

## Selected Abstracts from XXXVI National Congress of the Italian Society of Hypertension (SIIA), Rome, 26–28 September 2019

© Italian Society of Hypertension 2019

### Metabolic Aspects and Associated Risk Factors

#### VITAMIN D SUPPLEMENTATION AND INCIDENT PREECLAMPSIA: FINDINGS FROM A SYSTEMATIC REVIEW AND META-ANALYSIS OF CONTROLLED CLINICAL STUDIES

Silvia Fogacci<sup>1</sup>, Federica Fogacci<sup>1</sup>, Maciej Banach<sup>2</sup>, Eugenio R. Cosentino<sup>3</sup>, Daniela Degli Esposti<sup>3</sup>, Claudio Borghi<sup>1</sup>, Arrigo Francesco Giuseppe Cicero<sup>1</sup>, on behalf of the Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group

<sup>1</sup>Dip. di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna, Italy, <sup>2</sup>Facoltà di Medicina, Università di Lodz, Lodz, Poland, <sup>3</sup>Policlinico S. Orsola Malpighi, Bologna, Italy

**Introduction:** Recently, maternal vitamin D deficiency has been associated with an increased odd for preeclampsia, after adjustment for relevant confounders. Despite of that, the current evidence regarding the efficacy in preventing preeclampsia is controversial.

**Aim:** For this reason, we aimed to assess the impact of vitamin D supplementation on the risk of preeclampsia through a systematic review of the literature and a meta-analysis of the available clinical studies.

**Methods:** The primary outcome was preeclampsia. Subgroups' analyses were carried out considering the timing for the supplementation, the type of intervention and the study design. Meta-regression analysis, including the amount of vitamin D and maternal age, were planned to explore heterogeneity.

**Results:** Data were pooled from 29 clinical studies comprising 65 arms, which included overall 5297 subjects, whom 2833 in the vitamin D-treated arm and 2464 in the control one. Vitamin D administration in pregnancy was associated with a reduced risk of preeclampsia (odds ratio [OR] = 0.37, 95% confidence interval [CI]: 0.26, 0.52;  $I^2 = 0\%$ ). Moreover, if the vitamin D supplementation was started up to 20 weeks gestation, the odd for pregnant women was even much lower (OR = 0.35, 95% CI 0.24, 0.50,  $P < 0.001$ ). The effect was largely independent from the ending of the supplementation (until delivery or not), type of intervention (vitamin D alone or in association with calcium), and study design (open-label or blinded). Furthermore, increasing dose of vitamin D was negatively associated with increasing risk of preeclampsia (slope:  $-1.1$ ; 95% CI  $-1.73$ ,  $-0.46$ ; two-tailed  $p < 0.001$ ). On the opposite side, the risk of preeclampsia was not associated with maternal age ( $p > 0.05$ ).

**Conclusions:** Based on our data, vitamin D supplementation seems to be useful in preventing preeclampsia.

#### DIFFERENT PERFORMANCES IN THE SIX-MINUTES WALK TEST BETWEEN OBESE AND NORMAL-WEIGHT CHILDREN: ASSOCIATION WITH HAEMODYNAMIC PARAMETERS

A. Giontella<sup>1</sup>, F. Cattazzo<sup>1</sup>, A. Tagetti<sup>1</sup>, S. Bonafini<sup>1</sup>, I. Bresadola<sup>2</sup>, D. Marcon<sup>1</sup>, L. Branz<sup>1</sup>, P. Minuz<sup>1</sup>, C. Fava<sup>1</sup>

<sup>1</sup>Università degli Studi di Verona, Dipartimento di Medicina, Verona, Italy, <sup>2</sup>Università degli Studi di Verona, Dipartimento di Scienze Chirurgiche Odontostomatologiche e Materno-Infantili, Verona, Italy

**Introduction:** Physical activity plays an important role in preventing obesity and related cardiometabolic risk factors. The six-minute walk test (6MWT) is a clinical sub-maximal, easy and-cost effective test to assess functional capacity utilized also in epidemiological studies as predictor of cardiovascular disease.

**Aim:** We evaluated the association between the performance in the 6MWT with anthropometric and hemodynamic parameters collected before and after the test in a sample of children attending the 3rd and 4th classes in 4 primary schools in Verona South district.

**Methods:** The 6MWT was performed in a 36 m circuit and the total run distance was recorded. Before and after the end of the test some hemodynamic parameters, such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP). Sedentary activity (MET/min week) was assessed through a validated questionnaire (PAQ-C).

**Results:** Two hundred ninety-four (294) over 309 (95%) children were included in the study (Average age:  $8.64 \pm 9.0$  years; male: 50%). The mean 6MWT distance (6MWT-D) was  $548.0 \pm 57.0$  m. The 6MWT-D was lower in overweight or obese (OW & OB;  $n = 100$ ) children as compared to normal weight (NW;  $n = 194$ ) children [mean difference (OW & OB-NW):  $-18.0 \pm 7.0$  m,  $p = 0.007$ ]. The post 6MWT-rate pressure product (RPP =  $HR \cdot SBP$ , mean =  $10783.9 \pm 2282.4$  bpm\*mmHg) were significantly higher in the OW & OB group with respect to the NW group (mean difference =  $1227.1 \pm 272.1$  bpm\*mmHg,  $p = 9E^{-6}$ ). A better performance in the 6MWT-D was associated to higher RPP values ( $\beta = 9.33$ , SE: 0.209,  $p = 3.2E^{-5}$ ), adjusting for age, sex and height. This association is maintained in the NW group ( $\beta = 12.63$ , SE: 2.405,  $p = 4.2E^{-7}$ ) but not in the OW&OB group ( $\beta = 7.83$ , SE: 4504,  $p = n.s.$ ). Children classified as highly sedentary in PAQ-C score have higher values of  $\Delta$  RPP respect to the more active group (mean difference (post6MWT-pre6MWT) =  $1159.8 \pm 434.7$  bpm\*mmHg,  $p = 0.02$ ).

**Conclusions:** Obese and overweight children, despite a major hemodynamic challenge, as suggested by a higher RPP in overweight and obese children with respect to normotensive ones, have a worsen performance in the 6MWT. Lifestyle changes should aim not only to weight reduction but also to better body fit.

## DYSLIPIDEMIA IN HYPERTENSIVE PATIENTS: PREVALENCE, CONTROL RATES AND ROLE OF OVERWEIGHT AND OBESITY

Francesco Spannella<sup>1,2</sup>, Chiara Di Pentima<sup>1,2</sup>, Valentina Bordini<sup>1,2</sup>, Federico Giulietti<sup>1,2</sup>, Riccardo Sarzani<sup>1,2</sup>

<sup>1</sup>Internal Medicine and Geriatrics, “Hypertension Excellence Centre” of the European Society of Hypertension, and LIPIGEN Centre, IRCCS-INRCA, Ancona, Italy, <sup>2</sup>Department of Clinical and Molecular Sciences, University “Politecnica delle Marche”, Ancona, Italy

**Introduction:** Overweight and obesity play a key role in determining both arterial hypertension and dyslipidemia.

**Aim:** to evaluate the prevalence and control of dyslipidemia and the role of obesity in a large population of hypertensives evaluated with 24-h ambulatory blood pressure monitoring (ABPM).

**Methods:** Cross-sectional study on 1219 consecutive patients referred to our Centre for essential hypertension. Body mass index (BMI) and waist circumference (WC) were used as indices of adiposity. A complete lipid profile performed just before the clinical visit was considered in each patient. LDL cholesterol (LDLc) was calculated using the Martin-Hopkins coefficients. Dyslipidemia has been defined based on the ESC/EAS 2016 Guidelines.

**Results:** Mean age:  $56.5 \pm 13.7$  years; male sex: 55.6%. Prevalence of dyslipidemia: 91.1%. Mean BMI:  $27.8 \pm 4.6$  kg/m<sup>2</sup>. Mean WC:  $98.9 \pm 11.7$  cm. Overweight/obese patients (BMI  $\geq 25$  kg/m<sup>2</sup>): 70.2%. Overweight/obesity was associated with significantly higher glycemia, non-HDLc, triglycerides, non-HDL/HDLc and with lower HDLc levels. Significant correlations emerged between BMI and glycemia ( $\rho = 0.213$ ,  $p < 0.001$ ), triglycerides ( $\rho = 0.259$ ,  $p < 0.001$ ), HDLc ( $\beta = -0.215$ ,  $p < 0.001$ ), non-HDLc ( $\beta = 0.113$ ,  $p < 0.001$ ), non-HDLc/HDLc ( $\rho = 0.251$ ,  $p < 0.001$ ), even after adjustment for sex, age and lipid-lowering therapy. The same results emerged for the WC. Only 23.1% of patients took statin therapy, but only 28.5% of patients achieved the LDLc target. Paradoxically, the prevalence of LDLc control decreased with the increase in individual cardiovascular risk ( $p < 0.001$ ), despite the greater use of lipid-lowering drugs ( $p < 0.001$ ). Only 25.9% of patients in secondary prevention took a high-intensity statin and also were less controlled than patients in primary prevention (OR 3.5;  $p < 0.001$ ).

**Conclusions:** Dyslipidemia is very common and still poorly treated in the hypertensive patient. In addition to the poor control of LDLc levels, overweight/obese patients show a particularly atherogenic lipid profile that exposes them to a greater cardiovascular risk.

## DEFINITION OF HYPERTENSION-ASSOCIATED ORAL PATHOGENS: ANALYSIS OF NHANES DATA

Rita Del Pinto, Davide Pietropaoli, Eleonora Ortu, Annalisa Monaco, Claudio Ferri

University of L'Aquila, Dept. of Life, Health and Environmental Sciences, Coppito (AQ), Italy

**Introduction:** Periodontal microbiota has been linked to several systemic conditions, including high blood pressure (BP). Antibodies to oral pathogens can be considered an indirect measure of periodontal bacterial burden.

**Aim:** We hypothesized that a relationship exists between systemic exposure to periodontal microbiota, in terms of relative antibodies, and BP.

**Methods:** We analyzed cross-sectional data from 7928 US adults aged  $\geq 40$  years enrolled in NHANES III, who underwent determination of BP and serum antibodies to 21 periodontal microorganisms. BP was examined as both continuous (mmHg) and binary ( $\geq 130/80$  mmHg, i.e. normal/controlled or high/uncontrolled BP according to AHA 2017 guidelines) variable. Pearson's and Spearman's correlations, restricted maximum likelihood, generalized additive models, and a machine learning approach were combined to verify any association between antibodies to periodontal microbiota and BP.

**Results:** Antibodies to *C. rectus*, *V. parvula*, and *P. melaninogenica* (hypertension-associated pathogens, HOP) were consistently associated with high/uncontrolled BP by about +3 mmHg of systolic and +2 mmHg of diastolic BP and with 10–13% higher odds of high/uncontrolled BP (crude odds ratio [OR]: 1.13, 95% confidence interval [CI] 1.08–1.17,  $p < 0.0001$ ; full adjusted OR accounting for age, gender, ethnicity, body mass index, smoking habits, diabetes, US region, urban code, C reactive protein, and periodontitis: 1.10, 95% CI 1.04–1.15,  $p < 0.0001$ ), as well as with more active periodontal disease. Antibodies to *C. rectus* resulted in the strongest association with BP.

**Conclusions:** We found an association between systemic exposure to periodontal microbiota and BP. Understanding the pathogenetic mechanisms that shape such relationship, and the relative potential impact on personalized medicine, is the challenge of future research.

## PROPOSAL OF AN OBSERVATIONAL STUDY ABOUT CARDIOVASCULAR RISK IN A YOUNG OBESE POPULATION

E. Fanelli<sup>1</sup>, E. Eula<sup>1</sup>, S. Di Monaco<sup>1</sup>, M. Pappaccogli<sup>1</sup>, F. Abate Daga<sup>2</sup>, A. Astarita<sup>1</sup>, G. Mingrone<sup>1</sup>, S. Totaro<sup>3</sup>, I. Carretto<sup>4</sup>, I. Rabbone<sup>4</sup>, M. Gollin<sup>2</sup>, F. Rabbia<sup>1</sup>, F. Veglio<sup>1</sup>

<sup>1</sup>Department of Medical Sciences, Internal Medicine and Hypertension Division, AOU Città della Salute e della Scienza, University of Turin, Turin, Italy, <sup>2</sup>Department of Physical Education and Sports, University of Turin, Turin, Italy, <sup>3</sup>Department of Emergency Medicine, AOU Città della Salute e della Scienza, Turin, Italy, <sup>4</sup>Department of Pediatrics, AOU Città della Salute e della Scienza, University of Turin, Turin, Italy

**Introduction:** Obesity in young adults is a pathological condition that has an increasing incidence and has been associated to an increased risk of developing cardiovascular and metabolic conditions. It has been associated to hypertension in 25% of cases.

**Aim:** To identify the better physical activity to reduce long term cardiovascular risk in this population.

**Method:** 30 obese subjects underwent clinical (anthropometric parameters, blood exams, HOMA index), cardiovascular (transthoracic echocardiogram, 20-min electrocardiography recording, PWV, PWA, ABPM) and anthropometric-metabolic evaluation (TBW, ECW, ICW, FFM, FM, ECMatrix, AT, AAT, IMAT, RMR, FI, VO2 max, HPA Axis Index). These assessments have been the preliminary evaluation to the enrolment in an exercise program, with randomized assignment to aerobic and anaerobic activities.

**Results:** The mean age was  $15.7 \pm 2.3$  years (range 13–24 years). Male prevalence was 43.3%. Mean BMI was  $32.9 \pm 4.5$  kg/m<sup>2</sup>. At ambulatory visit, among mean values of assessed parameters: SBP  $123.1 \pm 9.7$  mmHg, DBP  $75.3 \pm 8.6$  mmHg, CF  $83.7 \pm 12.9$  bpm; PWV  $5.6 \pm 0.7$  m/s; central SBP e DBP respectively  $102.9 \pm 11.3$  mmHg and  $72.6 \pm 10.5$  mmHg. Of note among anthropometric-metabolic values: FM  $37.1 \pm 12.1$  kg, AAT  $638.2 \pm 233.3$  cm<sup>2</sup>, IMAT  $2.18 \pm 0.60$  kg. Significant correlations between abdominal adipose tissue (AAT) and office SBP ( $r = 0.56$ ,

$p = 0.004$ ), between AAT and office DBP ( $r = 0.60$ ,  $p = 0.002$ ), between fatty mass (FM) and office DBP ( $r = 0.60$ ,  $p = 0.002$ ) have been detected.

**Conclusions:** Clinical, cardiovascular and anthropometric-metabolic evaluation of a small group of young obese patients have underlined the positive correlation between abdominal adiposity and office BP.

### PROGNOSTIC CUT-OFF VALUES OF SERUM URIC ACID ASSOCIATED WITH FATAL AND NON FATAL INCIDENT MYOCARDIAL INFARCTION INDEPENDENTLY OF ARTERIAL HYPERTENSION IN A LARGE COHORT

E. Casiglia<sup>1</sup>, V. Tikhonoff<sup>2</sup>, G. Desideri<sup>3</sup>, C. Ferri<sup>3</sup>, F. Galletti<sup>3</sup>, C. Giannattasio<sup>3</sup>, G. Iaccarino<sup>3</sup>, F. Mallamaci<sup>3</sup>, A. Maloberti<sup>3</sup>, S. Masi<sup>3</sup>, A. Mazza<sup>3</sup>, M. L. Muiesan<sup>3</sup>, P. Palatini<sup>3</sup>, R. Pontremoli<sup>3</sup>, P. Verdecchia<sup>3</sup>, M. Volpe<sup>3</sup>, A. Ungar<sup>3</sup>, G. Grassi<sup>3</sup>, A. Virdis<sup>4</sup>, C. Borghi<sup>5</sup>

<sup>1</sup>Studium Patavinum, Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>2</sup>Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>3</sup>Working Group on Uric Acid and Cardiovascular risk of the Italian Society of Hypertension, Bologna, Italy, <sup>4</sup>Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa, Italy, <sup>5</sup>Dipartimento di Scienze Mediche e Chirurgiche, Alma Mater Studiorum, Università di Bologna, Bologna, Italy

**Introduction:** Searching for a prognostic cut-off value of serum uric acid (SUA) in predicting myocardial infarction (MI) in a large regional-based Italian cohort of men and women in the frame of the URRAH study (URic Acid Right for heArt Health).

**Methods:** The ongoing large database URRAH collects data from studies and cohorts from hypertension centres and epidemiological laboratories, including subjects with at least 1 measure of SUA and a follow-up of ~ 20 years. Incident myocardial infarction (MI) was defined in 23,475 subjects on the basis of ICD10 codes and double-checked with general practitioners and hospital files. Multivariate dichotomic Cox regression models having fatal and morbid MI as dependent variables, adjusted for arterial hypertension (AH), age, sex, diabetes, hematocrit, LDL-cholesterol, smoking and chronic renal disease were preliminarily used to search for an association between SUA as a continuous variable and MI. Two prognostic cut-off values (one for fatal and one for morbid MI), identified by means of receiver operating curves (ROC) and able to discriminate between subjects doomed to develop the event, were then used as independent predictors to divide people into those  $\leq$  cut-off and  $>$  cut-off in further multivariate Cox models adjusted for the confounders listed above.

**Results:** In Cox analysis, SUA as a continuous variable was a significant predictor of fatal [odds ratio, OR, 1.457 (1.029–1.240),  $p < 0.001$ ] and morbid [OR 1.254 (1.111–1.306),  $p < 0.0001$ ] incident MI, independently of AH. ROC showed that  $> 5.70$  mg/dl (95% CI 5.10–6.42, sensitivity 46.6, specificity 71.3,  $p < 0.0001$ ) was the prognostic cut-off value for fatal MI and  $> 4.30$  mg/dl (95% CI 3.79–5.20, sensitivity 79.5, specificity 34.0,  $p < 0.0001$ ) for morbid MI. These two values were accepted as multivariate predictors in Cox analyses, the hazard ratios being 1.23 (95% CI 1.04–1.68,  $p = 0.022$ ) for fatal and 1.73 (95% CI 1.22–2.47,  $p = 0.002$ ) for morbid MI.

**Conclusions:** clear prognostic cut-off values of SUA for fatal ( $> 5.20$  mg/dl) and morbid ( $> 4.30$  mg/dl) MI do exist also after adjustment for confounders including AH.

### ASSOCIATION BETWEEN METABOLIC SYNDROME AND OSTEOPOROSIS IN AN ADULT FREE-LIVING CAUCASIAN POPULATION EXTRACTED FROM A GENERAL PRACTICE DATABASE IN SOUTHERN ITALY

M. Evangelista<sup>1</sup>, V. Abate<sup>1</sup>, A. Giaquinto<sup>1</sup>, I. Nuzzo<sup>1</sup>, R. Piccinocchi<sup>1</sup>, G. Piccinocchi<sup>2</sup>, Domenico Rendina<sup>1</sup>, L. D'Elia<sup>1</sup>, F. Galletti<sup>1</sup>, P. Strazzullo<sup>1</sup>

<sup>1</sup>AOU Policlinico Federico II, Napoli, Italy, <sup>2</sup>Società Italiana di Medicina Generale, Napoli, Italy

**Introduction:** Metabolic syndrome (MetS) and Osteoporosis (Op) are two common multifactorial disorders showing similar epidemiological pattern worldwide. The studies analysing the possible association between MetS and Op provided contradictory and thus inconclusive results.

**Aim:** Aim of this cross-sectional epidemiological investigation was to analyse the association between MetS and Op in a large cohort of free-living Caucasian population from Southern Italy.

**Methods:** From the database of general practitioners affiliated to the "COMEGEN" cooperative, on June 1st 2018 we extracted the medical records of patients who had undergone at any time evaluation of both the bone mineral density by Dual-energy X-ray absorptiometry and the assessment of the constitutive elements of MetS according to the American Heart Association/National Heart, Lung and Blood Institute criteria.

**Results:** In the entire study cohort ( $n = 13844$ ), a statistically significant association was detected between MetS and Op (odds ratio 1.19; 95% confidence interval 1.08–1.31). Among the MetS constitutive elements, however, whereas hypertension was the one more tightly associated with to increased Op risk high fasting glucose level and diabetes were associated with lower Op risk.

**Conclusions:** This study of a large clinical practice patient population demonstrates the occurrence a significant association between MetS and Op.

### SEVERITY OF CORONARY ATHEROSCLEROSIS AND RISK OF DIABETES MELLITUS

C. De Colle<sup>1</sup>, I. Colaioni<sup>3</sup>, E. Barbato<sup>1</sup>, J. Bartunek<sup>2</sup>, C. Morisco<sup>1</sup>, D. Franco<sup>1</sup>, G. Di Gioia<sup>1</sup>, A. Rapacciuolo<sup>1</sup>, C. Mancusi<sup>1</sup>, M. A. Losi<sup>1</sup>, G. De Simone<sup>1</sup>, B. Trimarco<sup>1</sup>, R. Izzo<sup>1</sup>

<sup>1</sup>Università Federico II, Napoli, Italy, <sup>2</sup>OLV Hospital, AALST, BELGIUM, <sup>3</sup>Campus Biomedico, Roma, Italy

**Introduction:** Cardio-vascular target organ damage predicts onset of type 2 diabetes (DM) in hypertensive patients. Whether increased incidence of DM is also in relation with severity of coronary atherosclerosis is unknown.

**Aim:** We evaluated the onset of DM in relation with extent and severity of coronary atherosclerosis, using the SYNTAX score (SS), in patients with stable angina or acute coronary syndromes referred for coronary angiography (CA).

**Methods:** We included 570 consecutive non-diabetic patients (mean age  $65 \pm 10$  years, 69% male), who underwent CA between 1st January and 31st December 2009. Patients with previous CA, myocardial infarction or coronary artery bypass graft were excluded. SS was computed (mean:  $6.3 \pm 7.6$ ; range 0–50). Cox regression analysis was performed to identify independent predictors of DM onset in low, medium and high SS.

**Results:** During a median follow-up of 79 months (IQR: 67–94), 74 patients (13%) developed DM. Compared with patients with low SS, risk of DM onset was significantly higher in patients with medium and high SS (HR [95% CI] 18 [5–66],  $p < 0.0001$ ; and 35 [10–119],  $p < 0.0001$ , respectively vs. low SS), even after adjusting the Cox regression for obesity, history of hypertension, impaired fasting glucose and cardiovascular therapy.

**Conclusions:** Severity and extent of coronary atherosclerosis, as evaluated by the SS, is a strong predictor of DM onset in patients referred to coronary angiography independently of their baseline clinical and metabolic profile at the index angiography.

## HIGH LEVEL OF URIC ACID IS ASSOCIATED TO COGNITIVE IMPAIRMENT THROUGH THE PERIPHERAL VASCULAR DAMAGE, PARTICULARLY IN MALES

P. Nazzaro, A. Nardecchia, G. Schirosi, M. Contini, F. Caradonna Moscatelli, L. De Benedittis, G. Aceto, M. F Decaro, A. M. Papagni

*Dept of Neurosciences, Hypertension Unit “AM. Pirrelli”, University of Bari “Aldo Moro”, Bari, Italy*

**Introduction:** Many studies showed that blood uric acid (UA) high levels (HUA) might represent an independent factor of vascular damage and cognitive impairment.

**Aim:** to recognize if these characteristics were independently associated in hypertensives with no treatment for HUA and if a sex predisposition occurred.

**Methods:** After medical visit (off), 400 hypertensives ( $134 \pm 15/81 \pm 1$ ), with similar history and state of hypertension, treated with ACEi or ARBs as monotherapy, underwent tonometry to measure arterial stiffness (PWVcf), videocapillaroscopy of the medial and distal phalanx of the 2nd, 3rd and 4th finger of the non-dominant hand during venous congestion (CVC) to determine structural capillary rarefaction, and assessment of cognitive impairment (CIS) by multiple choice (1–4) 18-item questionnaire investigating different neuropsychological functions. They were divided in 284 with normal UA (NUA), 57 HUA without (VD-) and 59 HUA with (VD+) vascular damage and, then, in 60 males (MHUA) and 56 females (FHUA).

**Results:** The patients ( $45 < \text{age} < 65$  years) showed a similar hypertensive state, ascertained by ABPM, but significant differences occurred in order of vascular damage and cognitive performance ( $m \pm s.d.$ :  $p < .05$ ,  $**p < .01$ ,  $***p < .001$  vs NUA o MHUA;  $\wedge p < .05$ ,  $\wedge\wedge p < .01$ ,  $\wedge\wedge\wedge p < .001$  vs HUVD-).

pts/var	UA	SBP/DBP	PWVcf	CVC	CIS
NUA	4.2±0.9	135±14/81±9	9.8±3.9	53.1±9.9	24.6±5.9
HUAVD-	6.9±0.7***	134±15/82±9	10.1±2.3	52.1±7.8	25.2±5.8
HUAVD+	6.9±0.8***	133±14/80±8	11.8±3.4*** <sup>^^^</sup>	44.1±7.8*** <sup>^^^</sup>	29.1±8.3***
MHUA	7.1±0.8	135±14/82±9	11.8±2.9	43.2±6.9	29.1±7.8
FHUA	6.9±0.7	132±16/80±9	10±2.9***	48.7±8.9**	24.8±5.1***

Pearson analysis highlighted the association between UA and CVC ( $- .516^{**}$ ) and CIS ( $.547^{**}$ ) in HUAVD+, but not in HUAVD-, and PWVcf ( $.521$ ), CVC ( $- .620^{**}$ ) and CIS ( $.720^{***}$ ) in MHUA, but not in FHUA.

**Conclusions:** The findings show that HUA induces the cognitive impairment only in hypertensives with vascular damage. The finding demonstrated that the male patients are more subjected to this detrimental interaction and, then, they necessitate a more aggressive

strategy to prevent the HUA and the VD. Female hypertensives might be more preserved, along the adult age, probably because the exposition to the endothelial estrogenic protective action.

## CORTISOL AVAILABILITY AFTER RAPID DEXAMETHASONE SUPPRESSION TEST AMONG PATIENTS WITH ESSENTIAL HYPERTENSION: EVIDENCE OF AN ASSOCIATION WITH INSULIN RESISTANCE AND ALTERED GLUCOSE METABOLISM

G.P. Fra<sup>1</sup>, C. Cortese<sup>2</sup>, F. Brustia<sup>1</sup>, A. Re<sup>2</sup>, S. Strada<sup>2</sup>, E. Avitabile<sup>2</sup>, S. Bianco<sup>2</sup>, M. Pirisi<sup>1,2</sup>

<sup>1</sup>Internal Medicine 1, AOU “Maggiore della Carità”, Novara, Italy, <sup>2</sup>Department of Translational Medicine, Università del Piemonte Orientale (UPO), Novara, Italy

**Introduction:** Given the role of cortisol in blood pressure homeostasis and in secondary/resistant hypertension, we wondered if it might also be important among patients with well-controlled primary hypertension.

**Aim:** to verify if, in a hypertensive population, plasma cortisol values after rapid dexamethasone suppression test (Nugent test), though within normal limits, could stratify patients in relation to glucose and insulin metabolism.

**Methods:** N. = 107 subjects with newly diagnosed primary (essential) hypertension ( $< 6$  months), well controlled with calcium channel blockers, underwent an oral glucose tolerance test (OGTT), with measure of plasma glucose and insulin at baseline and after 120 min, as well as a Nugent test. All had also measured BMI, waist circumference and HOMA insulin resistance Index. Based on the post-test cortisol value, we excluded six patients who had a post-test plasma cortisol  $> 1.79$  mg/dL and stratified the N. = 101 remaining patients into tertiles: the lower tertile (group A), with post-test cortisol  $< 0.91$   $\mu\text{g/dl}$  (n = 36); the median tertile (group B), with post-test cortisol  $> 0.9$  and  $< 1.21$   $\mu\text{g/dl}$  (n = 33); and the upper tertile (group C), post-test cortisol  $> 1.2$   $\mu\text{g/dl}$  (n = 32).

**Results:** The percentage of hypertensive with normal glucose tolerance (NGT) after OGTT decreased progressively from group A to group B and C (respectively 80%, 61% and 53%,  $p < 0.02$ ). Significant increases from group A to group C were observed for BMI ( $p < 0.01$ ), waist circumference ( $p < 0.001$ ), plasma insulin at baseline and 120 min (respectively  $p < 0.001$  and  $< 0.002$ ), and HOMA ( $p < 0.05$ ). Similar results were observed considering only the N. = 66 hypertensives with NGT (n = 66).

**Conclusion:** Among patients with primary hypertension, an increased cortisol availability—though still within normal limits according to the Nugent test—is associated with altered glucose metabolism and greater resistance to insulin.

## NEUROADRENERGIC OVERDRIVE IN OVERWEIGHT AND OBESITY AND ITS CORRELATES: SYSTEMATIC REVIEWS AND META-ANALYSES

Fosca Quarti-Trevano<sup>1</sup>, Annalisa Biffi<sup>2</sup>, Gino Seravalle<sup>1</sup>, Raffaella Dell'Oro<sup>1</sup>, L.O. Parma<sup>1</sup>, J. Vanoli<sup>1</sup>, Giovanni Corrao<sup>2</sup>, Giuseppe Mancina<sup>3</sup>, Guido Grassi<sup>1</sup>

<sup>1</sup>Clinica Medica University of Milano-Bicocca, Italy, <sup>2</sup>Unit of Biostatistics, Epidemiology and Public Health, Dept Statistics and Quantitative Methods, University of Milano-Bicocca, Italy, <sup>3</sup>University of Milano-Bicocca, Milan, Italy

**Introduction:** Nerve traffic recordings (MSNA) have shown that sympathetic activation may occur in obese individuals (O). However, the small sample size of the available studies, presence of comorbidities, including sleep apnea, heterogeneity of the patients examined as well as presence of confounders represented major weaknesses not allowing to draw definite conclusions. This is particularly the case for overweight condition.

**Methods:** The present meta-analysis evaluated 1167 O recruited in 45 microneurographic studies. The analysis was primarily based on MSNA quantification in O of different clinical severity, excluding as concomitant conditions hypertension, sleep apnea and other comorbidities. Assessment was extended to the relationships of MSNA with other neuroadrenergic markers, such as venous plasma norepinephrine and heart rate (NE and HR, respectively), anthropometric variables, such as body mass index (BMI), waist-hip ratio (WHR) and metabolic variables.

**Results:** Compared to normal weight MSNA was significantly greater after adjustments for confounders in overweight and more so in O ( $37.0 \pm 4.1$  vs  $43.2 \pm 3.5$  and  $50.4 \pm 5$  bs/100 hb,  $P < 0.01$ ). MSNA was directly and significantly related to BMI and WHR ( $r = 0.41$  and  $r = 0.64$ ,  $P < 0.04$  and  $< 0.01$  respectively), clinic blood pressure ( $r = 0.68$ ,  $P < 0.01$ ), total cholesterol, LDL cholesterol, triglycerides and glucose ( $r = 0.91$ ,  $0.94$ ,  $0.80$  and  $0.59$ , respectively,  $P < 0.01$ ). No significant correlation was found between anthropometric indices and plasma insulin, HOMA index and plasma leptin. No correlation was found between MSNA and HR and NE.

**Conclusions:** Both O and overweight patients are characterized by sympathetic overactivity which mirrors the increase in BMI and WHR and the severity of the obese state and reflects metabolic alterations, with the exclusion of insulin. Neither HR nor NE appear to represent in O and in overweight faithful mirrors of the occurring sympathetic activation.

## INTERACTIONS BETWEEN GLUCOSE HOMEOSTASIS, VITAMIN D INSUFFICIENCY AND TARGET ORGAN DAMAGE IN ESSENTIAL HYPERTENSION

Cristiana Catena, Gian Luca Colussi, Andrea Palomba, Andrea Da Porto, Alessandro Frangipane, Andrea Duratti, Luca Bulfone, Giulia Candusso, Leonardo A. Sechi

Hypertension Unit, Department of Internal Medicine, University of Udine, Udine, Italy

**Introduction:** 25OH-vitamin D (25OHD) deficiency is associated to the target organ damage (TOD) in essential hypertension (EH). Furthermore, in our previous study, we found an independent and inverse association between 25OHD level and the glucose response to an oral

glucose tolerance test (OGTT) in non-diabetic essential hypertensive (EH) patients.

**Aim:** To evaluate if abnormalities in glucose homeostasis could be a link between 25OHD deficiency and presence of TOD in EH.

**Methods:** In 223 non-diabetic EH patients (age  $50 \pm 13$  years, 120 males, 94 naive) we evaluated 25OHD levels, area under the curve of glucose after an OGTT (G-AUC), glomerular filtration rate (GFR), 24-h urinary albumin excretion, intrarenal resistance indexes (IRI), left ventricular mass indexed (LVMI), TDI-e' velocity, E/A and E/e' ratios, presence of carotid plaques, carotid intima-media thickness (IMT), carotid coefficient of distension (CD), B-stiffness e Young elastic module (YEM) as indexes of carotid stiffness, and augmentation index (AIx) and pulse wave velocity (PWV) as indexes of aortic stiffness.

**Results:** 25OHD levels were significantly and inversely related to age, G-AUC, LVMI, E/A e E/e', presence of carotid plaques, IMT and IRI. G-AUC was significantly and positively related to age, BMI, LVMI, E/A, E/e', IMT, IRI, and inversely to TDI-e' velocity. We performed multivariate analysis with any TOD as dependent variable, and 25OHD level, G-AUC and other confounders that were related with both 25OHD level and G-AUC. LVMI was independently associated with BMI, E/A ratio was independently associated with age, the E/e' ratio was independently associated with a age, LVMI and G-AUC, the carotid IMT was independently associated with age and 25OHD, CD was independently associated with age, G-AUC and 25OHD, YEM was independently associated with age, IRI and presence of plaques were independently associated with age, AIx and PWV were independently associated with 25OHD levels e G-AUC.

**Conclusions:** The association between 25OHD deficiency and OGTT could be one of the mechanisms leading to the development of TOD in EH patients, but this association seems to be mediated by other factors influencing both 25OHD levels and glucose homeostasis.

## A MILD CORTISOL HYPERPRODUCTION IS ASSOCIATED WITH PROTHROMBOTIC MARKERS IN ESSENTIAL HYPERTENSIVE PATIENTS

Cristiana Catena, Gianluca Colussi, Marileda Novello, Rosangela Abrusci, Andrea Da Porto, Alessandro Frangipane, Agnese Presello, Andrea Palomba, Leonardo A. Sechi

Hypertension Unit, Department of Internal Medicine, University of Udine, Italy

**Introduction:** Cushing's syndrome and subclinical Cushing's syndrome are associated with a prothrombotic state. In patients with essential hypertension (EH) an activation of the prothrombotic system and the presence of hyperhomocysteinemia contribute to the development and severity of organ damage hypertension-related.

**Aim:** To evaluate possible relationships between cortisol production and prothrombotic system activation in EH patients.

**Methods:** In 134 EH patients (age  $49 \pm 14$  years, 75 males) we measured plasma levels of cortisol at 8, 17 and 11 pm, 24-h free urinary cortisol excretion, cortisol levels after a overnight 1 mg-dexamethasone suppression test (DST) and levels of fibrinogen, D-dimer, F1 + 2, PAI-1, t-PA, AT III, vWF antigen (vWFAg), homocysteine (Hcy) and reactive C protein (RCP).

**Results:** Patients have been subdivided into quartiles of cortisol level at 11 pm and after DST. High levels of cortisol at 11 pm and post-DST were associated with high levels of D-dimer ( $P = 0.012$ ) and vWFAg ( $P < 0.001$ ). Cortisol levels at 11 pm and post-DST were significantly and positively related to levels of D-dimer ( $r = 0.322$ ,  $P = 0.001$ ;  $r = 0.287$ ,  $P = 0.001$ , respectively) and vWFAg ( $r = 0.515$ ,  $P < 0.001$ ;  $r = 0.262$ ,  $P = 0.015$ , respectively), while only 11 pm

cortisol level was related to Hcy level ( $r = 0.300$ ,  $P = 0.002$ ). At multivariate analysis D-dimer level was independently associated with 11 pm and post-DST cortisol level, while vWFag and Hcy levels were independently associated only with 11 pm cortisol level.

**Conclusions:** In EH a mild and subclinical cortisol hyperproduction could leading to an induction of a procoagulative state and so contribute to the development and progression of the organ damage hypertension-related.

## IN ESSENTIAL HYPERTENSION THE ASSOCIATION BETWEEN VITAMIN D LEVELS AND PLASMA COULD BE MEDIATED BY THE ANGIOTENSIN-CONVERTING-ENZYME

Cristiana Catena, Gianluca Colussi, Andrea Da Porto, Andrea Palomba, Alessandro Frangipane, Francesca Spagnol, Agnese Presello, Leonardo Sechi

*Hypertension Unit, Department of Internal Medicine, University of Udine, ITALY*

**Introduction:** A 25OHD deficiency and the activation of the renin-angiotensin-aldosterone system (RAAS) are both known cardiovascular risk factors. Some studies have shown that 25OHD has a suppressive effect on RAAS but data in literature are conflicting.

**Aim:** To evaluate the relationships between 25OHD level and RAAS parameters in essential hypertensive (EH) patients free of severe renal failure and obesity.

**Methods:** In 153 EH subjects (age  $49 \pm 12$  years, 87 males, 123 naive, 30 studied after a wash-out period) we evaluated clinical characteristics, glomerular filtration rate (GFR), plasma levels of 25OHD, 1,25OHD, PTH, potassium, calcium, plasma aldosterone (PA), active renin (AR), angiotensin-converting-enzyme (ACE), 24-h urinary calcium (UrCa) and 24-h urinary sodium.

**Results:** 25OHD level was significantly and positively related to UrCa ( $r = 0.209$ ,  $P = 0.024$ ), ACE ( $r = 0.470$ ,  $P < 0.001$ ), PA ( $r = 0.272$ ,  $P = 0.001$ ), and inversely related to age ( $r = -0.301$ ,  $P < 0.001$ ) and PTH level ( $r = -0.188$ ,  $P = 0.025$ ). At multivariate analysis 25OHD level was independently associated with levels of PTH ( $B = -0.213$ ,  $P = 0.023$ ), ACE ( $B = 0.488$ ,  $P < 0.001$ ) and PA ( $B = 0.201$ ,  $P = 0.039$ ). PA level was positively related to level of 25OHD, 1,25-OHD ( $r = 0.256$ ,  $P = 0.026$ ), and ACE ( $r = 0.296$ ,  $P = 0.006$ ) and inversely related to age ( $r = -0.260$ ,  $P = 0.019$ ), potassium level ( $r = -0.261$ ,  $P = 0.001$ ) and alcohol intake ( $r = -0.224$ ,  $P = 0.007$ ). At a first model of multivariate analysis not including ACE, PA level was independently associated with levels of plasma potassium ( $B = -0.227$ ,  $P = 0.004$ ) and 25OHD ( $B = 0.197$ ,  $P = 0.018$ ). After inclusion of ACE in the analysis, PA level remained independently associated only with plasma potassium level ( $B = -0.244$ ,  $P = 0.015$ ) and alcohol intake ( $B = -0.244$ ,  $P = 0.016$ ). At multivariate analysis with ACE as dependent variable and 25OHD and PA as independent variables, ACE level was independently associated only with 25OHD level ( $B = 0.427$ ,  $P < 0.001$ ).

**Conclusions:** In EH there's a direct relation between 25OHD and PA levels that could be mediated by an effect of 25OHD on ACE levels.

## Atherosclerosis and Inflammation

### HYPERTENSIVE CHALLENGE ACTIVATE SUBFORNICAL ORGAN NEURONS PRIMING ADAPTIVE IMMUNITY BY THE ACTIVATION OF SPLENIC SYMPATHETIC NERVE IN MICE

<sup>1</sup>M. Perrotta, <sup>2</sup>F. Pallante, <sup>2</sup>L. Carnevale, <sup>2</sup>D. Iodice, <sup>2</sup>V. Fardella, <sup>1,2</sup>G. Lembo, <sup>1,2</sup>D. Carnevale

*<sup>1</sup>Department of Molecular Medicine, Sapienza University of Rome, Italy, <sup>2</sup>Department of Angiocardioneurology and Translational Medicine, IRCCS Neuromed, Pozzilli, Italy*

**Introduction:** Angiotensin II (AngII) is an important modulator of the sympathetic nervous system (SNS) acting through its type 1 neuronal AT receptors (AT1R) in cardiovascular control centers both in the brainstem and in the forebrain. Our most recent data have shown a brain-spleen connection, responsible for priming cells of the immune system. So far, the brain area controlling the activity of the splenic nerve through the efferent vagus nerve in hypertension has not been well identified. Circumventricular organs, such as the subfornical organ (SFO), are important brain regions involved in the control of cardiovascular functions like fluid homeostasis in response to AngII.

**Methods:** The experimental strategy used to study the role of this specific brain nucleus in the splenic sympathetic activation in hypertension, required a stereotaxic injection of a recombinant adenovirus encoding Cre-recombinase and a green fluorescence protein GFP (AdCreGFP) or GFP alone as control (AdGFP) in the SFO of AT1a<sup>fllox</sup> mice (mutant mice with the loxP sites upstream and downstream of exon 3 of the AT1R gene of type 1a).

**Results:** After evaluating the efficacy of the gene deletion procedure by ex vivo laser microdissection of SFO and real-time PCR on AT1aR mRNA, which was not produced anymore in the AT1a<sup>fllox</sup> compared to AT1a<sup>wt</sup> mice, we treated mice with AngII for 28 days and measured arterial pressure by tail cuff plethysmography and sympathetic activity of the splenic nerve by microneurography, which were significantly inhibited. Finally, in these mice we investigated the role of placental growth factor (PIGF) in the marginal area of the spleen in T cell activation, analyzing their egression and migration towards target organs of hypertension, as vessels and kidneys, by immunofluorescence.

**Conclusions:** These experiments allowed us to specifically target the AT1aR in the SFO to block splenic sympathetic activation, thus identifying a brain center controlling the immune response in hypertension.

### IN A CONTROLLED RHEUMATOID ARTHRITIS POPULATION THE CARDIOVASCULAR RISK FACTORS AND THE RESIDUAL DISEASE ACTIVITY ACCELERATE ATHEROSCLEROSIS

A. Dalbeni<sup>1</sup>, A. Giollo<sup>2</sup>, M. Bevilacqua<sup>1</sup>, G. Cioffi<sup>2</sup>, A. Tagetti<sup>1</sup>, F. Cattazzo<sup>1</sup>, G. Orsolini<sup>2</sup>, F. Ognibeni<sup>2</sup>, P. Minuz<sup>1</sup>, M. Rossini<sup>2</sup>, C. Fava<sup>1</sup>, O. Viapiana<sup>2</sup>

*<sup>1</sup>Division of General Medicine and Hypertension, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy, <sup>2</sup> Division of Rheumatology, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy*

**Introduction:** Patients with rheumatoid arthritis (RA) have an increased incidence of cardiovascular events. Ultrasound examination of the carotid arteries can show the presence of plaques and detect the atherosclerotic subclinical process mainly through the evaluation of intima-media thickness (cIMT) and the carotid segmental distensibility (cCD) measurement.

**Aim:** To identify the evolution of atherosclerosis (plaques, cIMT and cCD) after 1 year of follow-up in a sample of patients suffering from RA.

**Methods:** 137 patients with RA without previous CV events were enrolled. 105 (M/F: 22/83, age  $59.34 \pm 11.65$  years) were reassessed after one year using US of carotid arteries to detect atheromatous plaques and to measure cIMT and cCD.

**Results:** After 1 year, all the indexes of subclinical atherosclerosis worsened with respect to baseline ( $\Delta$ -cIMT =  $0.030 \pm 0.10$  mm,  $p = 0.005$ ;  $\Delta$ -cCD =  $-1.64 \pm 5.83$ ,  $10^{-3}$ /kPa,  $p = 0.005$ ;  $\Delta$ -plaques = 8.6%,  $p = 0.035$ ). Traditional CV risk factors (male sex, age, dyslipidaemia, hypertension) and corticosteroid therapy were independently associated with the acceleration of atherosclerosis. Interestingly, when considering RA patients divided according to the degree of disease activity (DAS28 [CRP]  $\geq 2.6$ ), the worsening of subclinical atherosclerosis indices was detectable exclusively in the group of patients with active disease. When we divided the population in quartiles, RA participants with cIMT above the 75<sup>th</sup> percentile assumed higher basal doses of DMARDs and lower dose of ACE inhibitors.

**Conclusions:** Our longitudinal study supports the hypothesis of an interaction between traditional CV risk factors, the activity of arthritic disease and progression of subclinical atherosclerosis in RA patients.

## THE SYSTEMIC TRANSFER OF A SINGLE HUMAN GENE ASSOCIATED WITH LONGEVITY REDUCES THE PROGRESSION OF ATHEROSCLEROSIS IN APOE KNOCKOUT MICE THROUGH A MECHANISM MEDIATED BY CXCR4

Albino Carrizzo<sup>1</sup>, Elena Ciaglia<sup>2</sup>, Antonio Damato<sup>1</sup>, Massimiliano De Lucia<sup>1</sup>, Chiara Spinelli<sup>3</sup>, Paola Lenzi<sup>4</sup>, Raffaele Izzo<sup>5</sup>, Valentina Trimarco<sup>5</sup>, Francesco Fornai<sup>1,4</sup>, Annibale Puca<sup>2,3</sup>, Carmine Vecchione<sup>1,2</sup>

<sup>1</sup>IRCCS Neuromed, Pozzilli, Italy, <sup>2</sup>Dipartimento di Medicina, Chirurgia e Odontoiatria Scuola Medica Salernitana, Università di Salerno, Salerno, Italy, <sup>3</sup>IRCCS Multimedica, <sup>4</sup>Dipartimento di Ricerca Traslationale e Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa, Italy, <sup>5</sup>Dipartimento di Scienze Biomediche Avanzate, Università Federico II di Napoli, Napoli, Italy

**Introduction:** Atherosclerosis, a multifactorial disease influenced by genetic and environmental factors, represents one of the main causes of death in the industrialized society. Since it is a slowly progressing disease, it is essential to find new treatments that can stop plaque progression and pro-inflammatory status.

**Aim:** To investigate the therapeutic effects of the longevity associated variant (LAV) -BPIFB4 on the atherogenic process.

**Methods:** ApoE knockout mice fed with high-fat diet were treated by injecting an adenoviral vector encoding the LAV protein and the WT-BPIFB4 protein or the empty vector (AAV-GFP). The primary endpoints of the study were: (i) to evaluate the vascular reactivity and (ii) the severity of the atherosclerotic disease, through imaging, histology and ultrastructural analysis. Furthermore, the ability of the LAV protein to influence the mono/macrophage phenotype of atherosclerotic mice and of the patients towards an anti-inflammatory phenotype was evaluated.

**Results:** Our results demonstrated the ability of LAV to restore the endothelial function of the mesenteric and femoral arteries from ApoE<sup>-/-</sup> mice; this effect was attenuated by pretreatment with AMD3100, a CXCR4 chemokine inhibitor. Mice treated with LAV-BPIFB4 showed an increase in circulating levels of anti-inflammatory interleukins such as IL-23 and IL-27. The study of dysfunctional arteries explanted from atherosclerotic patients showed that treatment with the recombinant LAV protein was able to improve endothelial function and to restore eNOS enzyme phosphorylation. Analysis of plasma levels of BPIFB4 protein in patients from 2 independent study groups showed the association between the reduced levels of plasma BPIFB4 with pathological carotid stenosis (> 25%) and intima media thickness (IMT) > 2 mm.

**Conclusions:** LAV reduces the atherogenic process and improves vascular function by acting through a CXCR4-dependent mechanism, thus opening new therapeutic perspectives in cardiovascular diseases. Heart

## EVALUATION OF CENTRAL BLOOD PRESSURE AND CENTRAL PULSE PRESSURE IN PRIMARY PREVENTION ADULT INDIVIDUALS STRATIFIED ACCORDING TO CARDIOVASCULAR RISK SCORE

Vivianne Presta<sup>1</sup>, Francesca Miceli<sup>1</sup>, Barbara Citoni<sup>1</sup>, Ilaria Figliuzzi<sup>1</sup>, Nadia Attalla El Halabieh<sup>1</sup>, Roberta Coluccia<sup>2</sup>, Andrea Ferrucci<sup>1</sup>, Massimo Volpe<sup>1,2</sup>, Giuliano Tocci<sup>1,2</sup>

<sup>1</sup>Hypertension Unit, Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, University of Rome Sapienza, Sant'Andrea Hospital, Rome, Italy, <sup>2</sup>IRCCS Neuromed, Pozzilli (IS), Italy

**Introduction:** European guidelines recommend use of SCORE risk charts to assess cardiovascular risk in primary prevention for guide the intensity of treatment and reduce the burden of cardiovascular events.

**Aim:** To evaluate both central blood pressure (cBP) and central pulse pressure (cPP) levels in a cohort of adult individuals according to risk stratification by SCORE algorithm.

**Methods:** We analysed data derived from a large cohort of adult individuals, without previous cardiovascular events, who consecutively underwent home, clinic and ambulatory BP monitoring at our Hypertension Unit for either diagnostic or therapeutic purposes. Clinic BP was measured with Mobil-O-Graph AND UA-1030T (A&D Medical, Sidney, Australia whilst central BP with Mobil-O-Graph PWA 24 h (IEM GmbH, Stolberg, Germany). Subjects were stratified into 5 groups according to SCORE risk: very low (SCORE < 1%), low (SCORE 1–2%), moderate (SCORE 2–5%), high (SCORE 5–10%), very high (SCORE  $\geq 10\%$ ).

**Results:** From an overall sample of 8,558 individuals we identified 7651 (93.8%) subject in primary prevention with valid calculated risk SCORE, among whom 2438 (32.6%) with very low cardiovascular risk, 1702 (22.7%) low CV risk, 935 (12.5%) moderate CV risk, 1288 (15.0%) high CV risk and 1288 (17.2%) very high CV risk. There were no statistically significant differences among groups with regard to cSBP ( $P = 0.311$ ) and cDBP ( $P = 0.175$ ), whilst cPP, pulse wave velocity (PWV) and vascular age showed a significant trend toward increase from very low to very high CV risk groups ( $P = 0.002$ ;  $P = 0.008$ ;  $P < 0.001$  respectively). Furthermore, cPP (Pearson:  $r = 0.241$ ;  $P = 0.13$ ), pulse wave analyses ( $r = 0.226$ ;  $P = 0.020$ ) and vascular age ( $r = 0.716$ ;  $P < 0.001$ ) were significantly associated to risk SCORE.

**Conclusions:** In our study cPP was associated with higher CV risk profile thus may be an alternative valid marker of hypertension-related organ damage and could help clinicians to assess individual CV risk profile.

## VASCULAR AGE AND HYPERTENSION RELATED CARDIAC ORGAN DAMAGE: A COMPARISON BETWEEN CLINIC AND AMBULATORY MEASUREMENT

Vivianne Presta<sup>1</sup>, Francesca Miceli<sup>1</sup>, Barbara Citoni<sup>1</sup>, Iliaria Figliuzzi<sup>1</sup>, Nadia Attalla El Halabieh<sup>1</sup>, Roberta Coluccia<sup>2</sup>, Andrea Ferrucci<sup>1</sup>, Massimo Volpe<sup>1,2</sup>, Giuliano Tocci<sup>1,2</sup>

<sup>1</sup>Hypertension Unit, Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, University of Rome Sapienza, Sant'Andrea Hospital, Rome, Italy, <sup>2</sup>IRCCS Neuromed, Pozzilli (IS), Italy

**Introduction:** Vascular age is a new parameter to improve individual's cardiovascular risk estimation but little consensus exists on its clinical value.

**Aim:** To evaluate the correlation between cardiac organ damage and both clinical and ambulatory vascular age in a cohort of patients affected by essential hypertension.

**Methods:** We analysed data derived from a large cohort of adult outpatient affected by hypertension, who consecutively underwent home, clinic and ambulatory BP monitoring at our Hypertension Unit. Clinic BP was measured with Mobil-O-Graph AND UA-1030T (A&D Medical, Sidney, Australia) whilst central BP with Mobil-O-Graph PWA 24 h (IEM GmbH, Stolberg, Germany).

**Results:** Clinical vascular age ( $56.1 \pm 17.7$  years) and ambulatory vascular age ( $48.2 \pm 14.7$  years) showed a significant correlation (Pearson:  $r = 0.949$ ;  $P < 0.001$ ). Both clinical ( $60.0 \pm 17.1$  vs.  $48.5 \pm 16.5$  years;  $P < 0.001$ ) and ambulatory vascular age ( $49.4 \pm 17.8$  vs.  $46.9 \pm 14.8$  years;  $P < 0.001$ ) were significantly higher in treated hypertensive patients compared to untreated individuals. Clinical vascular age was associated with Sokolow-Lyon index ( $r = -0.425$ ;  $P < 0.001$ ), MVS<sub>i</sub> ( $r = 0.387$ ;  $P = 0.16$ ), MVSh ( $r = 0.409$ ;  $P = 0.011$ ), MVSh<sup>2.7</sup> ( $r = 0.427$ ;  $P = 0.008$ ), and Em/Am ( $r = -0.581$ ;  $P = 0.002$ ), IVRT ( $r = 0.421$ ;  $P = 0.020$ ). Ambulatory vascular age showed no correlation with Sokolow-Lyon index ( $r = -0.275$ ;  $P = 0.086$ ), MVS<sub>i</sub> ( $r = 0.286$ ;  $P = 0.125$ ), MVSh ( $r = 0.301$ ;  $P = 0.106$ ), MVSh<sup>2.7</sup> ( $r = 0.197$ ;  $P = 0.296$ ), IVRT ( $r = 0.282$ ;  $P = 0.172$ ), with the exception of Em/Am ( $r = -0.611$ ;  $P = 0.004$ ).

**Conclusions:** In our cohort of adult hypertensive outpatients clinical vascular age seems to be better related with cardiac organ damage compared to ambulatory vascular age.

## FUNCTIONAL IMPROVEMENT AFTER CARDIAC REHABILITATION IS NOT RELATED TO IMPROVEMENT IN LEFT VENTRICULAR EJECTION FRACTION

A. Peretti<sup>2</sup>, A. Maloberti<sup>1,2</sup>, L. Garatti<sup>2</sup>, N. Triglion<sup>2</sup>, S. Sioli<sup>1</sup>, S. Bordoni<sup>3</sup>, L. Amoroso<sup>3</sup>, A. Pane<sup>3</sup>, D. Caroti<sup>1</sup>, F. Musca<sup>1</sup>, O. Belli<sup>1</sup>, B. De Chiara<sup>1</sup>, F. Casadei<sup>1</sup>, G. Sant'ambrogio<sup>1</sup>, F. Spano<sup>1</sup>, F. Esposito<sup>3</sup>, A. Moreo<sup>1</sup>, G. Beretta<sup>4</sup>, S. Riccobono<sup>1</sup>, C. Giannattasio<sup>1,2</sup>

<sup>1</sup>Cardiac Rehabilitation, Cardiology 4, ASST Niguarda Ca Granda Hospital, Milan, Italy, <sup>2</sup>School of Medicine and Surgery, Milan-Bicocca University, Milan, Italy, <sup>3</sup>Biomedical Science for Health Department, Milan University, Milan, Italy, <sup>4</sup>Rehabilitation Medicine, ASST Niguarda Ca Granda Hospital, Milan, Italy

**Introduction:** Cardiac rehabilitation (CR) improves the functional capacity and the prognosis of patients with coronary artery disease (CAD). Similar results have also been found in patients with dilated cardiomyopathy (DCM).

**Aim:** To assess the relationship between functional improvement (evaluated with 6-minute walking test-6MWT) and the improvement in left ventricular ejection fraction (LVEF) after CR.

**Methods:** we collected data from 260 patients that performed CR after an Acute Coronary Syndrome (ACS). The functional improvement after CR was expressed as the  $\Delta$  between distance covered at the final versus the initial 6MWT normalized for the initial 6MWT, while LVEF was calculated with transthoracic echocardiogram at the beginning and at the end of the CR.

**Results:** in the whole population functional improvement was 44.07% (baseline 6MWT 421.22 m vs follow-up 6MWT 597.28 m,  $p \leq 0.05$ ) while EF improvement was 2.48% (baseline EF 53.37% vs follow-up EF 55.91%,  $p \leq 0.05$ ). No significant correlation between the normalized  $\Delta$ meter and  $\Delta$ EF was founded. When patients were divided according to their pre-rehab LVEF ( $\geq 55$ , 40–55 and  $< 50\%$ ) we found a lower baseline 6MWT distance in the second and the third group with a higher improvement only in the second group (40 vs 50 vs 43% respectively,  $p = 0.001$ ). This latter group is also the one that presents the higher improvement in EF in comparison with the EF  $< 40\%$  group (5 vs 3%,  $p = 0.04$ ). No significant correlation between the normalized  $\Delta$ meter and  $\Delta$ EF was founded also when analysis was repeated in the different group depending on the EF values.

**Conclusions:** Our data confirm the CR related functional improvement that is not related to the relative increase in LVEF.

## THORACIC RADIOTHERAPY AS A RISK FACTOR FOR HEART ISCHEMIA IN SUBJECTS WITH CHEST IRRADIATION AND WITHOUT CLASSIC CARDIOVASCULAR RISK FACTORS

M. Palazzini<sup>1,2</sup>, P. Vallerio<sup>1</sup>, A. Maloberti<sup>1,2</sup>, C. Lestuzzi<sup>3</sup>, E. Grasso<sup>2</sup>, J. Sun<sup>2</sup>, A. Buono<sup>2</sup>, D. Sirico<sup>2</sup>, V. Gian<sup>2</sup>, V. Molinari<sup>2</sup>, M. Biolcati<sup>2</sup>, F. Lattuada<sup>2</sup>, S. Pezzini<sup>2</sup>, A. Moreo<sup>1</sup>, C. Giannattasio<sup>1,2</sup>

<sup>1</sup>Cardiology 4, ASST Niguarda Ca Granda Hospital, Milan, Italy, <sup>2</sup>School of Medicine and Surgery, Milan-Bicocca University, Milan, Italy, <sup>3</sup>Cardiology Unit, Oncology Department, CRO, National Cancer Institute, Aviano, Italy

**Introduction:** Radiation induced heart disease (RIHD) represents a late effect of chest irradiation, contributing in augmenting mortality in oncological patients by affecting pericardium, myocardium, valves and coronaries. Currently, regarding the risk of coronary heart disease (CAD), a cardiological screening involving exercise stress electrocardiography after 5–10 years from radiotherapy is advised.

**Aim:** We sought to determine the rate of ischemia at exercise stress electrocardiography in a population of patient without cardiovascular risk factors who sustained radiotherapy, using a cohort of high cardiovascular risk patients as control group.

**Methods:** A population of 115 patients who sustained chest irradiation, presenting without classic cardiovascular risk factors was evaluated with exercise stress electrocardiography. 135 patients with high

profile of cardiovascular risk candidate to stress testing for primary prevention or for atypical symptoms served as control group.

**Results:** The cohort of irradiated patients without classical cardiovascular risk factors was younger ( $48.7 \pm 10.1$  vs  $60.5 \pm 10.8$  years,  $p < 0.001$ ) and presents a lower percentage of males when compared with the control group. In this latter group 25.9% of subjects has diabetes, 62.9% dyslipidemia, 67.4% hypertension and 19.2% actively smoke. Despite this important differences regarding classic cardiovascular risk factor no significant differences were founded in the number of positive exercise stress electrocardiography ( $10.4$  vs  $5.9\%$ ,  $p = ns$ ).

**Conclusions:** Chest irradiation represent a strong cardiovascular risk factor, equalizing the rate of positive exercise stress electrocardiograms among two cohort of patients significantly different for the rate of classic cardiovascular risk factors.

### CARDIOVASCULAR REMODELING IN MILD HYPERTENSION: ROLE OF SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (sRAGE)

R. Corso, A. Grossi, N. Tandurella, S. Moretti, G. Cavallaro, L. Robustelli-Test, M. Agostinis, V. Pierobon, L. Tavecchia, V. Mancuso, C. Mongiardi, L. Montalbetti, A.M. Grandi, L. Guasti, A.M. Maresca

*Department of Medicine and Surgery, University of Insubria, Varese, Italy*

**Introduction:** Soluble Receptor for Advanced Glycation End Products (sRAGE) may be considered a marker inversely related to inflammation and its participation has been established in patients with advanced atherosclerotic vascular diseases. However, it is still unknown whether sRAGE reduction could be early metabolic change in the first stage of hypertension and initial hypertension-associated cardiac damage.

**Aim:** We sought to determine the sRAGE values in otherwise healthy, untreated and recently diagnosed mild hypertensives and evaluate their association with blood pressure (BP) values, metabolic parameters, and with subclinical initial signs of cardiac target organ damage (TOD).

**Methods:** sRAGE were measured in 100 hypertensive and 100 normotensive subjects matched for age, gender and body mass index (BMI), submitted to a clinic visit and both ambulatory BP monitoring and echocardiography to determine the presence of initial cardiac TOD (presence of signs of left ventricular hypertrophy: left ventricular mass indexed for height<sup>2.7</sup> (LVMI)  $> 48$  g/m<sup>2.7</sup> for men and  $> 44$  g/m<sup>2.7</sup> for women and/or increased left atrial volume 4-chamber indexed for body surface area (LAVi)  $> 34$  ml/m<sup>2</sup>).

**Results:** sRAGE levels were similar between hypertensive and normotensive subjects and were not significantly correlated with office and 24-h BPs values. However, when subgrouping the hypertensive patients in Hyp-TOD and HypwithoutTOD, sRAGE was found to be different among the three groups ( $p = 0.030$ ), being lower in the Hyp-TOD group than the values of both Hyp withoutTOD ( $p = 0.038$ ) and normotensives ( $p = 0.038$ ). In hypertensive patients sRAGE was negatively related with both LVMI ( $r = -0.239$ ,  $p = 0.034$ ) and LAVi ( $r = -0.315$ ,  $p = 0.005$ ) and was independently related to cardiac TOD also in multivariable analysis.

**Conclusions:** In this population of mild hypertensives, low circulating sRAGE may be a very early marker of initial TOD, suggesting the possible participation of oxidative stress in initial cardiac changes in human hypertension.

### INCIDENT LEFT VENTRICULAR HYPERTROPHY IN MASKED HYPERTENSION

F. Quarti<sup>1</sup>, C. Cuspidi<sup>2</sup>, R. Facchetti<sup>1</sup>, C. Sala<sup>3</sup>, G. Mancina<sup>1</sup>, G. Grassi<sup>1</sup>

<sup>1</sup>*Department of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy,* <sup>2</sup>*Istituto Auxologico Italiano, IRCCS, Milano, Italy,*

<sup>3</sup>*Department of Clinical Sciences and Community Health, University of Milan and Fondazione IRCCS Ospedale Maggiore Policlinico, Milan, Italy*

**Introduction:** In the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study, clinical variables, an echocardiogram as well as office and ambulatory blood pressure (ABP) were simultaneously measured at baseline and after a ten-year follow-up.

**Aim:** The study design allowed us to assess the value of Masked Hypertension (MH) as a predictor of new onset left ventricular hypertrophy (LVH).

**Methods:** The present analysis included 803 participants without LVH at baseline (LVMI  $< 115$  g/m<sup>2</sup> in men and  $< 100$  g/m<sup>2</sup> in women). Based on office and 24-h mean ABP values, subjects were divided into three groups: normal subjects (NT, office BP  $< 140/90$  mmHg and 24-h mean ABP  $< 130/80$  mmHg), MH (office BP normal and 24-h mean ABP elevated) and sustained hypertension (SH, office and 24-h BP both elevated).

**Results:** At entry, 57 subjects out of 803 fulfilled diagnostic criteria for MH (7.1%); 182 participants developed LVH (22.6%). Compared with subjects with normal in- and out-of-office BP, the risk of new onset LVH was greater in MH (OR = 2.23, CI 1.11–4.49,  $p = 0.02$ ) after adjustment for potential confounders. This was also the case for the absolute increase of LVMI.

**Conclusions:** Our study provides a new piece of evidence that MH, identified by office and ambulatory BP values, is associated with an increased risk of new onset LVH. Moreover, our findings convey the notion that office BP may inaccurately estimate the risk of incident LVH in the general population.

### BENEFICIAL EFFECTS OF DAAS ON CARDIAC FUNCTION AND STRUCTURE IN HEPATITIS C (HCV) PATIENTS WITH LOW-MODERATE LIVER FIBROSIS

Andrea Dalbeni<sup>1,2\*</sup>, Simone Romano<sup>1\*</sup>, Michele Bevilacqua<sup>1</sup>, Anna Piccoli<sup>3</sup>, Egidio Imbalzano<sup>4</sup>, Anna Mantovani<sup>1,5</sup>, Marco Benati<sup>6</sup>, Martina Montagnana<sup>6</sup>, Angela Donato<sup>1</sup>, Gioia Torin<sup>1</sup>, Cinzia Monaco<sup>1</sup>, Filippo Cattazzo<sup>1</sup>, Angela Tagetti<sup>1</sup>, Veronica Paon<sup>1,2</sup>, Donatella Ieluzzi<sup>2</sup>, Laura Iogna Prat<sup>2,5</sup>, Davide Roccarina<sup>5</sup>, Flavio Ribichini<sup>3</sup>, Franco Capra<sup>2</sup>, Pietro Minuz<sup>1</sup>, Cristiano Fava<sup>1</sup>

<sup>1</sup>*Division of General Medicine and Hypertension, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy,* <sup>2</sup>*Division of Liver Unit, Department of Medicine, University and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy,* <sup>3</sup>*Division of Cardiology, Department of Cardiology, University and Azienda Ospedaliera Universitaria Integrata, Verona, Italy,* <sup>4</sup>*Division of Internal Medicine, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy,* <sup>5</sup>*UCL Institute for Liver and Digestive Health, Royal Free Hospital and UCL, London, UK,* <sup>6</sup>*Department of Neurosciences, Biomedicine and Movement Sciences, Section of Clinical Biochemistry, University of Verona, Verona, Italy*

**Introduction:** Hepatitis C virus (HCV)-related chronic infection has been associated with a higher incidence of cardiovascular (CV) diseases. This association might be explained by the presence of a systemic chronic inflammation, specific viral cytotoxicity on either the endothelium or the myocardium, and an unexpectedly high prevalence of CV risk factors. An altered morphology and function were described in HCV patients; however, the causality of the association is still debated.

**Methods:** 98 non-obese and non-diabetic HCV-patients ( $59.5 \pm 12.0$  years; males 52%) with Fibroscan-Transient Elastography assessed low-moderate liver fibrosis were eligible for the virus eradication with DAAs (Direct-Acting Antivirals). 56 were compared to 52 control subjects matched for age, sex and CV risk factors at baseline. A trans-thoracic echocardiography was performed at baseline (T0) and repeated in all HCV patients after eradication (6 months later eligibility, T1). TNF- $\alpha$  and IL-10 were measured at baseline and at T1.

**Results:** A concentric remodelling of the left heart in HCV participants was identified, whereas tricuspid annular plane systolic excursion (TAPSE), right indexed atrial volume (RAV), right basal ventricular diameter (RVD) inferior vena cava diameter (IVC) and pulmonary arterial pressure (PAP) were higher in HCV participants compared to matched controls. After virus eradication, left indexed atrial volume and all right cardiac chambers measures were lower than baseline. A significant reduction of TNF- $\alpha$  was shown at T1, while IL-10 did not change.

**Conclusion:** The study shows a concentric remodelling of the left ventricle and structural modifications in the right sections in HCV patients compared to controls. Virus eradication with DAAs was associated with a reduction of the main right atrioventricular parameter indicating a direct involvement of the HCV in cardiac changes.

## LEFT VENTRICULAR GEOMETRY AND PERIODONTITIS IN PATIENTS WITH THE METABOLIC SYNDROME

L. Nibali<sup>1</sup>, N. Donos<sup>1</sup>, V. Terranova<sup>2</sup>, A. Di Pino<sup>3</sup>, S. Di Marca<sup>2</sup>, V. Ferrara<sup>3</sup>, M. Pisano<sup>2</sup>, R. Scicali<sup>3</sup>, A.M. Rabuazzo<sup>3</sup>, F. Purrello<sup>3</sup>, L. Malatino<sup>2</sup>

<sup>1</sup>Centre for Oral Immunobiology and Regenerative Medicine and Centre for Oral Clinical Research, Institute of Dentistry, Bart's and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK, <sup>2</sup>Department of Clinical and Experimental Medicine, Ospedale Cannizzaro, University of Catania, Catania, Italy, <sup>3</sup>Department of Clinical and Experimental Medicine, Ospedale Garibaldi-Nesima, University of Catania, Catania, Italy

**Introduction:** The presence of periodontal disease (PD) in subjects affected by the metabolic syndrome (MetS) may affect their risk of developing cardiovascular disease.

**Aim:** The aim of this cross-sectional study was to investigate the systemic impact of PD in MetS, by assessing measures of sub-clinical atherosclerosis and left ventricular mass and geometry.

**Methods:** A total of 103 patients undergoing treatment for MetS were examined for confirmation of diagnosis, blood sampling, and measures of pulse wave velocity (PWV), carotid intima-media thickness (c-IMT), left ventricular mass index (LVM), and relative wall thickness (RWT). All subjects underwent a detailed dental assessment, including measurements of DMFT (decayed-missing-filled teeth) and periodontal parameters.

**Results:** Ten patients (10%) were diagnosed with healthy-mild periodontitis, 38 patients (37%) were diagnosed in the moderate periodontitis group, and 55 (53%) had severe periodontitis. A total of 37% of subjects were affected by dental caries. Linear regression analysis revealed that patients with severe PD had increased average ventricular RWT (adjusted  $p = 0.032$ ). Average full mouth probing pocket depth (PPD) was also associated with RWT (adjusted  $p = 0.006$ ). No associations between PD and c-IMT, PWV, and LVM were detected after adjusted analyses.

**Conclusions:** This study suggests that periodontitis may be associated with concentric left ventricular remodeling, a predictive index of cardiovascular events. The presence of periodontitis in patients with MetS might have an effect on left ventricular geometry. These findings stress the importance of prevention, diagnosis, and management of periodontitis in patients with MetS.

## ASSOCIATION BETWEEN HEART RATE TRESHOLDS FOR CARDIOVASCULAR RISK DEFINED BY NEW ESC/ESH GUIDELINES AND NEUROADRENERGIC MARKERS

Raffaella Dell'Oro<sup>1</sup>, Margherita Gardini<sup>1</sup>, Gino Seravalle<sup>2</sup>, Fosca Quarti-Trevano<sup>1</sup>, Giacomo Marro<sup>1</sup>, Giuseppe Mancina<sup>2</sup>, Guido Grassi<sup>1</sup>

<sup>1</sup>Clinica Medica, Ospedale San Gerardo Monza, University of Milan-Bicocca, Milan, Italy, <sup>2</sup>University of Milan-Bicocca, Milan, Italy

**Introduction:** The ESC/ESH Guidelines for hypertension issued in 2018 identify resting heart rate (HR) values greater than 80 beats/minute as predictors of cardiovascular risk, with the undocumented evidence that this detection might represent the occurrence of a sympathetic cardiovascular overdrive. In the present study we tested this hypothesis throughout the use of direct and indirect markers of sympathetic neural function.

**Methods:** In 167 untreated and uncomplicated mild-to moderate essential hypertensives recruited for different investigations and aged  $51.8 \pm 3.2$  years (mean  $\pm$  SEM) without other cardiovascular or non-cardiovascular disease, we measured clinic and ambulatory blood pressure (BP), HR (EKG), venous plasma norepinephrine (NE, HPLC assay) and efferent postganglionic muscle sympathetic nerve traffic (MSNA, microneurography). We then subdivided the study population in 2 groups according to HR values  $\leq$  or  $>$  80 beats/minute.

**Results:** Sixty-eight patients displayed resting HR  $>$  80 beats/minute while the remaining 99 below this threshold value, the 2 groups showing superimposable age values and gender distribution. Body mass index, clinic and ambulatory BP were similar in the 2 groups this being the case also for LVMI and metabolic variables. In contrast MSNA values were significantly greater ( $P < 0.02$ ) in the former than in the latter group both when expressed as bursts incidence over time ( $49.2 \pm 1.8$  vs  $39.5 \pm 1.4$  bs/min) and when corrected for HR ( $60.7 \pm 3.0$  vs  $51.4 \pm 2.5$  bs/100 hb). NE showed a tendency to be greater in the former group without achieving, however, statistical significance. In the whole population there was a significant direct relationship between MSNA and HR values ( $r = 0.61$ ,  $P < 0.01$ ).

**Conclusions:** Thus hypertensive patients displaying HR  $>$  80 beats/minute are characterized by a marked sympathetic overdrive, particularly when direct adrenergic markers are employed. This finding suggests that cardiac and peripheral sympathetic activation may participate at the increased cardiovascular risk detected in this group of patients.

## RELATIONSHIP BETWEEN COMMON CAROTID DISTENSIBILITY/AORTIC STIFFNESS AND CARDIAC LEFT VENTRICULAR MORPHOLOGY AND FUNCTION IN A GROUP OF ARTHRITIC PATIENTS: AN OBSERVATIONAL STUDY

A. Dalbeni<sup>1</sup>, A. Giollo<sup>2</sup>, M. Bevilacqua<sup>1</sup>, F. Cattazzo<sup>1</sup>, A. Tagetti<sup>1</sup>, G. Orsolini<sup>2</sup>, G. Cioffi<sup>3</sup>, F. Ognibeni<sup>3</sup>, P. Minuz<sup>1</sup>, M. Rossini<sup>2</sup>, O. Viapiana<sup>2</sup>, C. Fava<sup>1</sup>

<sup>1</sup>Department of Medicine, General Medicine and Hypertension Unit, University of Verona and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy, <sup>2</sup>Department of Medicine, Division of Rheumatology, University of Verona & Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy, <sup>3</sup>Department of Cardiology, Villa Bianca Hospital, Trento, Italy

**Introduction:** Arterial stiffness indices are known to be associated with atherosclerosis, cardiac remodelling and cardiovascular diseases. In recent studies, in healthy population or with hypertension, common carotid artery rigidity could better predict cardiac morphology and function as compared with aortic parameters.

**Aim:** to determine the relation between carotid and aortic markers of stiffness and the main echocardiographic parameters in patients affected by arthritis.

**Methods:** 208 patients participated (57.4 ± 11.4 year; males = 36.1%); 65.9% were previously diagnosed with rheumatoid arthritis (RA), 20.2% with psoriatic arthritis (PA) and 13.9% with ankylosing spondylitis (AS). For each subject medical history, use of drugs and gluco-metabolic parameters were assessed. Echocardiography, blood pressure (BP) measurement and carotid ultrasonography were performed. Carotid Distensibility (CD) and Aortic Stiffness (AoS) were measured as indices of arterial stiffness.

**Results:** Mean left ventricular mass indexed by body surface area (LVMI/BSA) and relative wall thickness (RWT) were 98.8 ± 20.7 g/m<sup>2</sup> and 0.46 ± 0.06, respectively. In multiple regression analysis, between traditional risk factors for cardiovascular disease, CD correlated with age ( $\beta = 0.325$ ,  $p < 0.0001$ ), mean arterial pressure (MAP) ( $\beta = 0.502$ ,  $p < 0.0001$ ), gender and dyslipidaemia while AoS was not associated with any anthropometric, glucometabolic and hemodynamic covariate. About cardiac measurements, DC was inversely correlated with LVMI/BSA ( $r = -0.20$ ,  $p = 0.005$ ) whereas AoS directly correlated with left E/e' (a diastolic function index) ( $r = 0.191$ ,  $p = 0.007$ ).

**Conclusions:** Our data show an association between DC and left cardiac hypertrophy and remodelling and between AoS and left ventricular diastolic function. Carotid ultrasonography could be a valid monitoring tool for an early detection of vascular damage that can even predict sub-clinic cardiac remodelling in patients affected by chronic arthropathies.

## ECHOCARDIOGRAPHIC ASPECTS OF ONCOLOGIC PATIENTS IN TYROSIN KINASE INHIBITORS TREATMENT

D. Degli Esposti, E. Ribuoli, G. Nicolini, G. Melillo, S. Bacchelli, A.F.G. Cicero, F. Fogacci, F. Ventura, I. Ricci Iamino, M. Landolfo, E.R. Cosentino, M. Veronesi, C. Borghi

Internal Medicine, Cardio-Thoraco-Vascular Department, S. Orsola-Malpighi Hospital-Bologna University, Bologna, Italy

**Introduction:** Cardiovascular death is the main secondary cause of death in patients with cancer. Aim of Cardio-Oncology is therefore to

reduce cardiovascular mortality of these patients. Cardiotoxicity mechanisms of classical chemotherapy are clear, whilst less known are those of new target therapy.

**Aim:** to evaluate if cardiac structural and functional modifications could occur in oncologic patients in tyrosin kinase inhibitors (TKI) treatment.

**Methods:** 22 patients (8 M, 14 F, main age 55.8 ± 13.4) in TKI therapy because of different neoplastic disease underwent clinical, blood pressure (BP) assessment in particular, and complete echocardiographic evaluation before starting therapy (T0), and after 3 (T1) and 6 (T2) months of treatment.

**Results:** No significant differences were observed in BP values at T1 (117/76 ± 10/8) and T2 (116/77 ± 10/6) respect to T0 (116/77 ± 10/6). Echocardiography showed a slight increment in left ventricle end-diastolic and end-systolic dimensions (T0 = 4.5/2.8 ± 0.4/0.3, T1 = 4.5/2.8 ± 0.4/0.4, T2 = 4.6/3 ± 0.4/0.5 cm;  $p = 0.01$ ), and in right ventricle dimensions, together with a not-significant trend toward fractional shortening (T0 = 39% ± 3, T1 = 37% ± 3, T2 = 36% ± 4) and ejection fraction (T0 = 69% ± 4, T1 = 67% ± 5, T2 = 66% ± 5) reduction, and a slight, but significant tissue Doppler S reduction (T0 = 8.8 ± 1.3, T1 = 8.7 ± 1.2, T2 = 8.2 ± 1.4 cm/s;  $p = 0.04$ ). No significant changes were observed in diastolic function parameters, apart from an E/E' reduction.

**Conclusions:** our study results suggest that TKI can cause slight cardiac structural and functional modifications, with a slight trend toward an increment in both ventricles dimensions in particular, together with a slight trend toward a worsening in left ventricular systolic function as well. However, albeit this slight left ventricular structural and functional worsening, echocardiographic parameters always remained in classical normal ranges, and was observed in the absence of heart failure clinical signs, and of BP modifications.

## SACUBITRIL/VALSARTAN IN HEART FAILURE PATIENTS WITH REDUCED SYSTOLIC FUNCTION: ECHOCARDIOGRAPHIC EVALUATION

D. Degli Esposti, R. Ricci, G. Nicolini, E.R. Cosentino, M. Landolfo, I. Ricci Iamino, F. Ventura, S. Bacchelli, A.F. G. Cicero, F. Fogacci, M. Veronesi, C. Borghi

Internal Medicine, Cardio-Thoraco-Vascular Department, S.Orsola-Malpighi Hospital-Bologna University, Bologna, ITALY

**Introduction:** Sacubitril/valsartan therapy has shown to induce important clinical improvement in heart failure patients with reduced ejection fraction. Still scanty are real life data, echocardiographic data in particular.

**Aim:** To evaluate the effect on echocardiographic aspects of sacubitril/valsartan when used in real life.

**Methods:** 29 patients (21 M, 8 F, age 75 years, range 55–91) with reduced ejection fraction heart failure and treated with sacubitril/valsartan underwent clinical and echocardiographic evaluation before starting therapy (T0) and after 3 months of treatment (T1). 55% had ischemic heart failure, and 86% had history of hypertension.

**Results:** At T0 18 patients (62%) were in NYHA class II, and 11 (38%) in NYHA III; at T1 12 (41%) were in NYHA I, 16 (55%) in NYHA II, and 1 (3%) in NYHA III. Among echocardiographic parameters, we observed a significant reduction in left ventricular end-diastolic (T0 = 154 ± 43, T1 = 118 ± 39,  $p = 0.02$ ), and end-systolic (T0 = 93 ± 38, T1 = 62 ± 32,  $p = 0.02$ ) volumes, together with a significant increment in left ventricular fractional shortening (T0 = 19 ± 6, T1 = 28 ± 6,  $p = 0.000$ ) and ejection fraction

( $T_0 = 32 \pm 10$ ,  $T_1 = 49 \pm 9$ ,  $p = 0.000$ ). No significant differences were observed among diastolic parameters, albeit we observed a trend toward a reduction in E/A and E/E', suggesting a trend toward a less damaged diastolic function (from pseudo-normal to compromised relaxation). Among biohumoral parameters, we observed a significant reduction in BNP ( $T_0 = 833 \pm 263$ ,  $T_1 = 329 \pm 261$ ,  $p = 0.000$ ), and in uric acid values ( $T_0 = 7.7 \pm 1.9$ ,  $T_1 = 6.7 \pm 2.2$ ,  $p = 0.055$ ), together with a trend toward an improving in lipid/metabolic parameters.

**Conclusions:** Together with clinical and biohumoral, BNP in particular, amelioration, sacubitril/valsartan can induce an improvement in left ventricular structural and functional aspects as well, as we can see by the reduction in left ventricular volumes and the increment in systolic indexes in particular, and by the trend toward a better diastolic function.

## PREVALENCE OF LEFT ATRIAL ENLARGEMENT IN A LARGE SAMPLE OF PATIENTS UNDERGOING AN ECHOCARDIOGRAM FOR CARDIOVASCULAR RISK STRATIFICATION AT AN ESH EXCELLENCE CENTRE IN ITALY

F. Bertacchini, A. Painsi, M. Salvetti, C. Aggiusti, D. Stassaldi, S. Capellini, G. Saccà, L. Verzeri, E. Agabiti-Rosei, M.L. Muiesan

*Medicina Interna and 2<sup>a</sup> Medicina, Università di Brescia and ASST Spedali Civili di Brescia, Brescia, Italy*

**Introduction:** Left atrial (LA) enlargement (LAE) is associated to an increased risk of cardiovascular complications, and in particular of atrial fibrillation. The 2018 ESH/ESC Hypertension guidelines suggested the use of LA volume instead of linear dimensions, and for the first time proposed the indexation to height<sup>2</sup>(h<sup>2</sup>).

**Aim:** Was to assess the prevalence of left atrial dilatation in a large sample of patients undergoing an echocardiogram for cardiovascular risk stratification at an ESH excellence centre in Italy.

**Methods:** 3872 subjects undergoing a diagnostic work-up for arterial hypertension (known or suspect) were analysed. The mean age was  $56 \pm 15$  years, BMI  $26 \pm 5$ , 44% normal weight, 39% overweight, 17% obese, 53% males. Left atrial volume was measured by the area-length method using the apical 4-chamber and 2-chamber views.

**Results:** The prevalence of left ventricular hypertrophy (LVH) was 11% when indexing for BSA and 12% when indexing for height<sup>2</sup>. LAE was observed in 30% of subjects when indexing for h<sup>2</sup> and in 9% when indexing for BSA. In obese or overweight subjects the prevalence of LAE was 38% of subjects when indexing for h<sup>2</sup> and in 11% when indexing for BSA. The different prevalence of LAE was particularly evident in extremely obese patients. LAE was very common in patients with LVH: 62% and 26% when indexing for h<sup>2</sup> and for BSA, respectively. Interestingly, it was frequent also in patients without LVH, in particular when the indexation for h<sup>2</sup> was used (25% as compared to 7% when indexing for BSA).

**Conclusions:** In a large sample of subjects undergoing a diagnostic work-up for arterial hypertension LAE was frequently observed, particularly when the new indexation proposed by the 2018 ESH/ESC hypertension guidelines was used. Even in the absence of clear-cut LVH, LAE was observed in one quarter of subjects. The indexation to BSA leads to an under-recognition of LAE, in particular in patients with overweight and/or obesity.

## RELATIONSHIP BETWEEN UNATTENDED AND ATTENDED BP VALUES AND CARDIAC HYPERTENSIVE TARGET ORGAN DAMAGE

A. Painsi, M. Salvetti, C. Aggiusti, F. Bertacchini, D. Stassaldi, S. Capellini, G. Saccà, L. Verzeri, C. Arnoldi, E. Agabiti-Rosei, M.L. Muiesan

*Medicina Interna and 2<sup>a</sup> Medicina, Università di Brescia & ASST Spedali Civili di Brescia, Brescia, Italy*

**Introduction:** It has been suggested that measurement of “unattended” or “automated oscillatory (AOBP)” blood pressure values may provide advantages over conventional BP measurement and some hypertension guidelines now suggest this approach as the preferred one for measuring office BP. Data on the relationship between AOBP and cardiovascular events are much less solid as compared to those obtained with the standard BP measurement; conflicting data are available on the relationship between hypertensive organ damage and “attended” and “unattended” BP.

**Aim:** To evaluate the relationship between “attended” or “unattended” BP values and cardiac hypertensive target organ damage in 564 subjects attending the outpatient clinic of an ESH Excellence Centre.

**Methods:** Both “unattended” BP (patient alone in the room, an oscillometric device programmed to perform 3 BP measurements, at 1 min intervals, after 5 min) and “attended” BP were measured with the same device, on the same day of arterial stiffness assessment, in random order.

**Results:** Patient’s mean age was  $61 \pm 14$  years, mean BMI  $26 \pm 4$ , 59% were male, 78% had a previous diagnosis of hypertension (63% treated). Systolic unattended BP was lower as compared to attended SBP ( $128.0 \pm 15.5$  vs  $134.5 \pm 19.9$  mmHg). Left ventricular mass index (LVMI) was similarly correlated with unattended and attended SBP ( $r = 0.194$  and  $r = 0.205$ ,  $p < 0.0001$ , respectively). LVMI was similarly correlated with unattended and attended pulse pressure (PP) ( $r = 0.301$  and  $r = 0.295$ ,  $p < 0.0001$ , respectively). The differences between correlations were not statistically significant (Steiger’s Z test). No significant difference was observed between the ROC curves of attended or unattended SBP for the presence of left ventricular hypertrophy (AUC 0.624 vs. AUC 0.605,  $p$  for the comparison = ns).

**Conclusions:** Measurement of BP “unattended” or “unattended” provides different values, being unattended BP lower as compared to attended BP. Our results suggest that attended and unattended BP values are similarly related with cardiac hypertensive target organ damage.

## DETERMINANTS OF AORTIC ROOT DILATATION OVER TIME IN HYPERTENSIVE TREATED PATIENTS: THE CAMPANIA SALUTE NETWORK

Grazia Canciello, Costantino Mancusi, Raffaele Izzo, Nicola de Luca, Bruno Trimarco, Emanuele Barbato, Giovanni de Simone, Maria-Angela Losi

*Hypertension Research Center Federico II University, Napoli, Italy*

**Introduction:** We demonstrated that aortic root (AR) dilatation assessed by standardized difference between observed and predicted values is present at baseline in about 30% of treated hypertensive patients and predicts cardiovascular (CV) events independently of left ventricular (LV) hypertrophy (LVH).

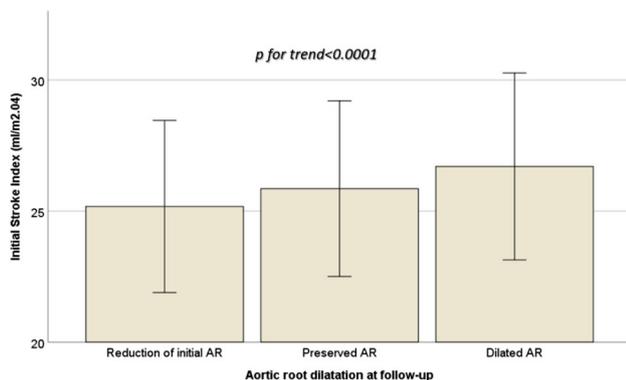
**Aim:** We investigate whether a CV phenotype exists predicting AR dilatation during follow-up of treated hypertensive patients.

**Methods:** 5301 hypertensive treated patients (age  $53 \pm 11$  years, 42% women) without prevalent CV disease and with normal ejection fraction ( $\geq 50\%$ ) were studied. AR dimension was measured in the parasternal long-axis view at the level of sinus of Valsalva in end-diastole, using the leading-edge to leading-edge method at first and last available echocardiograms. The z-score of AR dimension (AOz) was generated based on the difference between observed AR and predicted AR dimension, divided by sex-specific observed SD.

**Results:** Initial AOz exhibited a normal distribution and was correlated positively with age, male sex, systolic and diastolic blood pressure (BP), BMI, fasting glucose, and glomerular filtration rate (GFR, by EPI-CKD) and negatively with pulse pressure (PP) and cholesterol (all  $0.03 < p < 0.0001$ ). In multiple regression analysis, stroke index (SVi) was the most potent covariate of AOz, right after effect of BMI (both  $p < 0.0001$ ) and independently of age, sex, diastolic BP, lipid profile and GFR. Compared with initial values, at the last echocardiogram (5.5 years; IQR = 3.1–9.6 years), 417 subjects (8%) exhibited clear-cut aortic dilatation ( $> 75$ th percentile of the AOz distribution). Similar to baseline, initial SVi and BMI remained the most potent covariates of the final AOz (both  $p < 0.0001$ ), independently of significant effect of male sex, high diastolic BP, BMI, SVi, low PP, and low HDL-cholesterol. Variance inflation factor was  $< 2$  in both regression models. Figure 1 shows initial SVi in relation with AR at follow up.

**Conclusions:** We demonstrate that both volume (SVi) and pressure loads (diastolic BP) influence AR enlargement over time, AR dilatation is predictable in male obese patients with diastolic hypertension and other metabolic disturbances.

Figure 1



## THE INVOLVEMENT OF GRK2 IN STRESS RESPONSE TO RADIATION DURING CARDIOVASCULAR INVASIVE PROCEDURE

A. Fiordelisi<sup>1</sup>, G. Di Gioia<sup>1</sup>, I. Colaiori<sup>1</sup>, A. Katbeh<sup>2</sup>, J. Gambardella<sup>1</sup>, E. Barbato<sup>1</sup>, J. Bartunek<sup>2</sup>, D. Sorriento<sup>1</sup>, G. Iaccarino<sup>1</sup>

<sup>1</sup>Università Federico II Dipartimento di Scienze Biomediche Avanzate, Napoli, Italy, <sup>2</sup>OLV Hospital, AALST, Belgium

**Introduction:** G protein coupled receptor kinase type 2 (GRK2) has a pivotal role in the development and progression of cardiovascular diseases. Moreover, this kinase is a stress protein which is able to move quickly within the cell in response to acute stimuli such as ionizing radiation exposure (IR). Indeed, we have previously shown that in HEK-293 cells the acute exposure to IR promotes GRK2 translocation in different cellular compartment. The cardiovascular invasive procedures such as coronary angiography or percutaneous coronary interventions (PCI) are diagnostic examination, that use a

tolerated dose of X-ray. In PBMCs, GRK2 levels increase during acute myocardial infarction and are associated with worse cardiac function.

**Aim:** To evaluate the effects of IR exposure on GRK2 levels in PBMCs isolated from patients undergoing cardiovascular interventions and in Human Endothelial Progenitor cells (EPC) after IR exposure.

**Methods:** GRK2 levels are evaluated by western blot analysis in PBMCs isolated from peripheral blood by Ficoll gradient before, immediately after, at 24 h from the procedure. GRK2 levels are evaluated also in EPC cells by western blot analysis 24 h after IR exposure.

**Results:** In PBMCs from patients undergoing cardiovascular invasive procedure, changes in GRK2 levels are recorded in response to IR exposure occurring during procedure. In particular GRK2 levels are inversely proportional with dose-area product (DAP) of patients undergoing PCI both immediately after and 24 h from the procedure. To evaluate the direct effects of IR on cells and to confirm the trend observed in patients undergoing PCI, GRK2 levels are measured in EPC cells whose source of origin is represented by PBMCs. In detail, in these cells the GRK2 levels are assessed after 24 h from IR, by using radiation doses (0.3 Gy and 1 Gy) comparable with IR exposure of cardiovascular invasive procedure. Similarly to PCI, also in EPC cells the GRK2 levels are inversely proportional with radiation dose after 24 h from IR exposure. These in vitro results confirm the changes of GRK2 levels in response to IR, reflecting the trend observed in PBMCs of patients undergoing PCI.

**Conclusions:** These preliminary data suggest that GRK2 could be involved in stress response associated to IR exposure during cardiovascular interventions. The pathophysiologic relevance of this damage is to be established.

## SERUM URIC ACID, INDEPENDENTLY OF ARTERIAL HYPERTENSION, PREDICTS FATAL HEART FAILURE IN A LARGE COHORT OF MEN AND WOMEN. SEARCH FOR A CUT-OFF VALUE

C. Borghi<sup>5</sup>, G. Desideri<sup>3</sup>, V. Tikhonoff<sup>2</sup>, M. Cirillo<sup>3</sup>, P. Cirillo<sup>3</sup>, C. Ferri<sup>3</sup>, F. Galletti<sup>3</sup>, G. Grassi<sup>3</sup>, G. Iaccarino<sup>3</sup>, S. Masi<sup>3</sup>, M. L. Muijesan<sup>3</sup>, P. Palatini<sup>3</sup>, G. Parati<sup>3</sup>, R. Pontremoli<sup>3</sup>, M. Rattazzi<sup>3</sup>, P. Verdecchia<sup>3</sup>, M. Volpe<sup>6</sup>, A. Ungar<sup>3</sup>, E. Casiglia<sup>1</sup>, A. Virdis<sup>4</sup>, on behalf of the Working Group on Uric Acid and Cardiovascular Risk of the Italian Society of Hypertension

<sup>1</sup>Studium Patavinum, Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>2</sup>Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>3</sup>Working Group on Uric Acid and Cardiovascular risk of the Italian Society of Hypertension, Bologna, Italy, <sup>4</sup>Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa, Italy, <sup>5</sup>Dipartimento di Scienze Mediche e Chirurgiche, Alma Mater Studiorum, Università di Bologna, Bologna, Italy, <sup>6</sup>Hypertension Unit, Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine and Psychology, University of Rome Sapienza, Sant'Andrea Hospital, Rome, and IRCCS Neuromed, Pozzilli (IS), Italy

**Introduction:** Searching for a prognostic cut-off value of serum uric acid (SUA) in predicting incident heart failure (HF) in a large regional-based Italian cohort of men and women in the frame of the URRAH study (URic Acid Right for heArt Health).

**Methods:** The ongoing large database URRAH collects data from studies and cohorts from hypertension centres and epidemiological laboratories including subjects with at least 1 measure of SUA and a follow-up of  $\sim 20$  years. Incident HF was defined in 23,475 subjects

on the basis of ICD10 codes and double-checked with general practitioners and hospital files. Multivariate dichotomic Cox regression models having fatal and morbid HF as dependent variables, adjusted for arterial hypertension (AH), age, sex, diabetes, hematocrit, LDL-cholesterol, smoking and chronic renal disease were used to search for an association between SUA as a continuous variable and HF. Two prognostic cut-off values (one for fatal and one for morbid HF), identified by means of receiver operating curves (ROC) and able to discriminate between subjects doomed to develop the event, were then used as independent predictors to divide people into those < cut-off and > cut-off in further multivariate Cox models adjusted for the confounders.

**Results:** In Cox analysis, SUA as a continuous variable was a significant predictor of fatal [odds ratio, OR 1.101 (1.011–1.200),  $p = 0.028$ ] and morbid [OR 1.179 (1.031–1.349),  $p = 0.016$ ] incident HF, independently of AH. Diuretics reduced the risk of fatal HF only [OR 0.448 (0.259–0.774),  $p = 0.005$ ]. ROC showed that  $> 5.70$  mg/dl (CI 4.40–6.77, sensitivity 42.67, specificity 71.15,  $p < 0.0001$ ) was the univariate prognostic cut-off value for fatal HF, and  $> 4.20$  mg/dl (CI 3.36–6.05, sensitivity 75.06, specificity 31.14,  $p < 0.003$ ) for non-fatal HF. Nevertheless, only the cut-off for fatal HF was accepted as multivariate predictor in Cox analysis, the hazard ratios being 1.645 (1.284–2.109,  $p < 0.0001$ ), with diuretic acting as a protective factor ( $p = 0.007$ ), while that for morbid HF was rejected ( $p = 0.4$ ).

**Conclusions:** a clear prognostic cut-off value of SUA for fatal HF exists ( $> 5.70$  mg/dl) also after adjustment for confounders including AH, while SUA did not predict morbid HF.

## RELATIONSHIP BETWEEN COMMON CAROTID DISTENSIBILITY/AORTIC STIFFNESS AND CARDIAC LEFT VENTRICULAR MORPHOLOGY AND FUNCTION

A. Dalbeni<sup>1</sup>, M. Bevilacqua<sup>1</sup>, A. Giollo<sup>2</sup>, A. Tagetti<sup>1</sup>, G. Orsolini<sup>2</sup>, G. Cioffi<sup>2</sup>, F. Ognibeni<sup>2</sup>, P. Minuz<sup>1</sup>, M. Rossini<sup>2</sup>, O. Viapiana<sup>2</sup>, C. Fava<sup>1</sup>

<sup>1</sup>Department of Medicine, General Medicine and Hypertension Unit, University of Verona and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy, <sup>2</sup>Department of Medicine, Division of Rheumatology, University of Verona and Azienda Ospedaliera Universitaria Integrata of Verona, Verona, Italy

**Introduction:** Increased arterial stiffness is associated with atherosclerosis, cardiac remodelling and cardiovascular adverse events. Common carotid artery rigidity could accurately predict cardiac abnormalities in morphology and function as well as ascending aortic parameters.

**Aim:** To determine the relation between carotid and aortic markers of stiffness and the main echocardiographic parameters in patients affected by different types of chronic arthritis.

**Methods:** 208 patients participated ( $57.4 \pm 11.4$  years; males = 36.1%); 65.9% were previously diagnosed with rheumatoid arthritis, 20.2% with psoriatic arthritis and 13.9% with ankylosing spondylitis. For each subject medical history, use of drugs and gluco-metabolic parameters were assessed. Echocardiography, blood pressure (BP) measurement and carotid ultrasonography were performed. Carotid Distensibility (CD) and Aortic Stiffness index (AoS) were measured and taken as indices of arterial stiffness.

**Results:** Mean Left Ventricular Mass indexed by body surface area (LVM/BSA) and Relative Wall Thickness (RWT) were  $98.8 \pm 20.7$  g/m<sup>2</sup> and  $0.46 \pm 0.06$ , respectively. In multiple regression analysis, between traditional risk factors for cardiovascular disease, CD correlated with age ( $\beta = 0.325$ ,  $p < 0.0001$ ), mean arterial

pressure (MAP) ( $\beta = 0.502$ ,  $p < 0.0001$ ), gender and dyslipidaemia while AoS was not associated with any anthropometric, gluco-metabolic and hemodynamic covariates. About cardiac measurements, CD was inversely correlated with LVM/BSA ( $r = -0.20$ ,  $p = 0.005$ ) whereas AoS directly correlated with left E/e' (a diastolic function index) ( $r = 0.191$ ,  $p = 0.007$ ).

**Conclusions:** Our data show an association between CD and left cardiac hypertrophy and remodelling and between AoS and left ventricular diastolic function. Carotid ultrasonography could be a valid monitoring tool for an early detection of vascular damage that can even predict sub-clinic cardiac remodelling in patients affected by chronic arthropathies.

## A CASE OF HEART FAILURE IN A PATIENT WITH CARDIOMYOPATHY INDUCED BY GLUCOCORTICOID EXCESS

A. Concistrè<sup>1</sup>, L. Petramala<sup>1</sup>, V. Bisogni<sup>1</sup>, F. Olmati<sup>1</sup>, V. Saracino<sup>1</sup>, A. Ciardi<sup>2</sup>, G. Iannucci<sup>3</sup>, G. De Toma<sup>4</sup>, A. Frustaci<sup>5</sup>, C. Letizia<sup>1</sup>

<sup>1</sup>Department of Translational and Precision Medicine, Unit of Secondary Arterial Hypertension, "Sapienza" University of Rome, Rome, Italy, <sup>2</sup>Department of Radiological, Oncological and Anatomy-Pathological Sciences, "Sapienza" University of Rome, Rome, Italy, <sup>3</sup>Department of Internal Medicine and Medical Specialties, "Sapienza" University of Rome, Rome, Italy, <sup>4</sup>"Pietro Valdoni" Surgery Department, "Sapienza" University of Rome, Rome, Italy, <sup>5</sup>Department of Cardiovascular, Nephrologic, Anesthesiologic and Geriatric Sciences, "Sapienza" University of Rome, Rome, Italy

**Introduction:** Cushing's syndrome (CS) is an endocrine disorder characterized by inappropriate glucocorticoid secretion which determines typical manifestations such as hypertension, truncular obesity, osteoporosis and metabolic alterations. Cardiomyopathy secondary to excess glucocorticoids is an uncommon manifestation that can rarely begin with acute heart failure.

**Clinical case:** A 63-year-old woman with arterial hypertension, facies lunaris and hyperglycemia developed in the last year was studied in our Secondary Hypertension Department. Laboratory and radiological data suggested an ACTH-independent hypercortisolism due to a right adrenal lesion. During admission to the Surgery Department, before the adrenalectomy, the patient presented acute heart failure with pulmonary edema. After transfer to Cardiology Department, an echocardiogram was performed showing dilated left ventricle (LVEDD 62 mm) and severe reduction in overall systolic function (LV EF25%). For this reason, she underwent coronary angiography, ventriculography and endomyocardial biopsy which showed coronary arteries without significant stenosis, left ventricular dilatation, hypokinesia of the basal segments and antero-apical akinesia. Cardiac histology revealed myocardiocyte hypertrophy, myofibrillogenesis and sarcomeric disorganization. After clinical improvement, right adrenalectomy was performed with the resolution of hypercortisolism. A year later, a normalization of the size of the left ventricle (LVEDD 53 mm) and global systolic function recovery (LV EF55%) were found. After obtaining informed consent, 1 year after adrenalectomy, the patient underwent to endomyocardial biopsy with histological finding of reduction in the size of myocardiocytes and myofibrillogenesis and sarcomeric reorganization. We presented a case of heart failure secondary to cardiomyopathy caused by an adrenal disease.

**Conclusions:** This clinical manifestation, although uncommon in CS, suggests the role of hypercortisolism in the pathogenesis of cardiac myocyte alterations. The cardiac remodeling is also reversible after the normalization of circulating cortisol levels.

## FIRST-MINUTE HEART RATE INCREASE IN ERGOMETRIC STRESS TEST PREDICTS CARDIORESPIRATORY FITNESS PARAMETERS

F. Buono, M. Marzullo, L. Marotta, E. Di Vaia, A. Cuocolo, G. Iaccarino

*Dept. of Advanced Biomedical Sciences, Federico II University, Naples, Italy*

**Introduction:** Cardiorespiratory fitness (CF) is an important predictive factor of death due to any cause. Scientific evidences suggest that CF should be measured quantifying oxygen uptake (VO<sub>2</sub>). Due to complexity in measuring VO<sub>2</sub> in clinical practice, indirect parameters are used to estimate CF during stress test.

**Aim:** To verify if first-minute heart rate increase in stress test (EST) can be used as an indirect parameter to predict CF in non-sedentary population.

**Methods:** We analyzed data from 76 treadmill stress test performed by healthy volunteers in April 2019 at Sports Medicine Center of AOU "Federico II", Naples. According to the established protocol, slope and velocity increased every minute, up to seven steps. Tests were stopped when 85% of theoretical maximal heart rate was reached. Two steps of recovery (1 min and 2 min) were observed.

**Results:** We considered anthropometric measurements, hemodynamic parameters during rest and EST. Mean  $\pm$  SE age of volunteers is  $25 \pm 1.8$  years. Male to female ratio is 54/22. BMI is  $22.39 \pm 0.45$ . Rest heart rate (HR<sub>0</sub>) is  $78.6 \pm 1.8$  bpm. Blood pressure during rest is  $117 \pm 2.2/77 \pm 1.4$  mmHg. At maximal effort, mean slope is  $17.4 \pm 0.2\%$  and mean treadmill speed is  $7.7 \pm 0.1$  km/h with  $14.61 \pm 0.2$  METS calculated. Mean EST time is  $373 \pm 13$  s. Heart rate at the end of recovery phase (HRR) is  $104.9 \pm 2$  bpm. First minute heart rate variation mean percentage (DHR1) is  $30 \pm 2\%$  (min 12%, max 92%).

**Conclusions:** DHR1 indirectly correlates with HR<sub>0</sub> ( $F = 10.96$ ,  $R^2 = 146$ ,  $p < 0.0015$ ) and directly correlates with HRR ( $F = 5.606$ ,  $R^2 = 0.078$ ,  $p < 0.02$ ). In conclusion, DHR1 correlates with CF parameters as heart rate during rest and heart rate at the end of recovery phase and represents an additional parameter to predict CF at EST. This parameter might be of use in submaximal EST.

## ADAPTIVE CARDIAC REMODELING TO CHRONIC PRESSURE OVERLOAD REQUIRES THE EXPRESSION OF PLACENTAL GROWTH FACTOR IN THE SPLEEN AND DEPLOYMENT OF ADAPTIVE/REPARATIVE MACROPHAGES TO THE LEFT VENTRICLE

Sara Perrotta<sup>1</sup>, Roberta Iacobucci<sup>2</sup>, Lorenzo Carnevale<sup>2</sup>, Valentina Fardella<sup>2</sup>, Raimondo Carnevale<sup>2</sup>, Fabio Pallante<sup>2</sup>, Giuseppe Lembo<sup>1,2</sup>, Daniela Carnevale<sup>1,2</sup>

<sup>1</sup>Department of Molecular Medicine, "Sapienza" University of Rome, Italy, <sup>2</sup>Department of Angiocardioneurology and Translational Medicine, IRCCS Neuromed, Pozzilli (IS), Italy

**Introduction:** Cardiac remodeling to pressure overload is a complex process of adaptation of the left ventricle (LV) that involves various cell types, including cells of the immune system. We found that Placental Growth Factor (PIGF), a growth factor of the VEGF family, is necessary for adaptive remodeling to pressure overload and modulates the recruitment of innate immune cells in the LV.

**Aim:** To investigate the role of PIGF as an immunomodulator in response to pressure overload induced by transverse aortic coarctation (TAC).

**Methods:** We analyzed the cardiac monocyte/macrophage infiltrate by flow cytometry, to discriminate resident and recruited macrophages using the CD11b/CD64/Tim4/Ly6C/CCR2 markers.

**Results:** After TAC WT mice, but not the PIGF KO, showed a significant infiltrate of non-resident macrophages, suggesting that PIGF is involved in the recruitment of immune cells. Since TAC induces the expression of PIGF both in the heart and in the spleen, we generated chimeric mice through the spleen transplantation between WT and PIGF KO mice. PIGF KO mice with WT spleen showed a typical adaptive cardiac remodeling, as evidenced by echocardiographic analysis. In contrast, WT mice with a PIGF KO spleen subjected to TAC exhibit early heart failure (HFrEF) and reduced recruitment of monocytes/macrophages in the LV, as showed by flow cytometry. To investigate the potential role of the spleen as a reservoir of myeloid cells with adaptive/reparative functions, we subjected to TAC splenectomized mice that developed early HFrEF. To characterize the contribution of adaptive/reparative macrophages, characterized by the expression of the CX<sub>3</sub>CR1 receptor, and of the pro-inflammatory monocytes expressing CCR2, we subjected CX<sub>3</sub>CR1 KO and CCR2 KO mice to TAC. While CCR2 KO mice showed adaptive remodeling such as WT, CX<sub>3</sub>CR1 KO mice developed HFrEF similar to splenectomized mice and PIGF KO mice.

**Conclusions:** Overall our results indicate that pressure overload induces PIGF in the spleen as an immunomodulator capable to deploy adaptive/reparative macrophages that sustain adaptive remodeling of the LV.

## RELATIONSHIPS BETWEEN BNP LEVELS PRE- AND POST-SALINE LOAD SUPPRESSION TEST, RENIN-ANGIOTENSIN-ALDOSTERON PARAMETERS AND SYSTOLIC AND DIASTOLIC FUNCTIONAL INDEXES OF LEFT VENTRICLE IN ESSENTIAL HYPERTENSION

Cristiana Catena, Gianluca Colussi, Andrea Da Porto, Luca Bulfone, Alessandro Frangipane, Agnese Presello, Francesca Spagnol, Leonardo Sechi

*Hypertension Unit, Department of Internal Medicine, University of Udine, Italy*

**Introduction:** Some studies have shown a relation between BNP levels and morphofunctional parameters of left ventricle (LV) in essential hypertension (EH) but with conflicting results.

**Aim:** To search for relationships between levels of BNP pre- and post a saline infusion load test (SLT), plasma aldosterone (PA), active renin (AR), and morphofunctional parameters of LV in EH patients free of heart failure or valvular diseases.

**Methods:** In 155 EH patients (age  $48 \pm 12$  years, 92 males, 64 naïve, the remaining after a wash-out period), we evaluated clinical parameters, glomerular filtration rate (GFR), we performed a SLT (SF 0.9% 2 L in 4 h) with measurement of levels of PA, AR, BNP pre- and post-test (pre-BNP, post-BNP). An echocardiography with Tissue Doppler Imaging (TDI) was performed, with measure of LV mass indexed (LVMI), ejection fraction (EF), TDI-S velocity, E/A and E/e' ratios and TDI-e' velocity.

**Results:** Pre-BNP level was higher in females than males, and in patients on previous antihypertensive treatment than in naïve patients. Pre-BNP level was significantly and positively related to age, LVMI, E/e', and inversely to GFR, AR, TDI-S, E/A, and TDI-e'. Post-BNP

levels was higher in females and in previously treated patients, and it was positively related to age, E/e' ratio, and inversely to GFR, AR, TDI-S, E/A, and TDI-e'. At multivariate analysis pre-BNP level was independently associated with age, female gender, GFR, AR, while post-BNP level was independently associated with age, AR, and previous antihypertensive therapy.

**Conclusions:** In EH patients the BNP levels pre- and post a SLT are related to LV systolic and diastolic function and LVMI, but this relationship seems to be mediated by age and gender. However, measurement of BNP could be useful to identify and in follow-up of subclinical LV abnormalities in EH.

## Epidemiology and Clinical Aspects

### ELEVATED PULSE PRESSURE IN HYPERTENSION OF THE YOUNG: DIFFERENT PATHOGENETIC BACKGROUND IN MEN AND WOMEN

F. Saladini, C. Fania, L. Mos, A. Mazzer, G. Garavelli, G. Zanata, P. Spinella, E. Casiglia, P. Palatini

<sup>1</sup>Università degli Studi di Padova, Dipartimento di Medicina, Padova, Italy, <sup>2</sup>Cardiologia, Ospedale di San Daniele Del Friuli, Udine, Italy, <sup>3</sup>Medicina, Ospedale di Vittorio Veneto, Treviso, Italy, <sup>4</sup>Medicina, Ospedale di Cremona, Cremona, Italy, <sup>5</sup>Medicina, Ospedale di Pordenone, Pordenone, Italy

**Introduction:** The prognostic role of elevated pulse pressure (PP) in the young is still controversial. An elevated PP seems to have an unfavourable prognosis among women but not in men.

**Aim:** To identify clinical, metabolic and haemodynamic characteristics associated with raised PP in young hypertensive adults, investigating these associations according to gender.

**Methods:** We examined 1207 young stage I hypertensives (878 males) from the HARVEST Study, mean age  $33.1 \pm 8.5$  years, blood pressure (BP)  $145.5 \pm 10.6/93.5 \pm 5.7$  mmHg. Patients were divided into PP tertiles. All comparisons were tested with two-way ANCOVA.

**Results:** Stroke volume was higher in men than women ( $82.1 \pm 15.7$  ml vs  $70.8 \pm 16.4$  ml,  $p < 0.001$ ), while peripheral resistances did not differ significantly. Twenty-four-hour urinary norepinephrine/creatinine was higher in women than men ( $68.2 \pm 59.6$  vs  $54.4 \pm 66.5$  mcg/mg,  $p = 0.023$ ) whereas epinephrine was similar. PP was  $52.8 \pm 11.4$  mmHg in men and  $49.4 \pm 9.4$  mmHg in women ( $p < 0.001$ ). Men in the top PP tertile were younger and had lower BMI than those in the bottom tertile ( $p < 0.001$  and  $p = 0.002$ ), while the opposite trend was found for women ( $p < 0.001$  and  $p = 0.002$ ;  $p$  for PP-sex interaction  $< 0.001$  for both). Heart rate and systolic white coat effect progressively increased across PP tertiles in both genders ( $p < 0.001$  for both). Glucose and triglycerides increased with increasing PP among women while the opposite was found for men (with a significant trend for glucose  $p = 0.025$ ). At the end of follow-up (mean 7.9 years) females in the top PP tertile presented higher systolic BP ( $p = 0.004$ ), diastolic BP ( $p = 0.071$ ) and heart rate ( $< 0.001$ ), compared to males of the corresponding tertile.

**Conclusions:** Young hypertensive women are characterized by increased sympathetic activity, elevated BMI and worse metabolic profile, whereas men by a hyperkinetic state and better metabolic data. These differences may account for the worse prognosis of isolated systolic hypertension in female gender.

### EXTREME DIPPING: ALWAYS MEANS NOCTURNAL HYPOTENSION?

Elisa Gherbesi<sup>1</sup>, Giovanni Caffi<sup>2</sup>, Raffaella Dell'Oro<sup>2</sup>, Carla Sala<sup>1</sup>, Guido Grassi<sup>2,3</sup>, Giuseppe Mancia<sup>2</sup>, Cesare Cuspidi<sup>2,4</sup>

<sup>1</sup>Department of Clinical Sciences and Community Health, University of Milano and Fondazione IRCCS Policlinico di Milano, Italy, <sup>2</sup>Department of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy, <sup>3</sup>IRCCS Multimedica, Sesto San Giovanni, Italy, <sup>4</sup>Istituto Auxologico Italiano, IRCCS Milano, Italy

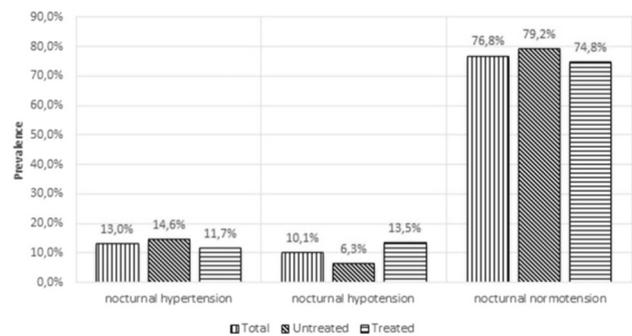
**Introduction:** Although nocturnal hypotension is considered the key factor responsible for the increased cardiovascular risk associated with the extreme dipping (ED) pattern no information is available on its prevalence in this setting.

**Methods:** We analyzed a total of 7074 ambulatory blood pressure monitoring (ABPM) records from a cohort of patients referred to a single out-patient hypertension center.

**Results:** A total of 339 patients (4.5%) exhibited an ED pattern (207 had a night-time reduction in both systolic and diastolic BP  $\geq 20\%$  compared to day-time values and 132 a night-time reduction in diastolic BP  $\geq 20\%$ ). In the total sample (Fig. 2), the prevalence of nocturnal hypotension varied from 9.1 to 45.0% depending on the criteria used (i.e. mean night-time BP  $< 90/50$  mmHg or  $< 100/60$  mmHg), and the prevalence of nocturnal hypertension (i.e. mean night-time BP  $\geq 120/70$  mmHg) was 19.5%. As compared to untreated patients, those taking anti-hypertensive drugs were more likely to have nocturnal hypotension and less likely to have nocturnal hypertension.

**Conclusions:** Our findings support the view that ED pattern is a condition not always associated with nocturnal hypotension, since a large fraction of ED patients have normal or elevated mean BP nocturnal values.

Figure 2



### THE LONG-TERM REPRODUCIBILITY OF MASKED (MUCH) AND WHITE COAT UNCONTROLLED HYPERTENSION (WUCH) IS LIMITED. DATA FROM THE ELSA STUDY

M. Bombelli, R. Facchetti, G. Corrao, C. Cuspidi, G. Grassi, G. Mancia

Department of Internal Medicine, Department of Statistics and Quantitative Methods, University of Milan Bicocca, S. Gerardo Hospital of Monza (MB), Istituto Auxologico, Milano, ITALY

**Aim:** To evaluate the long-term reproducibility of MUCH and WUCH, crucial information for defining the prognostic value of these conditions.

**Methods:** The reproducibility of MUCH and WUCH was evaluated in 1664 moderate hypertensive subjects enrolled in the European Lacidipine Study on Atherosclerosis (ELSA), a prospective multi-center, double-blind randomized study, treated with atenolol or lacidipine (in addition to any additional drugs), for a 4 year period. Every year each subject was subjected to measurement of Office blood pressure (BP) and to Ambulatory blood pressure monitoring (ABPM), thus allowing repeated subsequent reclassifications of the subjects in the MUCH and WUCH conditions.

**Results:** After 1 year of treatment, 21.1% of subjects were classified as MUCH while 17.8% were classified as WUCH. These prevalence values remained quite similar even in the surveys of the following years but a significant proportion of subjects modified their condition: only 1/3 of the subjects classified as MUCH or WUCH based on the Office BP and the ABPM of a set of measurements maintained the same condition in the surveys of the following years. The percentage of subjects that persisted in the same condition in the 4 years of treatment was only 4.5% (MUCH) and 6.2% (WUCH). The reproducibility of MUCH and WUCH was lower than that of the condition of persistent control or persistent non-therapeutic control of BP, both when the control was based on the Office measurement and when it was based on ABPM.

**Conclusions:** the conditions of MUCH and WUCH show poor reproducibility over time. This data must be taken into account when assessing their long-term prognostic value.

## IS GENDER SUFFICIENTLY TAKEN INTO CONSIDERATION BY SCIENTIFIC STUDIES ON HYPERTENSION?

Enrico Strocchi, Caterina Viggì, Angela Lucia Riva, Federico Cotti, Claudio Borghi

*University of Bologna, Bologna, Italy*

**Introduction:** Even though there are no doubts about the convenience of treating high blood pressure in both genders, the available evidence for men and women may not be equal and/or the presence of possible differences between genders might not have been systematically investigated.

**Aim:** In other words the questions to be answered are: (1) were both genders equally represented in hypertension researches; (2) Possible differences between genders have been investigated in all studies or not?

**Methods:** To try to find an answer to the above questions we performed a search of scientific literature to check whether women have been underrepresented in epidemiological and controlled clinical trials (CCT) and in which percentage of CCTs a gender specific analysis of the results was performed.

**Results:** As far as epidemiology both meta-analysis available (that of the Prospective Study Collaboration and that of the Asian Pacific Study Collaboration) included less than 40% of women; in CCTs the percentage of women included has increased from less than 30% in the early trials to almost 50% in the latest ones but large differences still persist among the studies. Moreover a gender-specific analysis of the results is not routinely performed. Among the latest 34 CCTs that were included in our analysis, results were reported separately for men and women only in half of the trials even though when searched some cases between genders were present. The situation is even worse for meta-analysis; of the 17 most relevant meta-analysis published between 1990 and 2018, two were dedicated to sex differences and

only 3 others analyzed the presence of potential differences between genders.

**Conclusions:** Even though the prevalence of hypertension in women is equal to that in men or even higher in older women, the attention given to the presence of potential differences in epidemiology, physiopathology and treatment is less than optimal and could be improved.

## THE IMPACT OF NEW BLOOD PRESSURE TARGETS IN CLINICAL PRACTICE

Enrico Strocchi, Eugenia Gamberini, Claudio Borghi

*University of Bologna, Bologna, Italy*

**Introduction:** 2018 ESH guidelines for diagnosis and treatment of hypertension have lowered the blood pressure (BP) targets to be reached with treatment especially for elderly subjects; this suggestion is based on the results of recent trials that demonstrate that lower blood pressures reduces the risk of cardiovascular events. However to attain a stricter blood pressure control is not always easy and requires intensified treatment.

**Aim:** To quantify the impact that new guidelines' BP targets could have on the clinical practice.

**Methods:** We analyzed 100 patient reports, related to visits performed in our outpatient clinic in a period preceding the publication of the 2018 guidelines (consecutive patients seen between March and May 2018); from the report we collected the BP values measured during the visit, the physician's evaluation of BP control and decision about treatment and prescribed drug therapy (class of drugs and dose, either full dose or low dose).

**Results:** 20 patients were excluded from subsequent analysis because it was their first visit and they were prescribed an antihypertensive treatment for the first time; in 63 of the remaining 80 patients, according to BP measured during the visit and overall BP control out of office, keeping in mind the target of previous guidelines, the physician decided to confirm the ongoing therapy because BP control was deemed satisfactory; in 3 more patients the BP control was partially unsatisfactory but the physician confirmed anyway the current therapy (an example of physician's inertia); in the remaining 14 patients the therapy was modified because of poor BP control. If we were to apply the new targets for BP, therapy should have been modified in 68 patients and that could be done with an increase of dose in 40 cases and with the addition of a new drug in the remaining 28 patients.

**Conclusions:** to reach the new targets for BP control is feasible but in many cases increases the number of drugs that have to be taken and this could have negative effects on adherence and therefore paradoxical effects on BP control.

## DETERMINANTS OF LONGITUDINAL CHANGES IN SUBMAXIMAL EXERCISE BLOOD PRESSURE IN A POPULATION OF YOUNG ATHLETES

Francesca Battista<sup>1</sup>, Daniel Neunhaeuserer<sup>1</sup>, Giulia Meneguzzo<sup>1</sup>, Sara Rovai<sup>1</sup>, Alessandro Patti<sup>1</sup>, Sara Ortolan<sup>1</sup>, Giacomo Pucci<sup>2</sup>, Andrea Ermolao<sup>1</sup>

<sup>1</sup>Department of Medicine, Sport and Exercise Medicine Division, University of Padua, Padua, Italy, <sup>2</sup>Unit of Internal Medicine, Terni University Hospital, Department of Medicine, University of Perugia, Italy

**Introduction:** In adults, a higher submaximal exercise blood pressure predicts the development of overt hypertension and future cardiovascular events.

**Aim:** To investigate correlates and determinants exercise blood pressure its longitudinal variations in in young athletes.

**Methods:** Longitudinal retrospective study conducted on adolescent athletes who underwent at least two pre-participation screening visits that included exercise test on treadmill by using standardized ramp incremental protocol. Blood pressure (auscultatory method) was assessed at rest (SBP<sub>rest</sub>), at 3rd minute of exercise (SBP<sub>3min</sub>) and at exercise peak (SBP<sub>peak</sub>).

**Results:** 351 young athletes (mean age at baseline 13 ± 2 years, 54% boys, average follow-up duration 3.4 ± 2.2 years) that showed, at baseline, mean SBP<sub>rest</sub> 103 ± 14 mmHg and mean SBP<sub>3min</sub> 124 ± 18 mmHg. Between-visit variation in SBP<sub>rest</sub> (ΔSBP<sub>rest</sub> 7.0 ± 17.4 mmHg; p vs baseline < 0.001) and ΔSBP<sub>3min</sub> (4.8 ± 11 mmHg; p < 0.001) were significant. BMI increased by 1.5 ± 1.8 kg/m<sup>2</sup> (p < 0.001). In a multivariate regression model independent determinants of baseline SBP<sub>rest</sub> were BMI (p < 0.0001) and age at baseline (p < 0.0001), while determinants of SBP<sub>rest</sub> at follow-up were gender (p < 0.0001), BMI at follow-up (p < 0.0001), SBP<sub>3min</sub> at baseline (p < 0.0001) and follow-up duration (p < 0.0001). Significant determinants of SBP<sub>3min</sub> at baseline were gender (p < 0.0001), BMI (p < 0.0001), SBP<sub>rest</sub> (p < 0.0001) and age (p < 0.04) at baseline, while SBP<sub>3min</sub> at follow-up was determined by gender (p < 0.0001), BMI (p < 0.0001) and SBP<sub>rest</sub> at follow-up (p < 0.0001). ΔSBP<sub>3min</sub> was significantly predicted by male gender (p < 0.01), baseline BMI (p < 0.01), ΔBMI (p < 0.01) and number of sports (p < 0.05). In a logistic regression model, ΔBMI was the only independent determinant of switching from a lower to an upper quartile of SBP<sub>3min</sub> (p < 0.001).

**Conclusions:** Increase in BMI during time is an independent determinant of the longitudinal increase of submaximal exercise blood pressure in a population of young athletes.

## ASSESSMENT OF CAROTID CROSS SECTIONAL AREA IN HYPERTENSIVE PATIENTS: PHENOTYPING AND PROGNOSTIC VALIDATION IN THE CAMPANIA SALUTE NETWORK

Costantino Mancusi, Raffaele Izzo, Maria Angela Losi, Emanuele Barbato, Valentina Trimarco, Carmine Morisco, Grazia Canciello, Maria Virginia Manzi, Francesco Rozza, Nicola De Luca, Giovanni de Simone, Bruno Trimarco

*Hypertension Research Center, Department of Advanced Biomedical Sciences, University of Naples Federico II, Italy*

**Introduction:** Increased intima media thickness (IMT) of common carotid artery (CA) is considered the hallmark of vascular hypertension-mediated target organ damage, even though vessel remodeling due to mechanical stress can be accompanied also by changes in diameter.

**Aim:** We developed a method computing both diameter and IMT of CA, and assessed correlates and prognostic impact of carotid cross sectional area (CCSA) in a large registry of treated hypertensive patients.

**Methods:** We selected 7049 hypertensive patients of the Campania Salute Network registry free of overt cardiovascular (CV) disease and with available CA ultrasound (54 ± 11 yrs; 57% male). CCSA was computed as:

$$\pi \times \left( \frac{(CA \text{ diameter}) + 2 \times (\text{mean IMT})}{2} \right)^2 - \pi \times \left( \frac{(CA \text{ diameter})}{2} \right)^2.$$

**Results:** CCSA was considered high if > 90th percentile of the sex-specific distribution (> 48 mm<sup>2</sup> in men and > 41 mm<sup>2</sup> in women). Higher CCSA correlated with older age, male sex, higher pulse pressure (PP), higher total and LDL cholesterol and presence of diabetes (p < 0.01 for all). During a median follow-up of 45 months (IQR 19–92), 324 incident composite major and minor CV events occurred. In Cox regression analysis high CCSA was associated with more than 100% increased risk of incident CV events (p < 0.0001), independently of the effect of older age, male sex, PP > 60 mmHg, presence of left ventricular hypertrophy (LVH), carotid plaque (CP), and less anti-RAS therapy (p < 0.05 for all).

**Conclusions:** In treated hypertensive patients, increased CCSA is associated with worse metabolic and lipid profile and predict incident CV events, independently of high PP, presence of LVH and CP.

## QUALITY OF LIFE AND BLOOD PRESSURE: ANALYSIS OF A NATIONAL SURVEY

Rita Del Pinto<sup>1</sup>, Silvia Pagliacci<sup>2</sup>, Giuliana Properzi<sup>1</sup>, Davide Grassi<sup>1</sup>, Giovambattista Desideri<sup>1</sup>, Claudio Ferri<sup>1</sup>

<sup>1</sup>University of L'Aquila, Dept. of life, Health and Environmental Sciences, Italy, <sup>2</sup>Federfarma-Sunifar, Italy

**Introduction:** For the World Hypertension Day 2018, Federfarma and SIIA have co-sponsored the initiative “Abbasso la Pressione!”, National survey in 3956 (21%) Italian pharmacies to raise awareness about blood pressure (BP) and others cardiovascular risk factors (CVRF).

**Aim:** We examined whether the quality of life (QoL) per city affects CVRF distribution and BP control.

**Methods:** The QoL composite index by city was extracted from accredited national sources available online. We calculated the prevalence of arterial hypertension (uncontrolled/controlled according to ESC/ESH 2018 guidelines; newly diagnosed) and of the other CVRF examined, as well as mean BP (using crude and progressively adjusted models incorporating gender, age, dyslipidemia, smoking, diabetes, sedentariness, eating habits, family history of CV diseases), according to tertiles of QoL (low, medium, high).

**Results:** In 47217 participants, the QoL was low for 33.2%, average for 35.3% and high for 31.5%, with a South-North gradient (high QoL: 0% in the South, 30.4% in the Center, 69.6% in the North, p < 0.001). Across the three tertiles, mean BP was 128.7 ± 17.5/76.7 ± 10.7 mmHg, 129.5 ± 18.1/76.7 ± 10.7 mmHg, and 129.6 ± 18.4/76.4 ± 10.8 mmHg, respectively (p < 0.001 for systolic BP). Participants in the higher tertile were older, leaner, dyslipidemic, non-smoker, non-diabetic, more active women, with family history of CV diseases, who used more vegetables and less salt (p < 0.001); there were more cases of newly diagnosed hypertension (p = 0.05). In the crude model, uncontrolled hypertensives showed a progressively increasing mean BP with increasing QoL (+ 2.1/+ 0.4 mmHg from the first to the third tertile, p < 0.05). In the adjusted model, mean BP increased with QoL (p < 0.0001) among both controlled (+ 1.1/+ 0.6 mmHg) and uncontrolled (+ 1.6/+ 0.3 mmHg) hypertensives.

**Conclusions:** In the examined sample, differences exist in CVRF and BP profile based on QoL per city. Living in a city with better QoL does not seem to be synonymous with good cardiovascular health.

## AIR POLLUTION AND BLOOD PRESSURE: ANALYSIS OF A NATIONAL SURVEY

Rita Del Pinto<sup>1</sup>, Silvia Pagliacci<sup>2</sup>, Giuliana Properzi<sup>1</sup>, Davide Grassi<sup>1</sup>, Giovambattista Desideri<sup>1</sup>, Claudio Ferri<sup>1</sup>

<sup>1</sup>University of L'Aquila, Dept. of life, Health and Environmental Sciences, Italy; <sup>2</sup>Federfarma-Sunifar, Italy

**Introduction:** For the World Hypertension Day 2018, Federfarma and SIIA have co-sponsored the initiative "Abbasso la Pressione!", National survey in 3956 (21%) Italian pharmacies to raise awareness about blood pressure (BP) and others cardiovascular risk factors (CVRF).

**Aim:** We examined whether fine particles (PM<sub>2.5</sub>) density per city affect CVRF distribution and BP control.

**Methods:** PM<sub>2.5</sub> density per city (year 2017) was extracted from accredited national sources available online. We calculated the prevalence of arterial hypertension (uncontrolled/controlled according to ESC/ESH 2018 guidelines; newly diagnosed) and of the other CVRF examined and the risk of uncontrolled hypertension (crude and progressively adjusted models incorporating gender, age, obesity, dyslipidemia, smoking, diabetes, sedentary life, eating habits), according to tertiles of PM<sub>2.5</sub> (lower = 0–15 mcg/m<sup>3</sup>; medium = 15–22 mcg/m<sup>3</sup>; upper = 22–34 mcg/m<sup>3</sup>).

**Results:** Among 37544 participants, the majority (36.9%) lived in cities with intermediate density of PM<sub>2.5</sub>, while 31.8% and 31.4% lived in cities with lower and higher density, respectively. There was a North–South gradient in microparticulate exposure (cities in the upper tertile: 94.8% in the North, 5.2% in the Center, 0% in the South,  $p < 0.001$ ). From the lower to the upper tertile, mean BP was  $128.4 \pm 17.7/76.5 \pm 10.8$  mmHg,  $129.6 \pm 18.2/76.8 \pm 10.9$  mmHg, and  $130.0 \pm 18.4/77.1 \pm 10.6$  mmHg, with new diagnoses of hypertension accounting for 11.8%, 12.9% and 12.5%, respectively ( $p < 0.001$ ). Participants in the upper tertile were older, lean, more active, dyslipidemic, non-smoking, non-diabetic women, who consumed more vegetables ( $p < 0.001$ ). The risk of uncontrolled hypertension was significantly higher among participants in the upper compared to the lower tertile (crude odds ratio [OR]:1.20, 95% confidence interval [CI] 1.11–1.30,  $p < 0.0001$ ; adjusted OR: 1.31 (95% CI 1.21–1.42),  $p < 0.0001$ ; N = 17176).

**Conclusions:** In the examined sample, differences exist in CVRF and BP profile based on PM<sub>2.5</sub> density per city. Improving air quality could represent a non-pharmacological strategy for cardiovascular prevention.

## HYPERTENSION IN A GENERAL MEDICINE PRACTICE

Marco Mucciarone<sup>1</sup>, Aldo Avincola<sup>2</sup>, Vincenzo Romano Spica<sup>3</sup>, Raffaele Landolfi<sup>1</sup>, Marco Mettimano<sup>1</sup>

<sup>1</sup>Center of Arterial Hypertension, University Hospital "Agostino Gemelli", Rome, Italy, <sup>2</sup>General Medicine practice, Rome, Italy, <sup>3</sup>Department of Human and Health Sciences, University "Foro Italico", Rome, Italy

**Aim:** To analyze prevalence, comorbidities and therapeutic choices in arterial hypertension basing on data collected throughout 2018 in a General Medicine practice located in the Ottavia district (Rome).

**Methods:** The study population is composed of 1375 patients, with an age and sex distribution comparable to the national one.

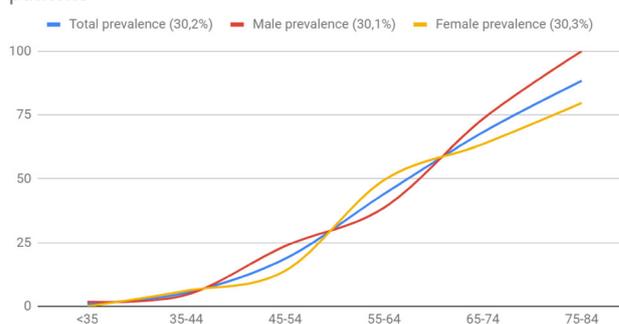
**Results:** The hypertensive patients were 415, with a global prevalence of 30.1% for men and 30.3% for women. The prevalence curve shows a general higher prevalence in men, except for 55–64 age

group, in which women had a greater prevalence. In the 75–84 age group the total prevalence of arterial hypertension reaches 88% (Fig. 3). The analyzed comorbidities were dyslipidemia and diabetes mellitus. Hypertension is mostly associated with diabetes mellitus and dyslipidemia with aging: while in the 45–54 age group, hypertensive patients with diabetes mellitus and/or dyslipidemia are 29%, in the 75–84 age group hypertensive patients with diabetes mellitus and/or dyslipidemia are 67%. The most used drugs were diuretics, followed by ACE-inhibitors, beta-blockers, sartans and calcium-antagonists. The most used association was ACE-inhibitors + diuretics. As the age ranges grow, there is a proportional increase in therapeutic associations.

**Conclusions:** Advancing age, hypertension can be considered an almost inevitable fate and it often manifests itself with diabetes mellitus and dyslipidemia. Therefore, pharmacological and behavioral therapy must manage hypertension focusing on comorbidities too.

Figure 3

Total prevalence and prevalence by sex of hypertensive patients



## RESISTANT ARTERIAL HYPERTENSION: FOLLOW UP

M. D'Avino, G. Caruso, F. Capasso, F. Ciaburri, B. A. Ferravante, S. Scarfiglieri, G. Zampa

AORN A. Cardarelli, Napoli, Italy

**Introduction:** Resistant arterial hypertension (RH) is the condition of PA > 140/90 while treating with three or more drugs. These patients show a 3 times greater risk of undergoing cardiovascular events than controlled pts.

**Aim:** To evaluate the occurrence of fatal and non-fatal events (IMA, Stroke, TIA, Aritmie) in pts with RH.

**Methods:** from January 2017 to January 2019 they were followed at our clinic of I.A. 179 pts (101 M) (average age  $57 \pm 7$ ) with PA > 140/90 (LG ESH 2013), without secondary IA, diabetes mellitus, dyslipidemia and smokers. 63 (Group A) had IVS, 48 (Group B) mid-intimal carotid thickening (IMT  $\geq 0.9$  mm), 50 (Group C) had signs of IVS and IMT. Only 68 (Group D) showed no signs of organ damage. The BP values were checked with clinical measurement and MAPA at T0, T1 (12 months) T2 (24 months). Patients were on ace-inhibitors, beta-blockers, angiotensin II antagonists, calcium channel blockers, diuretics, doxazosin and were on hypo-sodium therapy.

**Results:** 2 of Group D presented IMA, 3 Stroke including 1 fatal, 5 TIA and 7 arrhythmia from FA. Group A and Group C did not show any events. 3 of the C had ischemic heart disease, with coronary angiography and angioplasty. The largest number of events in all

groups occurred between the 1st and 2nd year of follow-up, when BP values were altered. The average PA was at T0 and T1 165/95; a significant reduction was achieved at T2. A reduction in BP to T2 was recorded at MAPA.

**Conclusions:** They showed patient cardiovascular events of the group without organ damage. The reduction of BP plays a fundamental role in the incidence of organ damage, the identification of which in patients with RH must induce to be very attentive to the optimization of therapy.

## BLOOD PRESSURE EFFECTS OF OBSTRUCTIVE SLEEP APNEA TREATMENT BY CONTINUOUS POSITIVE AIRWAY PRESSURE: SYSTEMATIC REVIEW, META-ANALYSIS AND EVALUATION OF PHENOTYPES PREDICTING RESPONSE

M. Pengo<sup>1</sup>, D. Soranna<sup>1</sup>, A. Giontella<sup>2</sup>, E. Perger<sup>1</sup>, E.I. Schwarz<sup>3</sup>, C. Lombardi<sup>1</sup>, G. Bilo<sup>1</sup>, A. Zambon<sup>4</sup>, J. Steier<sup>5</sup>, P. Minuz<sup>2</sup>, G. Parati<sup>1-6</sup>, C. Fava<sup>2</sup>

<sup>1</sup>Istituto Auxologico Italiano, Department of Cardiovascular, Neural and metabolic Science, IRCCS, Ospedale San Luca, Milan Italy,

<sup>2</sup>Department of Medicine, University of Verona, Verona, Italy,

<sup>3</sup>Department of Pulmonology and Sleep Disorders, Centre University Hospital, Zurich, Switzerland, <sup>4</sup>Department of Statistics and Quantitative Methods, Università di Milano Bicocca, Milan, Italy, <sup>5</sup>Centre for Human and Aerospace Physiological Sciences, Kings College London, London, UK, <sup>6</sup>Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy

**Introduction:** Treatment of obstructive sleep apnoea (OSA) has been shown to reduce blood pressure (BP). However, the effect size is modest and treatment of OSA is not recommended as the only treatment target when treating hypertension.

**Aim:** The aim of the present systematic review and meta-analysis was to identify potential predictors for BP response in patients with OSA undergoing CPAP treatment.

**Methods:** A systematic search was conducted in three databases (MEDLINE, Embase and Web of Science) using terms exploring obstructive sleep apnoea, CPAP and clinical trial. Inclusion criteria were: (i) randomized controlled clinical trials published between January 1st 1960 to December 31st 2017 and with a reasonable control group; (ii) OSA diagnosis using polysomnography; (iii) age > 18 years; (iv) OSA severity of at least 5 AHI/h. The random effect model was fitted to estimate the pooled BP reductions (difference between end-treatment minus baseline BP) in the CPAP and control group. Moreover, the original estimates have been stratified according to selected patient characteristics.

**Results:** Out of 2445 articles, 59 RCTs were included (n = 7.329 subjects) comparing CPAP with control groups. CPAP was associated with a net reduction in systolic BP of - 2.12 (95% CI - 2.82/- 1.42) mmHg and in diastolic BP of - 1.97 (95% CI - 2.46/- 1.48) mmHg, favoring treatment of OSA using CPAP (both p < 0.001). The subgroup analysis showed a greater reduction of SBP in subjects younger than 60 years (- 2.88 for age 40-50, - 2.78 for age 50-60 and - 0.61 for age more than 60 years, p = 0.007) and in patients with controlled BP at baseline versus uncontrolled BP (- 1.45 vs - 4.14, p = 0.002).

**Conclusions:** Younger patients (< 60 years) with uncontrolled BP at baseline are more likely to experience significant BP reductions with CPAP therapy. Phenotypisation of specific cohorts of patients can guide clinicians to target OSA treatment and help to optimize patients' cardiovascular risk.

## Genetics and Pharmacogenomics

### METHYLATION STATUS AND GENE EXPRESSION OF STEROIDOGENIC ENZYMES IN BENIGN ADRENOCORTICAL TUMORS

F. Fallo<sup>1</sup>, L. Morandi<sup>2</sup>, B. Rubin<sup>1</sup>, C. Pilon<sup>1</sup>, S. Asioli<sup>1</sup>, V. Maffei<sup>3</sup>, A. Fassina<sup>3</sup>, G. Di Dalmazi<sup>4</sup>

<sup>1</sup>Department of Medicine, Clinica Medica 3, University of Padova, Italy, <sup>2</sup>Department of Biomedical and Neuromotor Sciences, Section of Anatomic Pathology University of Bologna, Italy, <sup>3</sup>Department of Medicine, Cytopathology Unit, University of Padova, Italy, <sup>4</sup>Department of Medical and Surgical Sciences, Endocrinology Unit, University of Bologna, Italy

**Introduction:** DNA methylation has been recognized as a putative regulatory mechanism for *CYP11B2* in primary hyperaldosteronism.

**Aim:** To investigate the DNA methylation and the expression of a panel of genes encoding several enzymes involved in steroidogenesis in adrenocortical benign tumors.

**Methods:** We collected a total of 60 adrenocortical tissues, including 9 non-functioning adrenal adenomas, 9 adenomas associated with autonomous cortisol secretion, 17 adenomas associated with Cushing's syndrome, 13 Conn's adenomas and 12 tissues derived from adrenal gland adjacent to the Conn's adenomas. Non-functioning tumors and autonomous cortisol secretion were defined according to cortisol levels after 1 mg dexamethasone suppression test  $\leq$  or  $>$  50 nmol/L, respectively. The DNA methylation level of *CYP11A1*, *CYP11B1*, *CYP11B2*, *CYP17A1*, *CYP21A2*, *DHCR24*, *HSD3B1*, *HSD3B2*, *NR5A1*, *STAR*, and *TSPO* was evaluated by quantitative Bisulfite Next Generation Sequencing (bisulfite-NGS). Bioinformatic analysis was performed in a GalaxyProject environment and processed by BSPAT (Bisulfite Sequencing Pattern Analysis Tool). Spearman correlation coefficients were calculated using IBM SPSS 21 (IBM). *CYP11B1*, *CYP11B2*, *CYP17*, *CYP21*, *STAR* and  $\beta$ -actin gene expressions were examined by quantitative Real-Time PCR using a Sybr Green Assay kit (Thermo Fisher Scientific). The equation  $2^{-\Delta\Delta Ct}$  was used to calculate the fold changes in gene expression between the categories of samples.

**Results:** *CYP11B2* was significantly hypomethylated in Conn's adenoma, when compared to other adrenal tissues (P < 0.001). No difference in methylation status was found among groups for the remaining genes. *CYP11B2* mRNA levels were significantly higher in Conn's adenoma than in the remaining adrenal tissues (P = 0.001).

**Conclusions:** Overall, we found a negative correlation between *CYP11B2* expression and DNA methylation ( $\rho = -0.379$ ; P = 0.003). DNA methylation seems to be a pivotal regulatory mechanism for *CYP11B2* expression. It is feasible that epigenetic mechanisms may be responsible for aldosterone hypersecretion in Conn's adenoma.

## VARIATION IN THE CHROMOGRANIN B GENE INFLUENCES THE CIRCADIAN RHYTHM OF BLOOD PRESSURE AMONG NORMOTENSIVE AND NEWLY DIAGNOSED HYPERTENSIVE SUBJECTS

G.P. Fra<sup>1</sup>, S. Migliavacca<sup>2</sup>, V.M. Mallela<sup>2</sup>, M.N. Barbaglia<sup>2</sup>, F. Brustia<sup>1</sup>, C. De Benedittis<sup>2</sup>, E. Matino<sup>2</sup>, O. Vriz<sup>3</sup>, D. De Zanet<sup>2</sup>, E. Grossini<sup>2</sup>, R. Minisini<sup>2</sup>, M. Pirisi<sup>1,2</sup>

<sup>1</sup>AOU Maggiore della Carità, Novara, Italy, <sup>2</sup>Dipartimento di Medicina Traslationale, Università del Piemonte Orientale, Italy, <sup>3</sup>The Heart Centre, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

**Introduction:** The promoter variant A261T (rs236141) in the *CHGB* gene influences chromogranin B expression in vitro, as well as blood pressure (BP) in vivo (JACC 2010;55:1463–75). To date, whether this genetic trait may act on BP by altering its physiological circadian rhythm is unknown.

**Methods:** 126 apparently healthy subjects (N. = 77 females; aged 45–65) underwent 24-h ambulatory BP measurement for the purpose of cardiovascular screening. They were genotyped for rs236141 by restriction fragment length polymorphism of polymerase chain reaction amplicons.

**Results:** Based on 2018 ESC criteria, N. = 74/126 (59%) study participants were hypertensives. When compared to the group of N. = 52 normotensive subjects, male (53% vs. 22%,  $p < 0.001$ ) and overweight/obese subjects (49% vs. 21%,  $p = 0.003$ ) were overrepresented in the group with hypertension. rs236141 ancestral (p) allele frequency was = 0.607, variant (q) allele frequency was 0.393; the study population was in Hardy–Weinberg equilibrium. There was a nonsignificant trend for a larger prevalence of variant allele carriers among the group of hypertensives (65% vs. 48%,  $p = 0.088$ ). The median (IQR) average systolic BP values (in mm Hg) in the 24 h, daytime and nighttime BP recordings of wild-type homozygotes (N. = 44) vs. variant allele carriers (N. = 82) were 128 (121–144) vs. 136 (125–147) ( $p = 0.129$ ), 132 (125–148) vs. 137 (128–150) ( $p = 0.194$ ), and 112 (105–126) vs. 119 (109–135) ( $p = 0.027$ ), respectively. Nighttime systolic BP decreased less than 10% in comparison to daytime in 45/126 “non-dipper” subjects (36%; 26/45 were hypertensives): 35/45 (78%) were carriers of rs236141 variant allele ( $p = 0.020$ ). At multivariate analysis, being a non-dipper was predicted by carriage of the rs236141 variant allele (odds ratio = 2.46, 95% CI 1.07–5.68,  $p = 0.035$ ), independently of gender and body mass index.

**Conclusions:** Genetic variation in the *CHGB* locus influences BP mainly by hampering the physiological reduction of systolic BP values during nighttime.

## Resistant Hypertension

### HYPERTENSIVE EMERGENCIES AND URGENCIES: BLOOD PRESSURE MANAGEMENT AND ITS RELATIONSHIP WITH SHORT AND MEDIUM TERM OUTCOME

A. Maloberti<sup>1,2</sup>, G. Magni<sup>2</sup>, Cassano G<sup>2</sup>, Capsoni N<sup>2</sup>, Gheda S<sup>2</sup>, Magni G<sup>2</sup>, Azin GM<sup>2</sup>, Zacchino M<sup>2</sup>, Rossi A<sup>2</sup>, Campanella C<sup>2</sup>, Marta Bergamaschi<sup>2</sup>, Marta Battistini<sup>2</sup>, Tommaso Valobra<sup>2</sup>, A. Moreo<sup>1</sup>, A. Beretta<sup>3</sup>, A. Bellone<sup>3</sup>, C. Giannattasio<sup>1,2</sup>

<sup>1</sup>Cardiology 4, ASST Niguarda Ca Granda Hospital, Milan, Italy, <sup>2</sup>School of Medicine and Surgery, Milan-Bicocca University, Milan, Italy, <sup>3</sup>Emergency Department, ASST Niguarda Ca Granda Hospital, Milan, Italy

**Introduction:** Data regarding prevalence and clinical management of hypertensive emergencies and urgencies are lacking and heterogeneous.

**Aim:** To characterize patients with hypertensive emergencies and urgencies admitted to the emergency department (ED) of Niguarda hospital. In this population we also want to evaluate factors associated with organ damage, adherence to guidelines and the impact of blood pressure (BP) management on short-term (admission to hospital and hospital mortality) and medium-term outcomes (recurrence).

**Methods:** We performed a single-center retrospective study collecting data about all adult patients with systolic blood pressure  $\geq 180$  mmHg and/or diastolic blood pressure  $\geq 120$  mmHg admitted to our hospital's ED during 2017.

**Results:** Admission to ED for BP elevation were 706 (0.95% of total admission to ED), of whom 34.8% were hypertensive emergencies and 65.2% were hypertensive urgencies. Patients with hypertensive emergencies were older, mainly male, with more comorbidities and more symptomatic at ED admission. In the emergencies group, we observe a BP reduction rate of  $18.82 \pm 12.1\%$  within  $110.1 \pm 11.9$  min; the most used drugs were nitroglycerin, furosemide and labetalol. In the urgencies group, the BP reduction rate was 19% and the most used drug was short-acting nifedipine. Age, sex, smoking, clinical history of heart failure and chronic obstructive pulmonary disease, symptoms at ED admission and eGFR have been recognized as factors associated with organ damage. Instead, BP at ED admission and its management didn't appear to have a significant impact on outcomes.

**Conclusions:** Our study demonstrated good adherence to guidelines in the treatment of hypertensive emergency than of hypertensive urgencies. On the other hand, no significant association were found between the BP management in the ED and the short-term and medium-term outcomes.

## GENERAL AND PSYCHOLOGICAL CHARACTERISTICS OF PATIENTS WITH RESISTANT HYPERTENSION: A MULTICENTRE COHORT STUDY

Marco Pappaccogli<sup>1,2</sup>, Silvia Di Monaco<sup>1</sup>, Elvira Fanelli<sup>1</sup>, Elisabetta Eula<sup>1</sup>, Coralie Georges MG<sup>2</sup>, Géraldine Petit<sup>3</sup>, Francesca Severino<sup>2</sup>, Jean Renkin<sup>2,3</sup>, Philippe de Timary<sup>3</sup>, Franco Rabbia<sup>1</sup>, Alexandre Persu<sup>2,4</sup>

<sup>1</sup>Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy, <sup>2</sup>Division of Cardiology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, 1200 Brussels, Belgium, <sup>3</sup>Adult Psychiatry Department and Institute of Neuroscience, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, <sup>4</sup>Pole of Cardiovascular Research, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, 1200 Brussels, Belgium

**Introduction:** Management of resistant hypertension (RHTN) is challenging and often implies the use of interventional therapies.

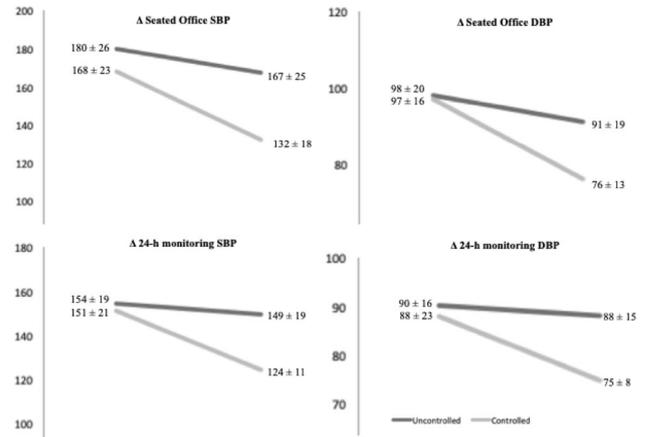
**Aim:** To depict the characteristic of a multicentre cohort of patients with RHTN and to look for differences between patients eventually controlled at the end of the follow-up and those who remained refractory.

**Methods:** Electronic medical files of all hypertensive outpatients referred to two expert centres in Brussels and in Turin were reviewed and clinical data, data on drug adherence and psychological profile were extracted. All patients with confirmed diagnosis of RHTN, according to Office and ambulatory monitoring (ABPM) measurements, were considered eligible.

**Results:** 313 patients (51% men; age:  $56 \pm 12$  years, office BP 177/89 mmHg; 24-h ABPM BP 153/90 mmHg) were included. At the end of the follow-up (median: 2 years [1–4]) both office and ABPM BP decreased by  $-19/-11$  mmHg and  $-9/-6$  mmHg, respectively, but only 26% of patients reached BP control (Fig. 4). Patients eventually controlled at the follow-up had lower pulse pressure (71 vs. 82 mmHg,  $p < 0.001$ ), less often myocardial infarction (6% vs. 20%,  $p < 0.005$ ) and a higher recourse to cognitive reappraisal when emotion regulation is concerned ( $4.8 \pm 1.1$  vs.  $3.9 \pm 1.2$ ,  $p = 0.009$ ; ERQ Questionnaire). Looking for predictors of controlled BP, only the psychological characteristic of cognitive reappraisal ("changing one's thoughts about a potentially emotion-eliciting event) remained significant (OR 1.95, IC 95% [1.11; 3.4],  $p = 0.019$ ).

**Conclusions:** Even in expert centred, only a minority of patients with RHTN reached BP control, irrespective of the centre involved or the interventions applied. Patients eventually controlled had lower arterial stiffness and less cardiac organ damage, suggesting a crucial role of both in promoting and sustaining RHTN. Besides these findings, the single predictor of BP control was the ability to modify the emotional impact of stressful situations. Hence, PP and psychological evaluation should be systematically incorporated in the approach of patients with RHTN.

Figure 4



## RESISTANT HYPERTENSION IN MOOD DISORDERS AND HYPOKALAEMIA: SEARCHING FOR A LINK

G. Santoro<sup>1</sup>, A. P. Sacco<sup>1</sup>, L. Schiavon<sup>2</sup>, C. Rossetti<sup>2</sup>, G. Torin<sup>3</sup>, S. Boschetti<sup>4</sup>, S. Benetti<sup>4</sup>, G. Grassetto<sup>5</sup>, M. R. Ballotta<sup>6</sup>, A. Mazza<sup>7</sup>

<sup>1</sup>UOS di Endocrinologia-UOC Medicina Interna-Ospedale di Rovigo, Rovigo, Italy, <sup>2</sup>UOC Medicina Interna-Ospedale di Rovigo, Rovigo, Italy, <sup>3</sup>UOC Medicina Generale ed Ipertensione-Università di Verona, Verona, Italy, <sup>4</sup>UOC Radiologia-Ospedale di Rovigo, Rovigo, Italy, <sup>5</sup>UOC Medicina Nucleare-Ospedale di Rovigo, Rovigo, Italy, <sup>6</sup>UOC Anatomia Patologica, Rovigo, Italy, <sup>7</sup>Centro Ipertensione di Eccellenza ESH, Rovigo, Italy

**Introduction:** A close relationship between cardiovascular diseases and psychopathological symptoms has been described in the literature. However, only few studies have reported mood disorders in patients with resistant hypertension (RH). On the contrary hypokalaemia is a finding suggestive of secondary hypertension. We discuss a case of RH and hypokalaemia in an otherwise healthy woman, and analyse the diagnostic and therapeutic approach followed.

**Clinical case:** A 70-year old woman referred to our Centre for a clinic blood pressure (BP) of 172/108 mmHg uncontrolled by 10 mg/day amlodipine, 10 mg/day ramipril, 50 mg/day hydrochlorothiazide, 5 mg/day amiloride, 25 mg/day spironolactone and 4 mg/day doxazosin started 2 months before due to hypertensives crisis with a BP of 192/126 mmHg and 216/130 mmHg respectively, without organ damage. The 24 h-ABPM showed a Reverse-Dipper profile of BP values. She referred a new-onset diabetes and a personality disturbance with generalized anxiety, panic disorder, impairment of memory and asthenia for which she had been treated with 150 mg/day venlafaxine and 0.50 mg/day alprazolam. She also had sleep disturbances such as middle insomnia and alteration of dreams which became more bizarre and vivid. Physical examination showed central obesity without abdominal striae, supra-clavicular fat pads, moon facies with easy bruising without hirsutism. An increase of the serum cortisol at the morning (22.4 mcg/dL) and at the evening (25.3 mcg/dL) and an increase of the 24 h-urinary free cortisol levels in two consecutive samples (754.8/748 µg/mL respectively) were found. The ACTH was suppressed ( $< 5$  pg/mL), DHEAS and Delta4-androstenedion were increased (7.36 µg/mL and 5.51 ng/mL) while

24 h-urinary metanephrines and normetanephrines and were normal. Hypokalaemia (3.2 mEq/L) and metabolic alkalosis were also found. A total-body TC scan revealed a right adrenal gland mass (11 × 9.5 × 8.5 cm on size) and many nodular focal lesions in the lung and liver suspected as replicating forms. A total body FDG-PET/CT scan showed an increased uptake of the tracer (SUVmax 29.5) in the right adrenal gland with lung and liver metastases. Despite a therapy with high doses of mitotane and metirapone 4 months after the initial observation the patient died for a cardio-circulatory arrest. Autopsy revealed a neuroendocrine tumour (NET) of the adrenal gland. The immune-histochemical study showed positive neoplasm staining for vimentin, synaptophysin and CD56 (all diffuse), NSE and Calretinin (focal). The proliferation marker Ki67 was positive in 30% of neoplastic cells.

**Conclusions:** A primitive NET of the adrenal gland is a rare and aggressive malignant neoplasm of the neuroendocrine system often diagnosed at an advanced stage. The combination of Cushing's syndrome is frequently found, but psychopathological symptoms are rare at the onset of a NET. Our case suggests not to consider as "depressed" and not to treat with antidepressant agents a hypertensive subject with an apparent RH without having ruled out an organic cause of psychiatric disease.

### ADRENAL VEIN SAMPLING—GUIDED ADRENALECTOMY. AN EFFECTIVE WAY TO RESOLVE DRUG-RESISTANT HYPERTENSION

Silvia Lerco<sup>1</sup>, Francesca Torresan<sup>2</sup>, Valeria Bisogni<sup>1</sup>, Giuseppe Maiolino<sup>1</sup>, Maurizio Cesari<sup>1</sup>, Giacomo Rossitto<sup>1</sup>, Rui Zhu<sup>1</sup>, Maurizio Iacobone<sup>2</sup>, Teresa Maria Seccia<sup>1</sup>, Gian Paolo Rossi<sup>1</sup>

<sup>1</sup>Clinica dell'Iperensione Arteriosa, DIMED, University of Padua, ITALY, <sup>2</sup>Endocrine Surgery Unit, Department of Surgery, Oncology and Gastroenterology, University of Padua, ITALY

**Introduction:** Drug resistant hypertension (RH) is characterised by a very high cardiovascular risk because of the presence of full-blown hypertension-mediated organ damage and it can be associated to a misdiagnosed Primary Aldosteronism (PA).

**Aim:** To examine if (i) adrenal vein sampling (AVS) is feasible in patients with RH and (ii) if AVS-guided adrenalectomy can resolve resistance to treatment.

**Methods:** Having a relatively large data set of hypertensive patients (total  $n = 1016$ ), we prospectively submitted them to AVS following the Endocrine Society Guidelines because they wished to achieve surgical cure of hypertension. Bilaterally selective AVS were held to denote lateralization of aldosteronism if the lateralization index was greater than 2.00.

**Results:** We identified a cohort of 25 patients (17 male and 8 female; mean age  $55.6 \pm 9.2$  years) with RH as defined by ESC/ESH 2018 Guidelines, with diagnosis of PA. AVS was bilaterally selective in all cases and showed clear-cut lateralization. 1 month after laparoscopic adrenalectomy serum potassium values raised from  $3.7 \pm 0.6$  mmol/L at baseline to  $4.6 \pm 0.4$  mmol/L at 1 month and to  $4.5 \pm 0.7$  mmol/L at 6 months after surgery. Systolic blood pressure (SBP) fell from  $162 \pm 25$  mmHg at baseline to  $129 \pm 8$  mmHg ( $P < 0.0001$ ) and diastolic BP (DBP) from  $98 \pm 15$  mmHg at baseline to  $82 \pm 6$  mmHg ( $P = 0.001$ ). 6 months after surgery SBP was  $133 \pm 14$  mmHg ( $P < 0.0001$ ) and diastolic BP  $84 \pm 9$  mmHg ( $P = 0.01$ ), notwithstanding the fall of number of drugs required achieving BP control (from  $3.7 \pm 1.0$  at baseline to  $1.3 \pm 1.3$  [ $P < 0.0001$ ] at 1 month and to  $1.2 \pm 1.0$  at 6 months after surgery [ $P < 0.0001$ ]). At 6 months of follow-up no one patient showed criteria for diagnosis of RH.

**Conclusions:** These results show that: (i) the AVS is feasible and can allow identification of lateralized aldosteronism even in patients with RH who, by definition, are on multiple antihypertensive drugs; (ii) AVS-guided adrenalectomy is a powerful tool to resolve drug-resistant hypertension.

### A NEW VAGAL STIMULATION TECHNIQUE TO ACTIVATE NEUROMODULATION OF SPLENIC IMMUNE RESPONSE: PHYSIOPATHOLOGICAL MECHANISMS IN EXPERIMENTAL MODELS OF HYPERTENSION

L. Carnevale<sup>1</sup>, M. Perrotta<sup>2</sup>, F. Pallante<sup>1</sup>, S. Fardella<sup>1</sup>, D. Carnevale<sup>1,2</sup>, G. Lembo<sup>1,2</sup>

<sup>1</sup>I.R.C.C.S. Neuromed, Pozzilli, Italy, <sup>2</sup>Università degli Studi di Roma La Sapienza, Roma, Italy

**Introduction:** Autonomic nervous system (ANS) and vagal tone regulation have a fundamental role in hypertension. Our group demonstrated that the ANS modulates the immune response involved in regulation of blood pressure (BP) in response to hypertensive stimuli as Angiotensin-II (AngII) or deoxycorticosterone acetate salt (DOCA), through a vagal efference modulating the splenic nerve.

**Methods:** In this work we set up a microneurographic method of peripheral nerves modulating the spleen: the splenic sympathetic nerve (splenic sympathetic nerve activity—SSNA) and the pre-ganglionic celiac vagus nerve (celiac vagus nerve activity—CVNA). Mice infused with AngII by subcutaneous osmotic pump and mice stimulated with DOCA-salt pellet (and matched controls) underwent surgical isolation of the splenic nerve or the celiac vagus nerve to record their activity.

**Results:** Both hypertensive stimuli resulted in an increase of SSNA and CVNA. At cellular level, the increase in vagal-splenic activity determined the recruitment of the co-stimulation process of T lymphocytes, necessary to raise BP. To determine how the nervous vagal-splenic coupling is established we exploited two different approaches. (1) Cut the celiac vagus nerve during SSNA in mice subjected to hypertensive stimuli. The results show that we obtain a significant reduction of SSNA and a subsequent inhibition of co-stimulation of T lymphocyte and their egression from the spleen to infiltrate target organs of hypertension. (2) Mimic the electric effect of hypertensive stimuli on the vagus nerve, in mice not subjected to AngII nor DOCA. By electrical stimulation of celiac vagus nerve we recorded a paired increase of SSNA, co-stimulation of lymphocyte T and their egression from the spleen.

**Conclusions:** We demonstrated that different hypertensive stimuli activate a stimulation pattern of the vagus nerve which recruits adaptive immunity through the splenic sympathetic activity.

### RESISTANT HYPERTENSION AND OBSTRUCTIVE SLEEP APNEA SYNDROME IN THERAPY WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

S. Lai<sup>1</sup>, M. Mordenti<sup>2</sup>, M. Mangiulli<sup>3</sup>, A. Galani<sup>4</sup>, V. Zingaretti<sup>5</sup>, A. Gigante<sup>5</sup>, R. Cianci<sup>5</sup>

<sup>1</sup>Department of Translational and Precision Medicine, Nephrology and Dialysis Unit, Sapienza University of Rome, Italy, <sup>2</sup>Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy, <sup>3</sup>Nephrology and Dialysis Unit, Sapienza University of Rome, Rome, Italy, <sup>4</sup>Department of Clinical and Experimental

**Introduction:** Resistant hypertension (RH) may be associated with obstructive sleep apnea (OSA), determining greater cardiovascular risk and an increased risk of progression to kidney disease.

**Aim:** To assess the effect of six months of continuous positive airway pressure (CPAP) treatment on blood pressure values, cardiovascular risk markers and exercise tolerance in patients with resistant hypertension and OSA.

**Methods:** 24 patients with RH and OSA were enrolled and 24-h ambulatory Blood Pressure (BP), intima media thickness (IMT), flow mediated dilatation (FMD), renal resistive index (RRI) and endurance cardiopulmonary exercise testing (CPET) were obtained before and after 6-month treatment.

**Results:** Our study showed a reduction in systolic BP, diastolic BP and mean arterial pressure (PAM) ( $p < 0.001$ ,  $p = 0.009$ ,  $p = 0.007$ ,  $p = 0.021$ ), an increase of excretion fraction ( $p = 0.035$ ) and a decrease in IMT and RRI after 6 months of CPAP therapy ( $p = 0.020$ ,  $p = 0.036$ ). We also found an improvement of all polysomnographic parameters (number of apnea/hypopnea per hour, Apnea Index, number of episodes of night-time hemoglobin desaturation (ODI) ( $p = 0.010$ ), an improvement in Epworth Sleepiness Scale ( $p = 0.03$ ), as well as an improvement in stress tolerance to CPET ( $p = 0.017$ ), after 6 months of CPAP therapy.

**Conclusions:** CPAP treatment for 6 months reduces BP and improvement cardiovascular risk in patients with RH and OSA. OSA can determine resistant hypertension, progression of renal disease and higher cardiovascular risk, so we suggest screening in patients with RH and a complete cardiovascular screening, considering the possible reversibility of some endothelial dysfunction and atherosclerotic markers after CPAP treatment. We also recommend the use of CPET, which is not yet widely used in clinical practice. Our study firstly showed a significant effect of ventilation treatment on exercise tolerance in this population.

## Cerebrovascular Diseases

### A FUNCTIONAL MRI (RESTING STATE FUNCTIONAL MRI RS-fMRI) HIGHLIGHTS ALTERED CONNECTIONS AND ALTERED FUNCTIONAL NETWORKS IN HYPERTENSIVE PATIENTS

L. Carnevale<sup>1,2</sup>, A. Maffei<sup>1,2</sup>, A. Landolfi<sup>1,2</sup>, G. Grillea<sup>1,2</sup>, D. Carnevale<sup>1,2</sup>, G. Lembo<sup>1,2</sup>

<sup>1</sup>I.R.C.C.S. Neuromed, Pozzilli, Italy, <sup>2</sup>Università degli Studi di Roma La Sapienza, Roma, Italy

**Introduction:** Hypertension is widely recognized as one of the main risk factors for the onset of vascular dementia and Alzheimer. To predict and hamper the onset of these pathologies it is fundamental the possibility to recognize the effects of the vascular risk factor on cognitive functions. By rs-fMRI it is possible to investigate the capability of the brain of modulating its basal activity, without executing any task, and analyze how a pathological condition like hypertension impacts on the cerebral functions.

**Methods:** Our study includes 37 subjects (18 normotensive vs 19 hypertensive) characterized for the structural connectivity with tractography in MRI (diffusion tensor imaging) and the cognitive profile with neuropsychological tests. Rs-fMRI analysis consists in the extraction of networks of functional connectivity, to evaluate cross-correlation of the signal between different cerebral areas. The network

obtained is analyzed to highlight differences between hypertensive patients and control subjects for correlation alterations and organization of the connectivity network.

**Results:** Hypertensive patients show altered connection between dorsal attention network (DAN) and sensorimotor network (SMN), between DAN and visual network, between DAN and frontoparietal network (FPN), while regions of the left hemisphere of FPN and salience network show alteration of network organization parameters, showing a reorganization of cerebral connectivity. Analysis of correlation between structural connectivity, cognitive tests and functional connectivity shows the modulation of different connections: superior longitudinal fasciculus fractional anisotropy and Montreal cognitive assessment (MoCA) score are correlated to different functional alterations, while execution of the Stroop test, which evaluates the emotional domain, modulates connection between Network Language and SMN.

**Conclusions:** our multimodal imaging data show how hypertension determines an alteration pattern of brain functional networks, correlated to cognitive dysfunction and to alteration of the structural connectivity.

### SERUM URIC ACID, INDEPENDENTLY OF ARTERIAL HYPERTENSION, PREDICTS NON-FATAL INCIDENT CEREBROVASCULAR EVENTS IN AN ITALIAN LARGE COHORT OF MEN AND WOMEN. SEARCH FOR A CUT-OFF VALUE

C. Borghi<sup>5</sup>, G. Desideri<sup>3</sup>, V. Tikhonoff<sup>2</sup>, M. Cirillo<sup>3</sup>, P. Cirillo<sup>3</sup>, C. Ferri<sup>3</sup>, F. Galletti<sup>3</sup>, G. Grassi<sup>3</sup>, G. Iaccarino<sup>3</sup>, S. Masi<sup>3</sup>, M.L. Muiesan<sup>3</sup>, P. Palatini<sup>3</sup>, G. Parati<sup>3</sup>, R. Pontremoli<sup>3</sup>, Marcello Rattazzi<sup>2</sup>, P. Verdecchia<sup>3</sup>, M. Volpe<sup>6</sup>, A. Ungar<sup>3</sup>, E. Casiglia<sup>1</sup>, A. Virdis<sup>4</sup>, on behalf of the Working Group on Uric Acid and Cardiovascular Risk of the Italian Society of Hypertension

<sup>1</sup>Studium Patavinum, Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>2</sup>Dipartimento di Medicina, Università di Padova, Padova, Italy, <sup>3</sup>Working Group on Uric Acid and Cardiovascular risk of the Italian Society of Hypertension, Bologna, Italy, <sup>4</sup>Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa, Italy, <sup>5</sup>Dipartimento di Scienze Mediche e Chirurgiche, Alma Mater Studiorum, Università di Bologna, Bologna, Italy, <sup>6</sup>Dipartimento di Medicina Clinica e Molecolare, Facoltà di Medicina, Università di Roma Sapienza, Roma, and IRCCS Neuromed, Pozzilli (IS), Italy

**Introduction:** Searching for a prognostic cut-off value of serum uric acid (SUA) for ischemic stroke in a large regional-based Italian cohort of men and women in the frame of the URRAH study (URic Acid Right for heArt Health).

**Methods:** The large database URRAH collects data from cohort epidemiological laboratories including subjects with at least one measure of SUA and a follow-up of ~ 20 years. Incident ischemic stroke was defined in 23,475 subjects on the basis of ICD10 codes and double-checked with general practitioners and hospital files. Multivariate Cox regression models having morbid and fatal stroke as dependent variables, adjusted for arterial hypertension (AH), age, sex, diabetes, hematocrit, LDL-cholesterol, smoking, chronic renal disease, and hematocrit, were preliminarily used to search for a predictive role of SUA as a continuous variable and stroke. Two prognostic cut-off values (one for morbid and one for fatal stroke), identified by means of receiver operating curves (ROC) and able to discriminate between subjects doomed to develop the event, were then used as independent predictors in further multivariate Cox models adjusted for the confounders listed above.

**Results:** In Cox analysis, SUA was a significant predictor of morbid stroke [odds ratio 1.499 (1.033–1.278),  $p < 0.01$ ], but not for fatal stroke, independently of AH. ROC showed that  $> 4.20$  mg/dl (95% CI 3.36–6.05, sensitivity 75.1, specificity 31.1,  $p < 0.003$ ) was a significant univariate cut-off of SUA for morbid stroke, and  $> 5.70$  mg/dl (CI  $> 4.40$  to  $> 6.77$ , sensitivity 42.67, specificity 71.15,  $p < 0.01$ ) at univariate cut-off for fatal stroke. Nevertheless, only the first one was accepted as a predictor in multivariate Cox analyses adjusted for the confounders listed above (hazard ratio 1.464, CI 1.019–2.103,  $p = 0.038$ ), while the second one was rejected ( $p = 0.2$ ).

**Conclusions:** after adjustment for AH, age, diabetes and renal disease, a prognostic cut-off value of SUA for morbid stroke ( $> 4.20$  mg/dl) does exist while fatal stroke cannot be predicted by SUA.

## Hormonal Mechanisms and Endocrine Hypertension

### WHEN MUSCLES DAMAGE PRESSURE

Chiara Grasselli, Angela Muoio, Elena Radighieri, Angelo Ghirarduzzi

*Hypertension Unit-Cardiovascular Medicine-Azienda Unità Sanitaria Locale di Reggio Emilia-IRCCS, Reggio Emilia, Italy*

**Introduction:** Exercising body muscles regularly with aerobic physical activity is recommended by the Guidelines to combat high blood pressure, but muscles are not always allies against hypertension.

**Clinical case:** GC, female, 45 years old, chronically mild hypertensive, was admitted after rheumatological examination due to suspected para-infectious myositis in recent auricular virosis. The Rheumatologist had been detecting myalgias in the lower limbs for a month and was performing normal autoimmunity and EMG which revealed mild myopathy without denervation. He proceeded with a muscle biopsy that detected atrophic fibers but no inflammatory infiltration. It concluded a likely self-limiting para-infectious myositis, but posed the suspicion of carnitine-palmitoyltransferase 2 deficiency, an hereditary disease of mitochondrial metabolism of long chain fatty acids, for which the patient carried out molecular analysis of the CPT2 gene at the Carlo Besta in Milan. However, routine examinations also showed persistent hypokalemia that required constant supplementation to be corrected, with improvement of myalgia and a marked reduction in myolysis indices. Hence, we also proceeded to investigate hypokalemia in hypertensive patient, highlighting high basal levels of plasmatic aldosterone concentration (PAC) with suppressed renin. PAC remained significantly elevated even after saline loading, configuring primary hyperaldosteronism with likely hypokalemic rhabdomyolysis at onset. Following tomographic evidence of a 2 cm nodule into the right adrenal gland. Adrenal venous sampling allowed to identify the consensual lateralization of aldosterone secretion, for which the patient was subjected to right VDL surrenectomy, with subsequent normalization of potassium and resolution of myalgia and asthenia.

**Conclusions:** Hyperaldosteronism is classified as a rare disease and, among primary aldosteronisms, those that begin with hypokalemic rhabdomyolysis are unusual. This case also underlines the importance of a multidisciplinary approach to the patient and the need for coordination of the team of Specialists by the Specialist in Internal Medicine.

## CHARACTERIZATION AND GENE EXPRESSION ANALYSIS OF SERUM-DERIVED EXTRACELLULAR VESICLES IN PRIMARY ALDOSTERONISM

Jacopo Burrello<sup>1</sup>, Chiara Gai<sup>2</sup>, Martina Tetti<sup>1</sup>, Tatiana Lopatina<sup>2</sup>, Maria Chiara Deregibus<sup>2</sup>, Franco Veglio<sup>1</sup>, Paolo Mulatero<sup>1</sup>, Giovanni Camussi<sup>2</sup>, Silvia Monticone<sup>1</sup>

*<sup>1</sup>Division of Internal Medicine 4 and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy, <sup>2</sup>Molecular Biotechnology Center, Department of Medical Sciences, University of Torino, Torino, Italy*

**Introduction:** Circulating extracellular vesicles (EVs) are nano-particles mainly released by inflammatory, platelet and endothelial cells and involved in inter-cellular communication; their characteristics reflect the activity of parental cells.

**Methods:** Patients with primary aldosteronism (PA) display an increased risk of cardiovascular events compared to essential hypertensives (EH). Endothelial dysfunction favours atherosclerosis and EVs could represent one of the mediators of vascular damage in these patients. The aim of this study was to characterize circulating EVs from patients diagnosed with PA and to explore their functional significance.

**Results:** Serum EVs were isolated from 12 patients with PA and 12 with EH, matched by sex, age and blood pressure, and compared with 8 NT controls. At nanoparticle tracking analysis, EVs concentration was 2.2 times higher in PA patients compared with EH and significantly correlated with serum aldosterone and potassium levels. FACS analysis demonstrated a higher absolute number of endothelial-derived EVs in PA, compared to both patients with EH and NT controls. Through EV mRNA profiling, 15 up-regulated and 4 down-regulated genes were identified in PA patients compared to EH; moreover, EDN1 was expressed only in patients with PA. Micro-array platform was validated by qRT-PCR on 4 genes (*CASP1*, *EDN1*, *F2R*, *HMOX1*) involved in apoptosis, inflammation and endothelial dysfunction. Following unilateral adrenalectomy, EVs number and expression of *CASP1* and *EDN1* significantly decreased in PA patients. Moreover, the incubation with PA-derived EVs reduced angiogenesis and induced apoptosis in vitro.

**Conclusions:** we characterized for the first time circulating EVs in patients with PA. EVs might not only represent a marker of endothelial dysfunction, but also contribute themselves to vascular dysfunction in PA patients.

## THE PRIMARY ALDOSTERONISM SURGICAL OUTCOME SCORE FOR THE PREDICTION OF CLINICAL OUTCOMES AFTER ADRENALECTOMY FOR UNILATERAL PRIMARY ALDOSTERONISM

Jacopo Burrello<sup>1</sup>, Alessio Burrello<sup>2</sup>, Michael Stowasser<sup>3</sup>, Tetsuo Nishikawa<sup>4</sup>, Marcus Quinkler<sup>5</sup>, Aleksander Prejbisz<sup>6</sup>, Jacques WM Lenders<sup>7,8</sup>, Fumitoshi Satoh<sup>9</sup>, Paolo Mulatero<sup>1</sup>, Martin Reincke<sup>10</sup>, Tracy Ann Williams<sup>1,10</sup>

*<sup>1</sup>Division of Internal Medicine and Hypertension, Department of Medical Sciences, University of Turin, Turin, Italy, <sup>2</sup>Department of Electronics and telecommunications, Polytechnic University of Turin, Turin, Italy, <sup>3</sup>Endocrine Hypertension Research Centre, University of Queensland Diamantina Institute, Greenslopes and Princess Alexandra Hospitals, Brisbane, QLD, Australia,*

<sup>4</sup>Endocrinology and Diabetes Center, Yokohama Rosai Hospital, Yokohama 222-0036, Japan, <sup>5</sup>Endocrinology in Charlottenburg, Berlin, Germany, <sup>6</sup>Department of Hypertension, Institute of Cardiology, Warsaw, Poland, <sup>7</sup>Department of Medicine III, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany, <sup>8</sup>Department of Medicine, Radboud University Medical Center, Nijmegen, The Netherlands, <sup>9</sup>Division of Clinical Hypertension, Endocrinology and Metabolism, Tohoku University Graduate School of Medicine, Sendai, Japan, <sup>10</sup>Medizinische Klinik und Poliklinik IV, Klinikum der Universität, Ludwig-Maximilians-Universität München, Munich, Germany

**Introduction:** Primary aldosteronism due to an aldosterone-producing adenoma (APA) is the most common surgically curable form of endocrine hypertension. Surgical resection of the dominant overactive adrenal results in a complete clinical success with resolution of hypertension without antihypertensive medication in less than half of patients with diagnosis of APA.

**Aim:** To develop a prediction model to discriminate patients for clinical outcomes after surgical unilateral adrenalectomy.

**Methods:** A linear discriminant analysis (LDA) model was built using data of 380 APA surgically-treated patients to classify post-surgical clinical outcomes. The cohort selected for analysis was randomly divided into training (280 patients) and test (100 patients) sub-groups to create and validate a score system to predict clinical outcomes. An online tool (PASO [primary aldosteronism surgical outcome] predictor) was developed to facilitate the use of the predictive score in clinical practice. Six variables were associated with a post-surgery complete clinical success: known duration of hypertension, sex, antihypertensive medication dosage, body mass index, target organ damage, and diameter of largest nodule at imaging.

**Results:** A 25-point predictive score was developed with an optimal cut-off of greater than 16 points (accuracy of prediction = 79.2%; specificity = 84.4%; sensitivity = 71.3%), with an area under the curve of 0.839.

**Conclusions:** This score and the PASO predictor can be used in a clinical setting to differentiate patients who are likely to be clinically cured after surgery from those who will need continuous surveillance after surgery due to persistent hypertension.

## THE EFFECT OF THYROID HORMONE NORMALIZATION ON ABPM IN HYPOTHYROID PATIENTS

N. Colapietro<sup>1</sup>, C. Xodo<sup>1</sup>, M. Rovina<sup>2</sup>, A. Da Rin<sup>1</sup>, F. Giudici<sup>1</sup>, S. Bernardi<sup>1</sup>, B. Fabris<sup>1</sup>

<sup>1</sup>Università degli studi di Trieste, Dipartimento di Scienze Mediche, Trieste, Italy, <sup>2</sup>Azienda Sanitaria Universitaria Integrata di Trieste, Trieste, Italy

**Introduction:** It is well known that thyroid hormones regulate cardiovascular function. Thyroid disease is extremely common with a prevalence of 9-15% in the general population.

**Aim:** To assess the effects of thyroid hormones on the changes of blood pressure and pulse wave in a cohort of hypothyroid patients.

**Methods:** A total of 22 patients with severe hypothyroidism, who were consecutively seen at the SS Endocrinologia ASUITS, were enrolled in this study. Follow-up data are available for 9 patients, after normalization of their thyroid hormone profile. At baseline and after normalization of thyroid hormone profile, patients underwent an ABPM and an arterial tonometry. Data were analysed with the statistical software R (version 3.0.3). In particular, patients were compared by Wilcoxon test for paired data, as they didn't have normal Gaussian distributions.

**Results:** Hypothyroid patients presented with overt thyroid disease (TSH  $54.15 \pm 16.72$ ). Our preliminary data show that after euthyroidism restoration (TSH  $3.75 \pm 1.58$ ), blood pressure variability was significantly reduced. In particular, this was observed for global diastolic variability, (p value < 0.01) as well as day (p value < 0.05) and night diastolic variability (p value < 0.05). We did not observe any difference in terms of mean arterial pressure, PWV, and the other pulse wave analysis parameters

**Conclusions:** Our preliminary data suggest that euthyroidism restoration with levothyroxine can significantly reduce blood pressure variability in hypothyroid patients. This confirms the importance of thyroid hormones for blood pressure control.

## RENAL DAMAGE IN PRIMARY ALDOSTERONISM: A SYSTEMATIC REVIEW AND META-ANALYSIS

Silvia Monticone<sup>1</sup>, Elisa Sconfienza<sup>1</sup>, Fabrizio D'Ascenzo<sup>2</sup>, Fabrizio Buffolo<sup>1</sup>, Fumitoshi Satoh<sup>3</sup>, Cristiana Catena<sup>4</sup>, Franco Veglio<sup>1</sup>, Paolo Mulatero<sup>1</sup>

<sup>1</sup>Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Torino, Torino, Italy, <sup>2</sup>Division of Cardiology, Department of Medical Sciences, University of Torino, Torino, Italy, <sup>3</sup>Division of Clinical Hypertension, Endocrinology and Metabolism, Tohoku University Graduate School of Medicine, Sendai, Japan, <sup>4</sup>Division of Internal Medicine, Department of Medicine, University of Udine, Udine, Italy

**Introduction:** In experimental animal models a significant association between exogenous aldosterone excess and the progression of renal disease has been observed. However, the evidence of an increased risk of renal damage in patients affected by primary aldosteronism (PA) remains controversial.

**Aim:** To assess the relationship between PA, renal target organ damage and its reversibility, by synthesizing available evidence from prospective and retrospective observational studies, through a meta-analysis.

**Methods:** We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials from January 1960 up to August 2017.

**Results:** Forty-four studies including 4,467 patients with PA and 8,234 patients with non-PA arterial hypertension were eligible for this meta-analysis. In 14 out of 44 studies, patients with different degree of renal impairment were excluded and for analysis purpose two subgroups have been generated (i.e. "renal disease excluded" and "renal disease not excluded"). After 8.5 years from the diagnosis of hypertension, while serum creatinine values did not differ between PA and non-PA hypertensive patients, the glomerular filtration rate (GFR) was significantly higher in the overall PA population (by 3.93 ml/min IQR [0.60; 7.26]). Of note, subgroup analysis indicated that the difference in GFR was significant only in those studies that included patients with renal disease (by 5.69 ml/min [1.15; 10.22]), while when considering the studies in which patients with renal disease were excluded, the mean GFR was not different between the two populations. Similarly, a more severe albuminuria (Std. mean difference 0.57 [0.11; 1.03]), resulting into a significant association with microalbuminuria (OR 2.15 [1.21; 3.84]) was observed in patients affected by PA. Following specific PA treatment, after a median follow-up of 12 months, a significant reduction in GFR was observed (by - 10.91 ml/min [- 13.61; - 8.21]) that was consistent in both surgically and medically treated patients. Consistently, a reduction in albumin excretion and an increase in serum creatinine were observed after specific treatment.

**Conclusions:** The results of the present meta-analysis further emphasize the importance of an early diagnosis of PA, since affected patients, compared with non-PA hypertensive patients, display a more pronounced renal organ damage, which can be at least partly reverted by the specific treatment.

### A RARE CASE OF PAROXYSMAL HYPERTENSION IN URINARY BLADDER PARAGANGLIOMA

Valeria Bisogni<sup>1</sup>, Monia Celi<sup>1</sup>, Federica Olmati<sup>1</sup>, Luigi Petramala<sup>1</sup>, Antonio Concistrè<sup>1</sup>, Gaia Oliviero<sup>1</sup>, Martina Mezzadri<sup>1</sup>, Maria Bonvicini<sup>1</sup>, Gino Iannucci<sup>1</sup>, Giorgio De Toma<sup>2</sup>, Antonio Cardi<sup>3</sup>, Claudio Letizia<sup>1</sup>

<sup>1</sup>Department of Translational and Precision Medicine, Unit of Secondary Arterial Hypertension, "Sapienza" University of Rome, Italy, <sup>2</sup>Surgery Department, "Pietro Valdoni" "Sapienza" University of Rome, Italy, <sup>3</sup>Department of Radiological Sciences, Oncology and Pathology "Sapienza" University of Rome, Italy

**Introduction:** Primary bladder paragangliomas (PGLs) are rare ectopic chromaffin-cells derived tumors. Clinical manifestations include micturition hypertension and/or palpitations, syncopes, hematuria, and frequent urinary tract infections. However, these symptoms, very often, are paroxysmal and non-diagnosed.

**Aim:** To focus the attention and better understanding this rare disease to prevent late diagnosis.

**Clinical case:** A young woman referred to our Unit for the first time when she was 17 years old, complaining, for about 4 years, for recurrent micturition episodes of throbbing frontal headache, associated to increased blood pressure (BP) values, palpitation, nausea, and flushing of legs. She had no family history for PGL. At the 24-h ambulatory blood pressure monitoring (ABPM) mean systolic and diastolic BP values were normal, but showed only paroxysms of blood pressure (BP) during micturition. We performed a screening for secondary hypertension without finding any pathological evidences. In particular, several measurements of 24-h urinary metanephrines were into the normal range. However, symptoms were very suggestive of PHEO, and the patient underwent to abdominal magnetic resonance (MR) that showed a thick-walled left adnexal mass (4.5 × 2 cm) abutting the urinary bladder, and confirmed by <sup>123</sup>I-MIBG scintigraphy as strongly uptaking mass. Laparotomic surgery was performed and the mass was removed without complications; the histologic exam confirmed diagnosis of bladder PGL. The genetic testing for SDH genes was negative for mutations. At 12-months of follow-up our patient is completely asymptomatic and her BP are well-controlled.

**Conclusions:** Our case showed that extra-adrenal PHEOs, often, are not associated with increased value of 24-h urinary metanephrines, especially when the over secretion is stimulated in particular situations, as in our case by bladder contraction. Thus, it is mandatory, whether clinical manifestations are suggestive, to perform further investigations in order to avoid late diagnosis.

### A RARE CASE OF PELVIC AND CAROTID PARAGANGLIOMA WITH PAROXYSMAL HYPERTENSION

F. Olmati<sup>1</sup>, V. Bisogni<sup>1,2</sup>, L. Petramala<sup>1</sup>, G. Oliviero<sup>1</sup>, M. Bonvicini<sup>1</sup>, M. Mezzadri<sup>1</sup>, A. Concistrè<sup>1</sup>, M. Celi<sup>1</sup>, V. Saracino<sup>1</sup>, G. Iannucci<sup>1</sup>, A. Ciardi<sup>4</sup>, G. De Toma<sup>3</sup>, C Letizia<sup>1</sup>

<sup>1</sup>Department of Clinical Sciences and Translational Medicine, Unit of Secondary Arterial Hypertension, "Sapienza" University of Rome, Italy, <sup>2</sup>UOSD Ipertensione-DIMED, University of Padua, Italy, <sup>3</sup>"Pietro Valdoni" Surgery Department, "Sapienza" University of Rome, Italy, <sup>4</sup>Department of Radiological Sciences, Oncology and Pathology, UOC Anatomia Patologica, "Sapienza" University of Rome, Italy

**Introduction:** Pheochromocytomas (PHEOs) and paragangliomas (PGLs) (together as PPGLs) are neuroendocrine tumors arising from chromaffin cells of adrenal medulla and paraganglia of the sympathetic and parasympathetic nervous system, respectively. PPGLs produce and secrete excess of catecholamines, leading to various symptoms including hypertension, headache, palpitations, and diaphoresis. Rare PPGLs have shown to be multiple and recurring after surgical treatment. Herein, we report a case of a woman with pelvic and carotid PPGLs associated to paroxysmal hypertension.

**Clinical case:** A 76-year-old woman referred to Our Center complaining of paroxysmal hypertension. She had no family history of PPGL. Hormonal screening test showed normal levels of 24-h urinary metanephrines. A computed tomography (CT) scan showed a mass of 52 mm diameter in the right pelvis. Strongest uptake of <sup>123</sup>I-Metaiodobenzylguanidine (<sup>123</sup>I-MIBG) deposited for a pelvic PGL. The patient underwent successful laparotomic surgery to remove the pelvic mass, without complications. Histologic examination confirmed PGL diagnosis. At 6-months follow-up the patient showed normalized levels of blood pressure with no medications. Although, during an ultrasonography evaluation of carotid arteries, an incidental oval mass of 20 mm of diameter, closed to right carotid siphon, was found and later confirmed by CT scan, as a tumor compatible with a carotid-PGL. Unfortunately, she refused surgical remove of this mass. The genetic testing of SDHx genes was negative for mutations.

**Conclusions:** It is important, in presence of PPGLs, to look for any other multiple lesions. Secondly, a genetic screening is mandatory to exclude hereditary syndromic PPGLs, in order to establish a proper treatment and follow-up.

### CLINICAL VALIDATION OF THE NEW AUTOMATED ALDOSTERONE LIAISON XL ASSAY ON THE ADRENAL VEIN SAMPLING CONFIRMATORY TEST

Gian Luca Salvagno<sup>1</sup>, Mariangela Veneri<sup>2</sup>, Giulia Sartori<sup>2</sup>, Elisa Danese<sup>1</sup>, Giuseppe Lippi<sup>1</sup>, Oliviero Olivieri<sup>2</sup>, Francesca Pizzolo<sup>2</sup>

<sup>1</sup>Section of Clinical Biochemistry, Department of Neurological, Biomedical and Movement Sciences, University of Verona, Verona, Italy, <sup>2</sup>Section of Internal Medicine, Department of Medicine, University of Verona, Italy

**Introduction:** Measurement of aldosterone is the cornerstone in Primary aldosteronism (PA) workup, for both screening and final diagnosis (as confirmatory test). Albeit several automated aldosterone chemiluminescent assays have become recently available as reliable alternatives to the well-established radioimmunometric methods

(RIA), little information is available on the diagnostic performance of the former methods using samples collected by adrenal vein sampling (AVS). AVS for aldosterone measurement is still considered the 'gold standard' procedure to differentiate aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA).

**Aim:** To assess the clinical utility of the new Aldosterone Liaison XL assay for AVS sampling compared with a traditional RIA method.

**Methods:** The study population consisted of 13 patients (11 males and 2 females) undergoing AVS. Aldosterone was measured with RIA (DSL800, Beckman coulter), and Liaison XL (Diasorin). Samples were taken step by step from both adrenal veins, and the superior and inferior vena cava (upper and below renal vein).

**Results:** Results of serum samples ( $n = 46$ ) were analysed. The median values (2.5–97.5 percentiles) for RIA and Liaison XL were 289 ng/mL (58–48550 pg/mL) and 203 ng/mL (64–39689 pg/mL), respectively. The nonparametric regression of Passing and Bablok and the Spearman's correlation showed excellent performance for Liaison XL Aldosterone compared to RIA (Liaison XL =  $0.44 \times$  RIA + 43.5;  $r = 0.97$ ,  $p < 0.001$ ). In all patients the lateralization ratio with RIA were confirmed with Liaison XL method. (7 patients had IHA; APA were 3 right and 3 left, respectively).

**Conclusions:** The rate of lateralization at AVS is identical when either RIA or LIAISON XL are used for aldosterone determination. We therefore conclude that the new Liaison XL Aldosterone is a suitable assay for the rapid quantification for the AVS procedure.

## ANGIOTENSIN II TYPE 1 RECEPTOR AUTOANTIBODIES: CAUSE OR CONSEQUENCE OF HUMAN PRIMARY ALDOSTERONISM?

M. Piazza<sup>1</sup>, T.M. Seccia<sup>1</sup>, B. Caroccia<sup>1</sup>, G. Rossitto<sup>2</sup>, G.P. Rossi<sup>1</sup>

<sup>1</sup>Department of Medicine-DIMED, University of Padua, Italy,

<sup>2</sup>University of Glasgow, UK

**Introduction:** In 2013 using an in-house made ELISA kit we found circulating autoantibodies to the Angiotensin II type 1 receptor (AT1AA) in patients with primary aldosteronism (PA), a finding thereafter confirmed by other groups. However, whether this AT1AA have a pathogenetic role remained unclear.

**Aim:** To investigate if the raised AT1AA titer in APA can be normalized by adrenalectomy and their biological role can be detected in vitro.

**Methods:** We measured serum AT1AA titer in 27 APA patients and its changes after adrenalectomy with commercially available ELISA kits. We next evaluated AT1AA bioactivity by using AT1R-transfected Chinese hamster ovary (CHO) and HAC15 cells. Aldosterone biosynthesis in adrenocortical cells stimulated with IgG was estimated by measuring aldosterone synthase (CYP11B2) mRNA with qRT-PCR.

**Results:** Two commercially available kits yielded higher levels in APA patients than in healthy subjects, which remained elevated at follow-up after cure of PA by adrenalectomy. HAC15 cells stimulation with IgG purified from sera of APA patients increased CYP11B2 gene expression (+ 40% vs healthy subjects); at variance, no detectable response to AT1AA was seen in CHO cells expressing AT1-R.

**Conclusions:** These findings support the contention that: (1) the raised AT1AA titer is not a consequence of hyperaldosteronism as it did not normalize after its cure; (2) AT1AA act as weak agonists stimulating aldosterone biosynthesis in hyperaldosteronism, but this can be identified only by using a sensitive in vitro technique.

## Blood Pressure Measurement

### LOOKING FOR THE APPROPRIATE SHAPE OF CUFFS TO OBTAIN ACCURATE BLOOD PRESSURE MEASUREMENTS IN OBESE SUBJECTS WITH LARGE ARMS

F. Saladini, C. Fania, F. Gasparotti, E. Benetti, P. Palatini

Università degli Studi di Padova, Dipartimento di Medicina, Padova, ITALY

**Introduction:** Published evidence has shown that tronco-conical cuffs are more suitable to correctly measure blood pressure (BP) in obese subjects because cylindrical cuffs overestimate true BP.

**Aim:** Due to the lack of published data regarding the exact shape of these tronco-conical cuffs, we investigated the anthropometric characteristics of the arm in a large ambulatory population.

**Methods:** We considered the upper arm either as a single tronco-conical shape or as the sum of two tronco-conical shapes, with bases at the proximal and middle arm circumference, respectively. Then we calculate the slant angles and the anthropometric characteristics of the arm in 777 adults, mean age  $55.0 \pm 16.9$  years, 49.9% males, mean BMI  $30.1 \pm 9.7$  kg/m<sup>2</sup>.

**Results:** The conical shape of the arm progressively increased with increasing arm circumference ( $r = 0.62$ ,  $p < 0.0001$ ). In the subjects with circumference  $\geq 42$  cm ( $N = 107$ ) the upper arm slant angle was  $85.0 \pm 1.4^\circ$ . In a multivariate analysis, independent predictors of the conical shape of the arm were arm circumference ( $p < 0.0001$ ) and length (negative relationship,  $p < 0.0001$ ), and BMI ( $p < 0.0001$ ). In the whole group, the arm upper angle and middle angle were similar ( $86.5^\circ$  for both). However, the difference between the two angles was related to the arm circumference ( $r = 0.41$ ,  $p < 0.0001$ ). In the subjects with a circumference  $\geq 42$  cm the average difference was  $> 2.0^\circ$  ( $86.1^\circ$  and  $83.9^\circ$ , respectively, for upper and middle angle), attesting a more pronounced tronco-conical shape of the lower half of the arm compared to the upper half. This shape was more frequent among the obese women, in whom the between-angle discrepancy was greater than in men ( $2.7 \pm 3.4^\circ$  versus  $1.4 \pm 2.8^\circ$ , age-adjusted  $p = 0.039$ ).

**Conclusions:** A tronco-conical cuff with an  $85^\circ$  slant angle should be used for BP measurement in subjects with extra-large arms. In addition, to properly fit the upper arm, the cuff should have a more pronounced tronco-conical shape in the lower half, especially for obese women.

### ROLE OF NON-MIDRIATIC DIGITAL RETINOGRAPHY IN THE EVALUATION OF HYPERTENSION MEDIATED ORGAN DAMAGE

M. Pierro<sup>1</sup>, A. Villarini<sup>1,2</sup>, A. Ratti<sup>1</sup>, N. Bitto<sup>1</sup>, M. Somaini<sup>1,2</sup>, R. Meazza<sup>1</sup>

<sup>1</sup>Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy, <sup>2</sup>Fondazione IRCCS-Istituto Nazionale dei Tumori, Milano, Italy

**Introduction:** to investigate the relationship between hypertensive retinopathy and the presence of Hypertension Mediated Organ Damage (HMOD), clarifying the potential role of retinopathy in cardiovascular risk stratification.

**Methods:** We evaluated 120 patients diagnosed with essential hypertension taking therapy. We studied the retinal microcirculation

using non-mydriatic digital retinography: through a dedicated software we calculated the AVR (arteriole: venule ratio), marker of retinal arteriolar narrowing, and classified the eventual presence of hypertensive retinopathy according to the Wong McIntosh classification of 2005. Patients were divided in two groups due to the presence or absence of hypertensive retinopathy. For each patient, medical history, Home Blood Pressure Monitoring (HBPM) and Ambulatory Blood Pressure Monitoring (ABPM) were collected. Blood chemistry tests were performed for the evaluation of the lipid and glucidic profile as well as the ultrasound examinations for the assessment of cardiac and carotid damage.

**Results:** Data analysis showed that patients with retinopathy (classified as mild in all of them) had average Systolic Blood Pressure higher compared to subjects without retinopathy (Table 2). In addition, we observed a significant increase in the risk of hypertensive retinopathy in patients with pathological ABPM. We found evidence of a direct correlation between left ventricular hypertrophy and presence of hypertensive retinopathy with a Spearman's Rho of 0.22 and a P value of 0.02. There was no statistically significant difference between levels of cholesterolemia, glycaemia or creatininemia in the two groups studied.

	All patients		P value
	Retinopathy (–)	Retinopatia (+)	
SBP (mmHg)	128.1 (± 9.1)	134.9 (± 12)	0.0036
DBP (mmHg)	78.1 (± 7.1)	79.7 (± 8.6)	0.3293
ABPM normal (%)	64.3	32.5	0.047
ABPM pathological (%)	35.7	67.5	

**Conclusions:** our data confirm the usefulness of non-mydriatic digital retinography in the clinical routine of hypertensive patients for the diagnosis of hypertensive retinopathy as an early marker of cardiac HMOD and poor blood pressure control. Therefore it is desirable to reassess hypertensive retinopathy in cardiovascular risk stratification.

## OFFICE, HOME AND AMBULATORY BLOOD PRESSURE LONG-TERM CHANGES IN THE GENERAL POPULATION: DATA FROM THE 3<sup>rd</sup> UPDATED 26 YEARS FOLLOW-UP OF THE PAMELA STUDY

R. Dell'Oro<sup>1</sup>, M. Bombelli<sup>1</sup>, F. Quarti<sup>1</sup>, R. Giovannini<sup>1</sup>, E. Marchesi<sup>2</sup>, R. Facchetti<sup>2</sup>, A. Vicini<sup>1</sup>, G. Mancina<sup>2</sup>, G. Grassi<sup>1</sup>

<sup>1</sup>Clinica Medica, Università Milano-icocca, Milan, Italy, <sup>2</sup>University of Milano-Bicocca, Milan, Italy

**Introduction:** The PAMELA is an epidemiological study performed on a large general population sample in which office, home and 24 h ambulatory blood pressure (BP) measurements were done. Measurements were made at baseline, after 11 years, and repeated in a 3rd new survey 26 years later.

**Methods:** A sample of 3200 subjects was randomly selected to be representative of the general population of Monza (North Italy) aged 25–74 years, stratified by gender and age. Each subject underwent a medical visit during which body mass index (BMI), office (mean of 3 sphygmomanometric values), home (mean of 2 values, semiautomatic oscillometric validated device) and 24 h (validated oscillometric device, set to obtain automatic BP measurements every 20 min) systolic (S) and diastolic (D) BP measurements were obtained.

Measurements also included heart rate (HR) and biochemical variables. All values were obtained at baseline (1st survey, 1990–91), 11 years later (2nd survey, 2001–02) and after further 15 years (3rd survey, 2016–17).

**Results:** 562 subjects (279/283 males/females, mean age ± SD 41.0 ± 10 yrs) participated at all the 3 surveys. Baseline average office, home and 24 h SBP/DBP were 122/81 ± 14/9, 116/73 ± 15/10, 116/73 ± 9/7 mmHg respectively and increased of 5/1 ± 14/9, 4/1 ± 14/9 and 4/2 ± 10/7 mmHg in office, home and 24 h SBP/DBP respectively at the 2nd survey. At the 3rd survey a further increase amounting to 11/2 ± 7/11, 8/3 ± 16/10 and 13/2 ± 15/9 mmHg was observed in office, home and 24 h BP respectively. The baseline-3rd survey office, home and 24 h SBP difference was unrelated to age, while the DBP increase inversely related to this variable ( $r = -0.32$ ,  $-0.39$  and  $-0.38$ , respectively,  $P < 0.0001$  for all). The baseline-3rd survey increase in office, home and 24 h DBP was significantly directly related to the concomitant BMI increase ( $r = 0.23$ ,  $0.17$  and  $0.14$ , respectively,  $P < 0.005$  for all). Office and home HR was similar in the 3 surveys while a reduction in 24 h HR was detected between the 1st and 3rd survey ( $-4.0 \pm 8.2$  b/min). At baseline the number of hypertensive subjects (including those treated) was 22.2% (office BP), 19.3% (home BP) and 20.7% (24 h BP), and increased to 37.7%, 33.8% and 43.5% at the 2nd survey and to 68.7%, 65.8% and 80.8% at the 3rd survey respectively.

**Conclusions:** The PAMELA 26-year follow-up represents the longest survey ever done describing the long-term changes of different types of BP measurements in the general population. The survey shows a long-term increase in office, home and 24 h BP which appears to be mainly related to the parallel BMI elevation and only partially accompanied by HR changes. There was concomitantly an increase in the prevalence of hypertension, particularly pronounced when defined on the basis of 24 h measurements.

## RELATIONSHIP BETWEEN BLOOD PRESSURE VALUES AND CHOROIDAL THICKNESSES IN HYPERTENSIVE PATIENTS

G. Mule', M. Vadala', G. Guarrasi, G. Geraci, K. Montalbano, L. Calandra, C. Carollo, E. Mancina, S. Cillino, S. Cottone

ESH Hypertension Excellence Centre and Nephrology Unit of the University of Palermo, Palermo, Italy

**Introduction:** The choroid is a pure vascular structure and its thinning may reflect a microvascular damage, that may be the local expression of a more generalised vascular injury. Per unit weight, it has the highest blood flow of any tissue in the body. At variance with the retina, the choroidal bed lacks an auto-regulatory mechanism for blood flow. Therefore, it may be more easily damaged directly by acute and chronic severe elevation of blood pressure (BP). However, the studies exploring the association of BP values with choroidal thickness yielded conflicting results

**Aim:** Our study was aimed to assess in hypertensive patients the relationships between choroidal thickness and "office" and 24-h BP readings.

**Methods:** We enrolled 158 hypertensive subjects (age:  $48 \pm 13$  years) recruited from those consecutively attending our Hypertension Centre. All the patients underwent clinic BP measurements, 24-h ambulatory BP monitoring (ABPM) and morphological evaluation of the retino-choroidal district by Swept-Source Optical Coherence Tomography (SS-OCT). The retinal and choroidal thicknesses were automatically calculated by the OCT mapping software. OCT measurements were performed according to the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol. The ETDRS map

divides the macula into 9 subfields. The circular grid is centered over the fovea and consists of 3 concentric rings of diameters 1, 3, and 6 mm, respectively. The inner and outer rings are further divided into quadrants: temporal, nasal, superior, and inferior to be included on the study, patients were required to have an estimated glomerular filtration rate (eGFR) of less than 30 mL/min, no intake of alkali within the previous 30 days, and the absence of pulmonary diseases and other clinical conditions at the time of the study that could explain an acute imbalance of the acid–base status, such as heart failure, hemorrhage, or sepsis. The study population was divided into two groups on the basis of the presence ( $n = 73$ ) or the absence of type 2 diabetes ( $n = 70$ ). Arterial blood samples were drawn in all the subjects and analyzed by the Radiometer ABL-800 FLEX blood-gas analyser.

**Results:** Age, sex distribution, serum creatinine, eGFR and proteinuria were not different in the two groups. Blood pH [7.406 (7.35–7.43) vs 7.384 (7.32–7.41),  $p = 0.02$ ], bicarbonate levels [22 (19.1–23.7) vs 20.5 (17.4–23.1);  $p = 0.05$ ] were higher and the prevalence of metabolic alkalosis (16.8 vs 8.4%) was greater in diabetic patients as compared to non diabetic ones. The positive associations between diabetes and pH values (beta: 0.186;  $p = 0.02$ ) and that between diabetes and metabolic alkalosis (odds ratio 2.68;  $p < 0.05$ ), were confirmed respectively in linear multiple regression analyses and in logistic multivariate models even after adjustment for potential confounding factors.

**Conclusions:** Our results, in agreement with those obtained in a previous study (Caracava et al., *Am J Kidney Dis* 1999) on the same issue, seem to suggest that metabolic alkalosis is more common than metabolic acidosis in diabetic patients with severe CKD. Further studies are needed in order to provide the pathophysiological explanations of these findings

## RELATIONSHIPS BETWEEN SHORT-TERM BLOOD PRESSURE VARIABILITY AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN HYPERTENSIVE PATIENTS

G. Mule<sup>1</sup>, E. Nardi, A. Di Maggio, G. Geraci, A. Sorge, E. Mancina, L. Calandra, M. Giambone, V. Imbrogio, S. Cottone

*ESH Hypertension Excellence Centre and Nephrology Unit- Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties-University of Palermo, Palermo, Italy*

**Introduction:** Although an accurate assessment of fast blood pressure (BP) fluctuations occurring within the 24 h, ideally requires continuous beat-to-beat recording, its assessment is also possible through non-invasive, intermittent 24 h ambulatory BP monitoring (ABPM). Short-term BP variability (SBPV) seems to be relevant to the pathophysiology of target organ damage and to the incidence of clinical events. However little is known about the association of SBPV with diastolic dysfunction.

**Aim:** To assess in hypertensive patients the relationships between some echocardiographic indices of DD and SBPV.

**Methods:** We enrolled 289 hypertensive subjects (age:  $54 \pm 16$  years) recruited from those consecutively attending our Hypertension Centre. All the patients underwent: a 24-h ambulatory BP monitoring (ABPM) and an echocardiogram. We calculated the following indices of SBPV: standard deviation and average real variability (ARV) of diurnal and nocturnal systolic (SBP) and diastolic BP (DBP), 24 h weighted SD and ARV of SBP and DBP. Diastolic function was assessed by measuring from the mitral inflow profile, the E-wave (E) and A-wave (A) peak velocities, E/A ratio and E-deceleration time. Isovolumic relaxation time was calculated

between aortic valve closure and the start of E-wave. Tissue Doppler imaging of the mitral annulus was obtained placing the sample volume in the lateral mitral valve annulus to evaluate: systolic peak velocity (Sm), early (Em) and late (Am) diastolic myocardial velocities. The E/em ratio was also calculated.

**Results:** All the indices of systolic SBPV examined showed significant correlations with A-wave and with Em ( $p < 0.01$ ). The correlations with the greatest strength were those between Em and ARV of 24 h SBP ( $r = -0.273$ ;  $p < 0.001$ ) and between Em and weighted SD of 24 h SBP ( $r = -0.307$ ;  $p < 0.001$ ). These associations held even after adjustment in multiple regression models for confounding factors, such as age, sex, average 24 h systolic BP and heart rate ( $p < 0.01$ ).

**Conclusions:** Our findings, showing an independent association between SBPV and some indices of diastolic dysfunction able to predict the development of heart failure, corroborate the concept that an increased short-term systolic BP variability may not be an innocuous phenomenon.

## STATIN THERAPY AND 24-HOUR BLOOD PRESSURE IN HYPERTENSIVE PATIENTS: A PROPENSITY SCORE ANALYSIS

Andrea Filippini<sup>1,2</sup>, Francesco Spannella<sup>1,2</sup>, Federico Giulietti<sup>1,2</sup>, Chiara Di Pentima<sup>1,2</sup>, Riccardo Sarzani<sup>1,2</sup>

*<sup>1</sup>Internal Medicine and Geriatrics, “Hypertension Excellence Centre” of the European Society of Hypertension, and LIPIGEN Centre, IRCCS-INRCA, Ancona, Italy; <sup>2</sup>Department of Clinical and Molecular Sciences, University “Politecnica delle Marche”, Ancona, Italy*

**Introduction:** Arterial hypertension and dyslipidemia often coexist and statins are fundamental in cardiovascular prevention. Statin therapy was associated with lower blood pressure (BP) values in previous studies.

**Aim:** To evaluate the association between statin therapy and 24-h BP in a large hypertensive population.

**Methods:** Retrospective observational study on 1827 consecutive outpatients referred to our Hypertension Centre for essential hypertension. All patients performed a 24-h ambulatory BP monitoring (ABPM). Anti-hypertensive treatment intensity score (TIS) was calculated to compare different drug associations. We used a “propensity score matching” to compare two equally-sized cohorts of patients with similar characteristics according to statin therapy. Matching was performed on log-transformed propensity score in a 1:1 fashion with a caliper of 0.1, in order to account for the different baseline characteristics between statins and non-statins groups. The variables included in the score were the following: age, sex, smoke, body mass index, estimated glomerular filtration rate, diabetes mellitus, TIS, mean 24 h pulse pressure.

**Results:** Mean age:  $58.1 \pm 13.8$  years; male sex: 55%. Patients on statin therapy: 402 (22%). These patients showed lower 24-h BP ( $-2.8/-7.0$  mmHg), daytime ( $-3.3/-7.5$  mmHg) and nighttime BP ( $-2.5/-6.0$  mmHg, all  $p < 0.001$ ). They also showed better BP control, even after adjustment for confounding factors. The analyses on the groups derived from the “propensity score matching” (228 patients in each group) confirmed these results (OR = 2.2 for 24-h BP control; OR = 1.9 for daytime BP control; OR = 1.9 for nighttime BP control, all  $p < 0.001$ ).

**Conclusions:** Statin therapy is associated with lower ABPM values in hypertensive patients. This result is not affected by the anti-hypertensive treatment intensity or by the several cofactors analyzed, but may depend on greater adherence to prescribed drug therapies. The

cardiovascular benefit of statins is mainly due to the reduction of blood cholesterol, but these drugs could also help in reducing BP in hypertensive patients.

## EVALUATION OF A SCREENING PROGRAM FOR ARTERIAL HYPERTENSION IN COMMUNITY PHARMACIES OF PIEDMONT, LIGURIA AND AOSTA VALLEY

S. Di Monaco<sup>1</sup>, L. Ravetto Enri<sup>2</sup>, M. Pappaccogli<sup>1</sup>, E. Fanelli<sup>1</sup>, C. Fasano<sup>1</sup>, I. Pignata<sup>2</sup>, F. Baratta<sup>2</sup>, F. Rabbia<sup>1</sup>, M. Mana<sup>3</sup>, F. Veglio<sup>1</sup>, P. Brusa<sup>2</sup>

<sup>1</sup>Division of Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy, <sup>2</sup>Department of Pharmaceutical Sciences and Technologies, University of Turin, Turin, Italy, <sup>3</sup>Federfarma Piemonte, Turin, Italy

**Introduction:** Arterial hypertension is a cardio-cerebrovascular risk factor. The diagnosis requires a correct and repeated measurement of blood pressure (BP). European guidelines recommend the promotion of BP measurement by increasing the role of pharmacists in the follow-up of hypertensive patients.

**Aim:** To evaluate the outcome of a screening for hypertension in the pharmacies of Piedmont, Liguria and Aosta Valley.

**Methods:** On 17/05/2017, 2731 subjects in 94 local pharmacies voluntarily joined the study. A questionnaire was administered for medical history and 3 blood pressure measurements were performed using the same Omron HEM 1040-E device.

**Results:** The screened population is mainly composed of women (58%) with an average age of  $58 \pm 16$  years. 41% of subjects declared themselves as treated hypertensive, 6% not-treated hypertensive, 41% normotensive and 12% said they did not know their BP status. The mean measured BP values were  $130 \pm 18$  mmHg for the SBP and  $79 \pm 10$  mmHg for the DBP. Considering 140/90 mmHg as the reference threshold for the diagnosis of arterial hypertension, 10% of the subjects who declared themselves normotensive and 35% of the patients not aware of their blood pressure were hypertensive. While, considering 130/80 mmHg as a BP threshold for hypertensive patients, 76% of the treated hypertensives and 86% of the non-treated hypertensives were not controlled.

**Conclusions:** The results of our study showed the significant number of unknown diagnoses of hypertension and the poor BP control of hypertensive patients. Pharmacies, thanks to the widespread diffusion in the territory, allow to reach a large portion of the population. However, the measurement methods in pharmacy are not yet standardized and neither the pressure cut-offs are defined.

## INVASIVE ASSESSMENT OF PULSE PRESSURE AMPLIFICATION AND ITS RELATIONSHIP WITH HEART RATE

G. Pucci<sup>1</sup>, F. Battista<sup>2</sup>, S. Notaristefano<sup>3</sup>, C. Cavallini<sup>3</sup>, G. Vaudo<sup>1</sup>

<sup>1</sup>Department of Medicine, University of Perugia-Unit of Internal Medicine, Terni University Hospital, Terni, Italy, <sup>2</sup>Sport and Exercise Medicine Division, Department of Medicine, University of Padova, Padova, Italy, <sup>3</sup>Unit of Cardiology, Perugia University Hospital, Perugia, ITALY

**Introduction:** The physiological meaning of the heart rate (HR) dependence of pulse pressure amplification (PPA) is still a matter of

controversy. Moreover, there is lack of data exploring such phenomenon invasively.

**Aim:** We aimed at investigating the relationship between invasive aortic-to-brachial PPA and HR in subjects undergoing cardiac catheterization.

**Methods:** 29 patients were evaluated during cardiac catheterization (radial approach). Exclusion criteria were: history of peripheral arterial disease, aortic aneurysm, absent pulses or known obstructive large artery atherosclerotic disease, active malignancy, hypotension (SBP < 90 mmHg), valvular heart disease, left ventricular dysfunction (EF < 50%) or arrhythmias. Intra-arterial ascending aortic BP was recorded and then the catheter was pulled back to the brachial artery site (using a pre-defined length) in about 5–10 s. A fluid-filled catheter was used for all hemodynamic recordings (ACIST medical systems, Eden Prairie, MN, USA). Invasive MAP was calculated by the integral of pressure waveform. Form factor (FF) was expressed as (MAP-DBP/PP).

**Results:** mean invasive brachial and aortic BPs were  $149/67 \pm 19/10$  mmHg and  $141/71 \pm 18/10$  mmHg, respectively. Mean PPA was  $1.18 \pm 0.19$ , mean HR  $68 \pm 10$  bpm; brachial and aortic FFs were  $0.37 \pm 0.06$  and  $0.41 \pm 0.04$ , respectively. The relationship between HR and PPA did not reach statistical significance (Pearson's  $R = 0.34$ ,  $p = 0.08$ ) in this cohort. In a multivariate linear regression model, HR (+ 7% each 10 bpm increase,  $p = 0.01$ ) and log-transformed age ( $p < 0.01$ ) were significant predictors of PPA. HR was positively associated with aortic FF ( $R = 0.56$ ,  $p = 0.01$ ), but not with brachial FF ( $R = 0.05$ ,  $p = n.s.$ ).

**Conclusions:** we found that HR is a significant predictor of invasively measured PPA. The aortic waveform shape is closely associated with HR, thus reflecting higher sensitivity to HR variations (less peaked aortic waveform shape at increasing heart rate) than brachial waveform shape. Our preliminary invasive results are in line with studies performed non-invasively, and needs to be confirmed in large scale datasets.

## EFFECTS OF ANTIHYPERTENSIVE DRUG CLASSES ON 24-HOUR PULSE PRESSURE AMPLIFICATION

G. Pucci<sup>1</sup>, M. Maggi<sup>1</sup>, B. Hametner<sup>2</sup>, S. Wassertheurer<sup>2</sup>, A. Cerasari<sup>1</sup>, G. Vaudo<sup>1</sup>

<sup>1</sup>Department of Medicine, University of Perugia-Unit of Internal Medicine, Terni University Hospital, Terni, Italy, <sup>2</sup>Center Health and Bioresources, AIT Austrian Institute of Technology-Biomedical Systems, Vienna, Austria

**Introduction:** Anti-hypertensive drug classes may have differential effects on central (cBP) and peripheral (pBP) office BP, and consequently on their relationship, namely pressure amplification (PPA).

**Aim:** We aimed at assessing the effect of anti-hypertensive treatment on PPA evaluated over the 24-h period.

**Methods:** 281 treated hypertensives ( $59 \pm 14$  years, 58% men) underwent ambulatory 24-h cBP and pBP monitoring (ABPM) using the Mobil-o-Graph, a validated oscillometric brachial cuff-based sphygmomanometer which determines cBP from brachial oscillometric pressure waveforms by applying a proprietary generalized transfer function. PPA was calculated as pPP/cPP. Patients with history of severe valvulopathy and LV dysfunction, arrhythmias, peripheral obstructive atherosclerotic disease, or low-quality ABPMs (n. of readings < 70% total) were excluded. Daytime and night-time intervals were calculated after removing intermediate shift hours, as 06.00–09.00 and 20.00–22.00 am respectively.

**Results:** 31% of patients were treated with monotherapy, 36% with  $\geq 3$  drugs. 84% of patients were treated with ACE/ARBs. Mean 24-h PPA was  $1.26 \pm 0.07$ , mean daytime PPA (dPPA) was  $1.31 \pm 0.09$ , mean night-time PPA (nPPA) was  $1.22 \pm 0.07$ . Mean 24-h pBP was  $128/78 \pm 14/9$  mmHg. In pairwise comparisons, subjects treated vs untreated with ACE/ARBs ( $60 \pm 14$  years vs  $54 \pm 15$  years,  $p = 0.01$ ), and with diuretics ( $63 \pm 13$  years vs  $58 \pm 14$  years,  $p < 0.01$ ) were older. Subjects treated with calcium-channel blockers (CCBs) were more frequently males (67% vs 50%,  $p < 0.01$ ), whereas individuals treated with  $\beta$ -blockers were more females (46% vs 66%,  $p < 0.01$ ), shorter (166 cm vs 170 cm,  $p < 0.01$ ), and with significantly lower heart rate (HR  $69 \pm 9$  bpm vs  $71 \pm 8$  bpm,  $p < 0.01$ ). In unadjusted comparisons,  $\beta$ -blockers were associated with lower 24-h PPA (1.24 vs 1.26,  $p = 0.04$ ) and dPPA (1.29 vs 1.32,  $p < 0.01$ ), whereas CCBs were associated with higher 24-h PPA (1.27 vs 1.25,  $p < 0.01$ ). After adjustment for age, sex and height,  $\beta$ -blockers were only associated with lower dPPA ( $p = 0.02$ ); such association, however, disappeared after further adjustment for HR ( $p = 0.49$ ).

**Conclusions:** With the exception of  $\beta$ -blockers, all the anti-hypertensive drug classes have similar impact on 24-h PPA. The use of  $\beta$ -blockers is associated with reduced dPPA, which is mainly explained by the associated HR-lowering effect, but not with reduced nPPA.  $\beta$ -blockers may be responsible for an increased central hemodynamic load during daytime.

## ASSOCIATION BETWEEN BLOOD PRESSURE VARIABILITY, CARDIOVASCULAR DISEASE AND MORTALITY IN TYPE 2 DIABETES: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Chiriaco<sup>1</sup>, A. Virdis<sup>1</sup>, E. Duranti<sup>1</sup>, M. Emdin<sup>2</sup>, S. Taddei<sup>1</sup>, S. Masi<sup>1</sup>  
<sup>1</sup>Department of Clinical and Experimental Medicine, Università degli Studi di Pisa, Italy, <sup>2</sup>Sant'Anna School of Advanced Studies, Pisa, Italy

**Introduction:** This meta-analysis sought to investigate the associations between blood pressure variability (BPV), in the form of long-term (visit-to-visit), short-term (ambulatory blood pressure monitoring, ABPM) and mid-term variability (home blood pressure monitoring, HBPM) and all-cause mortality, cardiovascular disease events, microvascular (MiC) and macrovascular complications (MaC) and hypertension-mediated organ damage (HMOD) in adult patients with type 2 diabetes (T2D).

**Methods:** PubMed, Medline, Embase, Cinahl, Web of Science, ClinicalTrials.gov and grey literature databases were searched. Studies were included if they contained data on patients with T2D, considered at least one measure of BPV (visit-to-visit, HBPM, ABPM), and a prospective or retrospective evaluation of the incidence of at least one of the following outcomes: all-cause mortality, adverse major cardiovascular events (MACEs), MiC and/or MaC and/or HMOD.

**Results:** 26 papers comprising 25 independent cohorts and a total of 377,305 T2D patients were analysed. Systolic blood pressure (SBP) variability was associated with an increased risk of CVD events (HR 1.10, 95% CIs 1.04–1.17), all-cause mortality (HR = 1.12, 95% CI 1.04–1.21), MiC (HR = 1.12, 95% CI 1.01–1.24) and MaC (HR = 1.08, 95% CI 1.02–1.15). Diastolic blood pressure (DBP) variability was not associated with a significant increase in risk of CVD events, MiC and MaC. The level of evidence for short-term and mid-term blood pressure variability on microvascular complications was greater than long-term variability. Qualitative analysis showed that BPV was associated with the presence of HMOD expressed as carotid intima-

media thickness, pulse wave velocity and left ventricular hypertrophy. Age and anti-hypertensive medication were not predictors of the magnitude of the association between SBP variability and MACEs, MiC or MaC.

**Conclusions:** Our results suggest that BPV might provide important clinical information on the risk of CVD in patients with diabetes, supporting the inclusion of its assessment in the tool for CVD risk stratification in this high-risk population.

## THE ORTHOSTATIC SYSTOLIC BLOOD PRESSURE CHANGE DURING THE MEDICAL VISIT AND ITS POTENTIAL CLINICAL SIGNIFICANCE

P. Nazzaro, A. Nardecchia, G. Schirosi, M. Contini, F. Caradonna Moscatelli, L. De Benedittis, G. Aceto, M.F. Decaro, A.M. Papagani

Dept of Neurosciences, Hypertension Unit "AM. Pirrelli", University of Bari "Aldo Moro", Bari, Italy

**Introduction:** Many studies showed the association between orthostatic hypotension and cardiovascular events, but very few of them considered the clinical findings related to systolic blood pressure (SBP) change at the orthostatic posture (OR) in the medical office.

**Aim:** To verify the association between SBPOR, the hemodynamic assessment and the quality of life in hypertensive patients treated with ACEi or ARBs as monotherapy.

**Methods:** In the medical office 340 hypertensives with similar hypertensive state and history, divided in tertiles of SBPOR at the 3rd min, underwent measurement of arterial stiffness (PWVcf) and central SBP (car) by tonometry, ambulatory blood pressure monitoring (ABPM) for SBP/DBP/HR circadian rhythm (day/night) and variability (s.d.), assessment of quality of life (SF-36) and of cognitive capabilities (CIS) by a questionnaire, with a satisfactorily internal coherence (alpha:0.87), composed by 18 gradual (1–4) multiple choice items related to different neuropsychological attitudes.

**Results:** The patients, divided in order of elevated (+) (n.:54), medium (=) (n.:219) or reduced (–) (n.:67) SBPOR, with similar metabolic state, age and SBP/DBP/HR in clinostatism ( $131 \pm 16/78 \pm 10/67 \pm 9$  vs  $133 \pm 15/78 \pm 9/65 \pm 11$  vs  $134 \pm 14/77 \pm 9/64 \pm 11$ , n.s., respectively) showed characteristic differences (m  $\pm$  s.d.; \*:p < .05, \*\*:p < .01, \*\*\*:p < .001 vs SBPOR +; ^:p < .05, ^^:p < .01, ^^=:p < .001 vs SBPOR=).

pts/var	SBPOR	PWVcf	SBPcar	SF-36	CIS
SBPOR+	11 $\pm$ 12	11.1 $\pm$ 2.8	124 $\pm$ 9	77.1 $\pm$ 18.5	26.1 $\pm$ 7.2
SBPOR=	1 $\pm$ 4***	9.4 $\pm$ 3.5***	121 $\pm$ 13	75.1 $\pm$ 19.5	25.3 $\pm$ 7.5
SBPOR-	-19 $\pm$ 7****^	12.5 $\pm$ 2.6****^	116 $\pm$ 11****^	68.1 $\pm$ 21.3****^	30.1 $\pm$ 9.4****^

ABPM showed similar SBP/DBP day ( $131 \pm 13/78 \pm 11$  vs  $128 \pm 17/77 \pm 11$  vs  $129 \pm 9/76 \pm 4$ , n.s.) and night ( $112 \pm 15/66 \pm 10$  vs  $111 \pm 13/65 \pm 9$  vs  $108 \pm 15/61 \pm 9$ , n.s.) but dayHRs.d. ( $16 \pm 3$  vs  $15 \pm 3$  vs  $11 \pm 1$ \*\*\*\*^), e nightHRs.d. ( $7 \pm 3$  vs  $7 \pm 2$  vs  $5 \pm 3$ \*\*\*\*^). were significantly reduced in SBPOR–. Pearson analysis highlighted the association between SBPOR and SBPcar (.250\*), dayHRs.d. (.477\*\*\*\*) and e nightHRs.d. (.296\*\*).

**Conclusions:** The findings show that an impaired SBPOR is associated to a major arterial stiffness and a restrained central SBP. The further association with the reduced day and night HR variability suggest a restrained left ventricular performance. These patients, coherently, also present a reduced quality of life and a cognitive impairment ascribable to parental cortex properties.

## Nutraceuticals

### NUTRITIONAL INTERVENTIONS AND BLOOD PRESSURE CHANGES

G.I.W. Germanò, E. Belmonte, R. Grillo, S. Rella, R. Germanò, A. Caparra, M. Cacciafesta

*Dipartimento di Malattie Cardiovascolari, Pneumologiche, Nefrologiche, Anestesiologiche e Geriatriche, Sapienza Università di Roma, Roma, Italy*

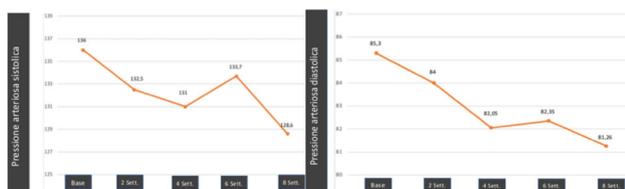
**Introduction:** Nattokinase is a serine protease isolated in 1987 from a fermented soy extract: Natto. The powerful fibrinolytic activity is linked to its property of activate plasmin and increase t-Pa levels. It is also stable after digestion and has no side effects or bleeding risk. The structure of the Nattokinase is identical to that of the subtilisin E and in experimental studies has inhibited ACE and clinical evidence has shown a reduction in blood pressure.

**Methods:** Hypertensive patients (10 males and 10 females,  $58 \pm 8$  and  $56 \pm 9$  years of age) in good blood pressure control with the drugs in daily use, took 8 weeks Nattokinase NSK-SD (Reonat-AB Pharma-Italy) at a dose of 100 mg (2000 fibrinolytic units). The blood pressure was measured at home once, three times in a row, a day (Microlife AFIB-Colpharma). At the beginning of the study and after 2, 4, 6, 8 weeks the values recorded and sent via e-mail were checked. At the beginning of the study and after 8 weeks blood tests were performed.

**Results:** The mean systolic and diastolic pressures at the beginning and at the end of the study are shown in the Fig. 5. The mean values of the systolic pressures were significantly reduced from 136.0 mmHg (SEM  $\pm$  1.80) to 128.6 mmHg (SEM  $\pm$  1.83— $p < 0.05$ ), the average of the diastolic pressures was reduced from 85.3 mmHg (SEM  $\pm$  1.9) at 81.2 (SEM  $\pm$  1.6). No changes in blood chemistry or no adverse events were noted.

**Conclusions:** It is therefore a preliminary observation on a nutritional intervention that reduces blood pressure. The Nattokinase, in addition to fibrinolytic and thrombolytic properties with clinical evidence by now established, can be considered a support in the control of high blood pressure values.

Figure 5



### COMBINED EFFECTS OF BIOACTIVE COMPOUND (CARDIOL FORTE<sup>®</sup>) ON LIPID PROFILE, SAFETY PROFILE AND ENDOTHELIAL FUNCTION IN PATIENTS WITH MILD-TO-MODERATE HYPERCHOLESTEROLEMIA. PRELIMINARY Results OF A DOUBLE-BLIND STUDY

N. Lomartire<sup>1</sup>, V. Pecchioli<sup>2</sup>, M.P. Gemmiti<sup>3</sup>, A. Colangeli<sup>4</sup>, G. Neroni<sup>2</sup>, M.P. Corsi<sup>3</sup>, G. Germanò<sup>5</sup>

<sup>1</sup>Anesthesiology and Intensive Care Unit-ASL Frosinone,

<sup>2</sup>Cardiovascular Prevention Unit-Hospital Department ASL

Frosinone, <sup>3</sup>Cardiology and Cardiological Intensive Care Unit-ASL

Frosinone, <sup>4</sup>Pneumology Unit-Department of Internal Medicine-

University of L'Aquila, <sup>5</sup>University Sapienza of Rome

**Introduction:** Endothelial dysfunction in hypercholesterolemic patients is in large part due to reduced bioavailability of nitric oxide(NO).

**Aim:** To evaluate the ability of the newly combined nutraceutical, Cardiol Forte<sup>®</sup> to lower LDL-C in patients with mild-to-moderate hypercholesterolemia and to assess the endothelial function and overall safety profile of the product.

**Methods:** In this double blind, placebo controlled, single center study, 80 outpatients with mild-to- moderate hypercholesterolemia were enrolled; 40 patients were assigned to an 8-week active nutraceutical compound with a low fat diet and 40 subjects to dietary regimens alone. The two groups of patients resulted cross-matched by baseline age, blood pressure, lipid, and glucose metabolism parameters.

**Results:** In comparing the nutraceutical group A effect with control group B in placebo, we observed that nutraceutical intake was associated with a significantly higher decrease in LDL-C ( $P < 0.001$ ) in group A vs 0.004 of group B. In group A, compared with the baseline FMD measurement we observed a significant increase ( $+ 18.8\% \pm 0.050$ ,  $P < 0.0001$ ). In group B we observed a lesser significant increase ( $+ 10.8\% \pm 0.03$ ,  $P < 0.001$ ). We observed a significantly higher increase in Endothelial function ( $P < 0.001$ ) in group A compared to the control group B. The study shows that 8 weeks is enough to achieve a reduction in cholesterol levels. A better decrease in TC and LDL-C was observed when compared to placebo. This result was associated with improved endothelial function as documented by (a more significant) increase of FMD than that of only diet in placebo group B. The significant effect on improving endothelial function is given not only by the inhibition monacolin K exerts on the inhibition of HMG-CoA reductase but also, above all, by the simultaneous administration of antioxidants such as coenzyme Q, olive oil polyphenols, omega 3 fatty acids and vitamin E.

**Conclusions:** In our study, monacolin K 10 mg and principal components of the bioactive compound (CARDIOL FORTE<sup>®</sup>) were well tolerated: no variations of liver, renal, and muscle safety parameters were recorded.

## RHO KINASE ACTIVITY, CONNEXIN40 AND ATRIAL FIBRILLATION: MECHANISTIC INSIGHTS FROM END STAGE RENAL DISEASE UNDER DIALYSIS PATIENTS

V. Ravarotto, G. Bertoldi, E. Pagnin, B. Rossi, F. Nalesso, L.A. Calò  
Department of Medicine, Nephrology, Dialysis and Transplantation Unit, University of Padova, Italy

**Introduction:** Evidence on cellular and molecular mechanisms that lead to atrial fibrillation (AF) are scanty. Increased expression of ROCK and myosin phosphatase target subunit 1 (MYPT-1), involved in ROCK signaling were shown in left atrial appendage biopsies of AF patients, which correlated with the expression of Connexin40 (Cx40), an integral membrane protein of heart gap junctions, fundamental for the rapid cell–cell transfer of action potential. AF is the most frequent cardiac arrhythmia in dialysis patients who, we demonstrated to present increased MYPT-1 phosphorylation, marker of ROCK activity, which correlated with their LV mass. Given the known role of ROCK in cardiovascular (CV)-renal remodeling together with its induction of impairment of cell-to-cell coupling and conduction of potential promoting AF initiation and perpetuation by reducing atrial wavelength, we evaluated in dialysis patients with AF, the phosphorylation state of MYPT-1, the expression of Cx40 and their relationship to support their mechanistic involvement in AF induction.

**Methods:** 11 AF-dialysis patients (AFDP) (chronic bicarbonate dialysis 3 times/week), 8 males, 3 females, 49–91 yo, 11 sinus rhythm-dialysis patients (DP), 7 males, 4 females, 53–91 yo, and 11 healthy subjects (C), 7 males, 4 females, 26–38 yo were enrolled. Mononuclear cells MYPT-1 phosphorylation and Cx40 expression were determined by Western blot. Data were expressed as mean  $\pm$  SE and evaluated by unpaired data ANOVA.

**Results:** In AFDP MYPT-1 phosphorylation was increased vs DP and C ( $1.57 \pm 0.17$  du vs  $0.69 \pm 0.04$  vs  $0.51 \pm 0.05$  respectively,  $p < 0.0001$ ). MYPT-1 phosphorylation in DP was also higher vs C,  $p = 0.009$ . Cx40 was higher in AFDP ( $1.23 \pm 0.12$  vs  $0.74 \pm 0.03$  vs  $0.69 \pm 0.03$ ,  $p < 0.0001$ ). MYPT-1 phosphorylation correlated with Cx40 expression ( $r = 0.67$ ,  $p < 0.001$ ) in all dialysis patients.

**Conclusions:** These data confirm at mechanistic level in dialysis patients a role for ROCK increased activity and Cx40 expression association as a possible mechanism leading to induction of AF. The correlation between MYPT-1 phosphorylation and Cx40 in all dialysis patients further strengthens this mechanistic relationship for AF induction. The clarification, on a mechanistic basis, of this relationship might give further insights for additional pharmacologic targeting of AF.

## DETERMINANTS OF END STAGE RENAL DISEASE IN IGA NEPHROPATHY: A FOCUS ON ACHIEVED BLOOD PRESSURE

E. Russo<sup>1</sup>, S. Drovandi<sup>1</sup>, G. Salvidio<sup>1</sup>, D. Verzola<sup>1</sup>, D. Lamperi<sup>1</sup>, A. Sofia<sup>1</sup>, F. Ferrario<sup>2</sup>, C. Pozzi<sup>2</sup>, F. Viazzi<sup>1</sup>, R. Pontremoli<sup>3</sup>, G. Garibotto<sup>1</sup>

<sup>1</sup>Clinica Nefrologica, Dialisi e Trapianto, Policlinico San Martino IRCCS-Genova, Italy, <sup>2</sup>Nefrologia e Dialisi, Ospedale Bassini-Cinisello Balsamo (ASST Nord Milano), Milano, Italy, <sup>3</sup>Clinica di Medicina Interna 2, Policlinico San Martino IRCCS-Genova, Italy

**Introduction:** While evidence for a role of corticosteroids in slowly progressive IgAN is not definitive, the value of optimized supportive care has increasingly more support. This term is usually taken to mean tight blood pressure control and titration of renin-angiotensin blockade accompanied by dietary salt restriction to minimize proteinuria, however, the debate regarding appropriate goals for blood pressure management remains controversial.

**Methods:** We retrospectively studied 248 patients with biopsy proven IgAN followed-up for at least 1 year from 1996 to 2018. We included the 154 subjects with available data about eGFR, proteinuria/day, and office BP values at the time of biopsy, at the end of the 6-month treatment and at least every year until the occurrence of the endpoint. All patients received Supportive Care, 39% was on RASB alone, 45% RASB and steroids, and 16% was treated with RASB and steroids plus other immunosuppressors. We analyzed the changes in eGFR and proteinuria during the follow-up and the need for RRT was the primary endpoint.

**Results:** During a mean follow-up of  $67 \pm 6$  months, 23% of the study patients ( $n = 33$ ) progressed to ESRD and 6% ( $n = 9$ ) died. Patients who reached the renal endpoint, went through a lower TA-eGFR and higher TA-proteinuria, proteinuria indexed and yearly eGFR decline. Moreover, they maintained a significantly higher TA-SBP ( $139 \pm 17$  vs  $130 \pm 13$ ,  $P = 0.0016$ ) and therefore they more likely showed a TA-BP  $> 130/80$  ( $85$  vs  $62\%$ ,  $P = 0.0249$ ) and less frequently reached optimal time updated BP control as compared to patients who did not require RRT.

**Conclusions:** The incidence of ESRD was higher in IgAN patients in the highest TA-SBP tertile as compared to those in the second and first one ( $32$  vs  $23$  vs  $9\%$ ,  $X^2 6.8$ ,  $P = 0.033$ ) (Log Rank  $P = 0.0015$ ). After adjusting for baseline SBP, baseline and TA proteinuria indexed, MEST-C score, and treatment, the association between TA-SBP and ESRD persisted.

RISK FACTORS	Univariate			Multivariate with TA-SBP			Multivariate with TA-SBP-130 mmHg		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
SBP	1.025	1.007-1.043	0.0066	0.968	0.956-1.021	NS	1.000	0.973-1.028	NS
TA-SBP	1.06	1.032-1.08	<0.0001	1.069	1.014-1.127	0.018			
BP at baseline $>140/90$ mmHg	2.704	1.254-5.832	0.012						
TA-SBP $<130$ mmHg	0.419	0.183-0.957	0.0389				0.329	0.111-0.972	0.0443
VVV	1.13	1.023-1.215	0.0156						
Proteinuria-indexed at baseline	1.08	1.029-1.148	0.0027	1.023	0.991-1.057	NS	1.028	0.995-1.063	NS
TA-Proteinuria Indexed	1.054	1.037-1.070	<0.0001	1.032	1.010-1.055	0.0048	1.038	1.015-1.062	0.0011
Annual slope eGFR, %	1.054	1.033-1.074	<0.0001						
M	0.476	0.205-1.101	0.0827	0.887	0.270-2.913	NS	0.962	0.300-3.088	NS
E	1.221	0.971-4.023	0.7424	1.044	0.114-9.528	NS	1.192	0.108-9.819	NS
S	1.448	0.762-3.565	0.2062	1.836	0.569-5.927	NS	1.662	0.519-5.213	NS
T	3.173	1.309-7.718	0.0110	1.658	0.543-5.063	NS	2.268	0.451-3.565	NS
C	2.742	1.154-6.519	0.0234	1.256	0.325-4.451	NS	1.024	0.264-3.982	NS
Arteriole hyalinosis	2.378	1.125-7.365	0.0274						
Treatment: RASB + Corticosteroids	reference								
RASB	3.20	1.19-8.60	0.0209	2.485	0.633-9.753	NS	2.361	0.625-8.912	NS
RASB + CS + immunosuppressors	5.33	1.76-15.84	0.0029	3.462	0.724-16.552	NS	3.657	0.838-15.956	NS

Cox Regression Hazard ratio (HR) in univariate and multivariate analysis for predicting ESRD in IgAN patients

While Supportive Care alone was more frequently complicated by the need for RRT as compared to Corticosteroids or Immunosuppressors treatment ( $p < 0.0109$ ), maintaining a SBP below 130 mmHg for most of the time showed to be independently

associated to a decreased risk of renal progression in IgAN (HR 0.33 [95% CI 0.11–0.97];  $P = 0.044$ ).

## TWO DAYS ABPM RECORDING PROVIDES PARAMETER OF STIFFNESS ABLE TO PREDICT MORTALITY IN HD PATIENTS

Francesca Cappadona, Francesca Viazzi, Giovanna Leoncini, Elena Ratto, Annalisa Gonnella, Barbara Bonino, Daniela Verzola, Giacomo Garibotto, Roberto Pontremoli

*Clinica Nefrologica Dialisi e Trapianto, University of Genova and Ospedale Policlinico San Martino-IST, Genoa, Italy*

**Introduction:** Blood pressure (BP) and arterial stiffness are known cardiovascular risk factors in hemodialysis patients.

**Aim:** This study examines the prognostic significance of 44-h BP circadian rhythm and ambulatory arterial stiffness index (AASI) in this population.

**Methods:** A total of 80 hemodialysis patients underwent 44-h ambulatory blood pressure monitoring (ABPM) with a TM-2430 monitor during a standard midweek interdialytic interval and followed-up for  $4.5 \pm 1.7$  years. The end point was all-cause mortality.

**Results:** About 76% of participants were hypertensive (40% uncontrolled), 62% were non-dippers and 23% risers during the first interdialytic day, while 73 and 44% in the second day, respectively. During follow-up, 31 patients (40%) died. These showed higher PP, AASI<sub>44</sub> and AASI<sub>22</sub> of the second inter-dialytic period. The incidence of all-cause mortality was higher in HD patients with AASI<sub>44</sub> > median, i.e. > 0.54 (IQR 14) (54% vs 28%  $\chi^2$  5.3,  $p = 0.021$ ) as compared to those with lower AASI<sub>44</sub>. Second, but not first day ABPM-derived parameters, namely non-dipping (log rank  $\chi^2$  6.10,  $P = 0.0134$ ) or reverse dipping status (log rank  $\chi^2$  5.32,  $P = 0.210$ ) and arterial stiffness index (log rank  $\chi^2$  6.61,  $P = 0.0101$ ) were significantly related to greater mortality.

**Conclusions:** These findings indicate a strong relationship between arterial stiffness and cardiovascular risk and support a wider use of 44-h ABPM recording for risk stratification in hemodialysis patients.

## INFLUENCE OF DIABETES ON ACID-BASE BALANCE IN HYPERTENSIVE PATIENTS WITH CHRONIC KIDNEY DISEASE

G. Mule<sup>1</sup>, C. Carollo, Cusumano, A. Ferrara, C. Giarratana, N. Sinatra, F. Vaccaro, M. Guarneri, S. Cottone

*ESH Hypertension Excellence Centre and Nephrology Unit of the University of Palermo, Palermo, Italy*

**Introduction:** Metabolic acidosis is a common complication of advanced chronic kidney disease (CKD). It has been associated with an increased risk of death and faster renal function decline. Diabetes mellitus is one of the most important cause of CKD. The dysregulation of glucose homeostasis may lead to many acid-base balance disorders. However, little is known whether or not there is any difference in the prevalence and severity of metabolic acidosis between CKD patients with and without diabetes.

**Aim:** Our study was aimed to compare blood acid-base status of diabetic patients with severe CKD with that of non-diabetic CKD subjects.

**Methods:** The study population included 143 CKD hypertensive subjects recruited from those consecutively attending our outpatient unit of Nephrology because of advanced renal failure. To be included

on the study, patients were required to have an estimated glomerular filtration rate (eGFR) of less than 30 mL/min, no intake of alkali within the previous 30 days, and the absence of pulmonary diseases and other clinical conditions at the time of the study that could explain an acute imbalance of the acid-base status, such as heart failure, hemorrhage, or sepsis. The study population was divided into two groups on the basis of the presence ( $n = 73$ ) or the absence of type 2 diabetes ( $n = 70$ ). Arterial blood samples were drawn in all the subjects and analyzed by the Radiometer ABL-800 FLEX blood-gas analyser.

**Results:** Age, sex distribution, serum creatinine, eGFR and proteinuria were not different in the two groups. Blood pH [7.406 (7.35–7.43) vs 7.384 (7.32–7.41),  $p = 0.02$ ], bicarbonate levels [22 (19.1–23.7) vs 20.5 (17.4–23.1);  $p = 0.05$ ] were higher and the prevalence of metabolic alkalosis (16.8 vs 8.4%) was greater in diabetic patients as compared to non diabetic ones. The positive associations between diabetes and pH values (beta: 0.186;  $p = 0.02$ ) and that between diabetes and metabolic alkalosis (odds ratio 2.68;  $p < 0.05$ ), were confirmed respectively in linear multiple regression analyses and in logistic multivariate models even after adjustment for potential confounding factors.

**Conclusions:** Our results, in agreement with those obtained in a previous study (Caracava et al., Am J Kidney Dis 1999) on the same issue, seem to suggest that metabolic alkalosis is more common than metabolic acidosis in diabetic patients with severe CKD. Further studies are needed in order to provide the pathophysiological explanations of these findings.

## INFLUENCE OF RENAL FUNCTION ON RETINAL VASCULAR DENSITY ASSESSED BY OCT ANGIOGRAPHY IN HYPERTENSIVE PATIENTS

G. Mule<sup>1</sup>, M. Vadala<sup>2</sup>, M. Castellucci<sup>2</sup>, C. Pugliese<sup>1</sup>, T. La Blasca<sup>1</sup>, G. Virone<sup>1</sup>, R. Dell'Utri<sup>1</sup>, A. Ferotti<sup>1</sup>, S. Cillino<sup>2</sup>, S. Cottone<sup>1</sup>

*<sup>1</sup>ESH Hypertension Excellence Centre and Nephrology Unit-Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties-University of Palermo, Palermo, Italy, <sup>2</sup>Department of Experimental Biomedicine and Clinical Neuroscience, Section of Ophthalmology, University of Palermo, Palermo, Italy*

**Introduction:** It is well known that the retinal vasculature may be regarded as a window through which the body microcirculation can be observed in life easily, safely and repeatedly. Alterations of the renal microcirculation have been documented in animal models with hypertensive renal damage and microvasculature changes have been suggested to play a mayor etiological role in a large proportion of subjects with chronic kidney disease (CKD). Optical coherence tomography angiography (Angio OCT) is a recently developed non-invasive diagnostic imaging technique that employs motion contrast extracted from high-speed OCT images to produce depth-resolved, high-resolution images of retinal and choroidal vasculature without dye injection.

**Aim:** Our study was aimed to assess in hypertensive patients the influence of renal function on retinal vascular density assessed by Angio-OCT.

**Methods:** We enrolled 120 hypertensive subjects (age:  $51 \pm 13$  years; males 68%) recruited from those consecutively attending our Hypertension Centre. All the patients underwent routine biochemical evaluation and angio-OCT. The retinal angiograms obtained allowed to assess vascular density of both superficial (DRS) and deep (DRP) network in the parafoveal area. Only one eye of each

subject was randomly selected for analysis. Glomerular filtration rate (GFR) was estimated by CKD-EPI equation.

**Results:** Twenty-six subjects exhibited a GFR value  $< 60$  ml/min/1.73 m<sup>2</sup>. These patients, when compared to those with higher GFR, showed significantly lower values of DRS ( $36.48 \pm 1.23$  vs  $37.29 \pm 0.78\%$ ;  $p < 0.001$ ) and of DRP ( $37.69 \pm 1.23$  vs  $38.34 \pm 0.97\%$ ;  $p = 0.005$ ). Moreover, the GFR correlated directly with DRP ( $r = 0.385$ ;  $p < 0.001$ ) and with DRS ( $r = 0.247$ ;  $p < 0.01$ ). These associations remain statistically significant even after adjustment for age, BP and other confounding factors in step-wise multiple linear regression analyses (respectively,  $\beta = 0.265$ ;  $p < 0.05$  e  $\beta = 0.211$ ;  $p < 0.05$ ).

**Conclusions:** Our study, showing a significant association between reduced retinal vascular density and renal function impairment, confirm the close link relating CKD with retinal vascular abnormalities.

## RENAL FUNCTION IMPROVES BY FACILITATING THE ACTION OF NATRIURETIC PEPTIDES: OUR EXPERIENCE WITH SACUBITRIL/VALSARTAN

Francesco Spannella<sup>1,2</sup>, Marco Marini<sup>3</sup>, Federico Giulietti<sup>1,2</sup>, Giulia Rosettani<sup>1,2</sup>, Matteo Francioni<sup>3</sup>, Gian Piero Perna<sup>3</sup>, Riccardo Sarzani<sup>1,2</sup>

<sup>1</sup>Internal Medicine and Geriatrics, “Hypertension Excellence Centre” of the European Society of Hypertension, and LIPIGEN Centre, IRCCS-INRCA, Ancona, Italy, <sup>2</sup>Department of Clinical and Molecular Sciences, University “Politecnica delle Marche”, Ancona, Italy, <sup>3</sup>Department of Cardiovascular Sciences, Ospedali Riuniti, Ancona, Italy

**Introduction:** Randomized clinical trials (RCTs) show that Sacubitril/Valsartan has neutral or favorable effects on renal function in patients with heart failure and reduced ejection fraction (HFrEF), despite reduced blood pressure (BP) values. However, data from clinical practice are still scant.

**Aim:** To evaluate the renal effects of Sacubitril/Valsartan in a “real life” sample of HFrEF patients.

**Methods:** Prospective observational study of 54 consecutive HFrEF patients with clinical indication to Sacubitril/Valsartan. Patients were evaluated at baseline (T0), at 6 months (T6) and 12 months (T12) after starting Sacubitril/Valsartan. A historical control group (30 HFrEF patients) treated with inhibitors of the renin-angiotensin-aldosterone system (RAAS) was used in the analyses.

**Results:** Mean age:  $65.5 \pm 11.7$  years. Older patients (age  $\geq 65$  years): 29 (53.7%). Mean estimated glomerular filtration rate (eGFR):  $59.4 \pm 19.2$  ml/min/1.73 m<sup>2</sup>. Patients with chronic kidney disease (CKD = eGFR  $< 60$  ml/min/1.73 m<sup>2</sup>): 29 (53.7%). There were no significant changes in the diuretic dosage during follow-up. Blood pressure decreased during follow-up ( $119.0 \pm 14.3/72.2 \pm 10.1$  mmHg at T0;  $113.3 \pm 15.5/67.3 \pm 11.1$  mmHg at T6;  $114.8 \pm 15.8/67.5 \pm 10.0$  mmHg at T12,  $p = 0.014$  and  $p = 0.002$ , respectively), while ejection fraction slightly increased ( $p < 0.001$ ). Renal function improved at 12 months, compared with the historical control group ( $+ 6.2$  vs  $- 7.2$  ml/min/1.73 m<sup>2</sup>,  $p$  for interaction  $< 0.001$ ). Patients aged  $< 65$  years ( $p$  for interaction = 0.002) and those with CKD ( $p$  for interaction = 0.009) showed the greatest benefits. There was a statistically ( $p = 0.009$ ), but not clinically significant increase in serum potassium, regardless of age and CKD.

**Conclusions:** Our “real life” data show an eGFR improvement after 12 months, despite a significant BP reduction, in patients treated with Sacubitril/Valsartan. This represents an important confirmation,

outside of the peculiar world of RCTs, of the beneficial role on renal function exerted by simultaneous RAAS antagonism and facilitation of natriuretic peptides activity in patients with HFrEF.

## SUBCLINICAL TARGET ORGAN DAMAGE IN A SAMPLE OF CHILDREN WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

L. Branz<sup>1</sup>, D. Marcon<sup>1</sup>, A. Tagetti<sup>1</sup>, M. Bevilacqua<sup>1</sup>, A. Giontella<sup>1</sup>, M. Brugnara<sup>2</sup>, F. Malesani<sup>1</sup>, P. Minuz<sup>1</sup>, C. Fava<sup>1</sup>

<sup>1</sup>Department of Medicine, University of Verona, Italy, <sup>2</sup>Department of Odontostomatological and Maternal-Infantile Surgical Sciences, University of Verona, Italy

**Introduction:** Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common monogenic hereditary kidney disease, characterized by the development of cysts along the renal tubule. Its prevalence is estimated at 1 per 1000 population. Previous studies suggest that hypertension and vascular damage can start during childhood.

**Aim:** To evaluate markers of vascular damage and left ventricular geometry in a sample of children with ADPKD.

**Methods:** Several vascular measurements were obtained: ambulatory blood pressure monitoring (ABPM), carotid intima media thickness (cIMT), carotid distensibility (CD), pulse wave velocity (PWV) and Echocardiographic measurements: relative wall thickness (RWT) and left ventricular mass index (LVMI).

**Results:** 11 children with ADPKD were recruited (4 females and 7 males, mean age  $9.5 \pm 3.2$  years): 3 children were overweight, 8 were normal weight. Five children resulted hypertensive at the ABPM, 4 were normotensive, 2 ABPM were not available. One child was already on therapy with an ACE-inhibitor. RWT was tendentially high (mean  $0.47 \pm 0.39$ ) while cIMT was above the 95<sup>o</sup>percentile for sex and height in 20% of children ( $0.5 \pm 0.005$  mm). Average PWV and CD were between the normal range ( $5.5 \pm 4.6$  m/s and  $89.6 \pm 16.1 \times 10^{-3}$ /kPa respectively). We observed a positive correlation between the PWV and RWT ( $r = 0.616$ ;  $p = 0.044$ ) and a negative correlation between CD and RWT ( $r = - 0.770$ ;  $p = 0.015$ ). None of the subjects have altered glomerular filtration rate (GFR).

**Conclusions:** Increased RWT and high cIMT, indicating subclinical organ damage, are present in ADPKD children. The level of RWT was significantly correlated to that of CD and PWV, implying that vascular stiffening is associated with cardiac remodelling. None of the children has an alteration of renal function, suggesting that subclinical cardiovascular alterations may precede the overt decline in Glomerular Filtration Rate. These data underline the importance of a comprehensive cardiovascular screening in all the children with ADPKD.

## Therapy, Pharmacoeconomy and Pharmacosurveillance

### COST-EFFECTIVENESS OF ROSUVASTATIN/EZETIMIBE IN FIXED-DOSE COMBINATION IN HIGH-RISK HYPERTENSIVE PATIENTS WITH UNCONTROLLED HYPERCHOLESTEROLEMIA COMPARED TO A PREVIOUS SIMVASTATIN/EZETIMIBE TREATMENT

Alberto Mazza<sup>1</sup>, Ciro Rossetti<sup>2</sup>, Cosimo D'Amicis<sup>3</sup>, Gioia Torin<sup>4</sup>, Laura Schiavon<sup>2</sup>, Salvatore Lenti<sup>5</sup>, Stefano Cuppini<sup>2</sup>

<sup>1</sup>ESH Excellence Hypertension Centre, Unit of Internal Medicine, AULSS5 Polesana, Rovigo, Italy, <sup>2</sup>Unit of Internal Medicine, S. Maria della Misericordia General Hospital, AULSS 5 Polesana, Rovigo, Italy, <sup>3</sup>Freelance, Master in Statistics, Bologna, Italy, <sup>4</sup>Unit of Internal Medicine C and Hypertension, Department of Medicine, University of Verona, Verona, Italy, <sup>5</sup>Hypertension Centre, Internal Medicine and Geriatrics, San Donato General Hospital, Arezzo, Italy

**Introduction:** Combination therapy may help achieve low-density lipoprotein cholesterol (LDL-C) goals in high-risk patients (i.e. < 70 mg/dL). The role of rosuvastatin and ezetimibe (RE) has not been fully characterized in high-risk hypertensive outpatient subjects.

**Aim:** To evaluate the cost-effectiveness of RE in fixed-dose combination in patients with uncontrolled hypercholesterolemia by a simvastatin and ezetimibe (SE) therapy and to compare the costs between the two therapies.

**Methods:** 32 subjects (46.8% men, mean age 67.8±11.1 years) with uncontrolled LDL-C levels (109.4±14.2 mg/dL) and treated with SE (40 mg and ezetimibe 10 mg daily, 56.3% in fixed-dose combination), were switched to once-daily fixed-combination therapy with RE 10/10 mg (n = 18) or 20/10 mg (n = 14). The monthly cost for treating patients with SE and RE was estimated using pharmacy dispensing records. The change of LDL-C level, the tolerability analyses (i.e. AST, ALT and CPK values) and the costs of treatment were compared also using parametric and non-parametric statistic tests.

**Results:** After a median time of 76 days, RE treatment were associated with significant decrease of LDL-C levels (- 25%, Wilcoxon signed-rank test p < 0.001) and costs reduction (- 39.4%). The LDL-C target value was reached in 32% of cases. The average cost of RE therapy is also lower than the minimum cost of the SE combination (26.64 vs. 33.76 €, p < 0.01). No adverse event was observed during the RE treatment and safety parameters was not-different.

**Conclusions:** RE in fixed-dose combination therapy was safe and cost-effective on improving LDL-C levels.

### EFFECTS OF BENZODIAZEPINES ON ORTHOSTATIC BLOOD PRESSURE IN OLDER PEOPLE

G. Rivasi<sup>1</sup>, R. A. Kenny<sup>2</sup>, A. Ungar<sup>1</sup>, R. Romero-Ortuno<sup>2</sup>

<sup>1</sup>Referral Centre for Hypertension in the Elderly, Department of Geriatrics and Geriatric Intensive Care Unit, Careggi Hospital and University of Florence, Italy, <sup>2</sup>Discipline of Medical Gerontology and Falls and Syncope Unit, Mercer's Institute for Successful Ageing, St. James's Hospital, Dublin, Ireland

**Introduction:** Older people taking benzodiazepines (BDZs) have higher risk of falling, which is mainly attributed to unfavorable drug-related effects on cognition and psychomotor functioning. BDZs may also have hypotensive effects, but evidence concerning the relationship between BDZs and orthostatic blood pressure (BP) behaviour in older people is scarce.

**Aim:** We investigated the effects of BDZs on BP response to an orthostatic active stand test.

**Methods:** We performed a retrospective analysis of data from the Technology Research for Independent Living (TRIL) Clinic in St James's Hospital, Dublin, Ireland, where people aged 60 or older underwent a comprehensive geriatric assessment between August 2007 and May 2009. Non-invasive beat-to-beat orthostatic BP was measured during active stand, with systolic BP assessed at each 10-s interval. Information on regular BDZs use was collected. Factors independently associated with orthostatic systolic BP were investigated using multiple linear regression.

**Results:** Of 624 community-dwelling people who underwent a clinic assessment, information on regular BDZs use was available in 538 people. Of 538 participants, mean age was 72.7 ± 7.2, 67.7% were female and 33 (6.1%) reported regular use of BDZs. History of falls (p = 0.027) and fear of falling (p < 0.001) were more prevalent in this subgroup. During active stand, participants on BDZs showed a significantly greater systolic BP drop 10 s after the posture change ("immediate" BP drop). No significant differences were detected in orthostatic systolic BP in the latter phases of the active stand. After adjusting for possible confounders, BDZs use was independently associated with a mean immediate systolic BP drop of 12 mmHg after standing.

**Conclusions:** BDZs may confer higher risk of an immediate systolic BP drop after standing in older people, which may contribute to their known falls risk. BDZ should be avoided in older people at risk of falling.

### OCCUPATIONAL THERAPY IN THE PREVENTION OF RISK OF FALL CONCERNING ELDERLY PEOPLE AFFECTED BY HYPERTENSION

F. D'Amico<sup>1,2</sup>, R. Grasso<sup>1</sup>, R. D'Amico<sup>1</sup>

<sup>1</sup>Department of Geriatrics and Long Term Care, Center of Hypertension, Hospital of Patti, <sup>2</sup>School of Medicine, University of Messina

**Introduction:** This study assessed the efficiency of an Occupational Therapy support to reduce incidence of falls in elderly people with controlled hypertension and high risk of fall.

**Methods:** 33 women (mean age 78 ± 3) and 21 men (mean age 77 ± 4) already diagnosed controlled hypertension have been included in the study (group A). They have been compared with a control group of 23 women (mean age 76 ± 2) and 12 men (mean age 78 ± 5) without Hypertension (group B).

**Results:** In group A 8 women and 6 men had a mean 14 ± 5 score showing a high risk of fall. In group B 4 women and 5 men had a mean 16 ± 2 score indicating a high risk of fall. Group A subjects with a high Tinetti score, therefore a high risk of fall, also showed significant connections between risk of fall and physical efficiency assessed through SBBP Scale (p < 0.05). Group B did not confirm the same relation. Throughout a 6-month-period we applied a model of Occupational Therapy at home focused on the prevention of falls. The therapists studied necessary space each patient with a lower physical efficiency and a higher risk of fall (p < 0.01) needed for mobility.

Such evaluation was based on the ability by patients to perform BADL and IADL at home.

**Conclusions:** This study found out: (1) a significant relation among Hypertension, high risk of fall and reduced physical efficiency in elderly subjects; (2) the importance of an occupational therapy model focused on making the domestic environment more friendly and safe both to patient and caregiver. The latter was previously instructed by the therapist on how to move the patient and to take care of his body.

## Vessels and Endothelium

### CORRELATION OF ANKLE-BRACHIAL INDEX WITH FRAILTY STATUS IN OLD HOSPITALIZED PATIENTS

<sup>1</sup>A. Maloberti<sup>1,2</sup>, E. Motto<sup>2</sup>, D. Caroti<sup>2</sup>, P. Vallerio<sup>1</sup>, F. Fibbri<sup>2</sup>, F. Panzeri<sup>2</sup>, L. Occhi<sup>2</sup>, N. Triglione<sup>1</sup>, F. Musca<sup>1</sup>, B. De Chiara<sup>1</sup>, A. Agrati<sup>3</sup>, F. Colombo<sup>3</sup>, C. Giannattasio<sup>1,2</sup>

<sup>1</sup>Cardiology 4, ASST Niguarda Ca Granda Hospital, Milan, Italy, <sup>2</sup>School of Medicine and Surgery, Milan-Bicocca University, Milan, Italy, <sup>3</sup>Internal Medicine Department, ASST Niguarda Ca Granda Hospital, Milan, Italy

**Introduction:** Frailty is a state of vulnerability due to poor recovery of homeostasis after stressor event and is a consequence of cumulative decline in many physiological systems, including the cardiovascular one. Atherosclerosis causes a chronic reduction of vascularization of tissues, contributing in this way to the functional and cognitive decline of the elderly. The Ankle-Brachial Index (ABI), obtained by the ankle/brachial blood pressure ratio, as an indicator of atherosclerosis, could be used as a marker of frailty.

**Methods:** Our cross-sectional monocentric study selected 100 patients of  $\geq 65$  years old (average age  $80 \pm 6.9$  years) hospitalized in the Internal Medicine department of our institution. Subjects were evaluated with ABI and frailty indexes (death, hospitalization length, delirium, falls, cognitive impairment, ADL and I-ADL).

**Results:** At the correlation analysis of the various indexes of frailty considered, the only significant correlations with the ABI were represented by the cognitive impairment ( $r = -0.298$ ;  $p = 0.003$ ) and the ADL index ( $r = 0.198$ ;  $p = 0.048$ ). At the subsequent multivariate regression, the ABI index remained a statistically significant determinant of cognitive impairment ( $\beta = -5.818$ ;  $p = 0.01$ ) but not of ADL ( $\beta = 0.328$ ;  $p = 0.729$ ).

**Conclusions:** Lower ABI is associated with worse cognitive performance in old age, possibly because of long-term exposure to atherosclerotic disease. This would accentuate the functional disability of the elder, even in the simplest daily actions, and support the hypothesis that the ABI can be used as a marker of frailty in elderly people.

### EFFECTS OF CHRONIC HEART FAILURE UNCONVENTIONAL THERAPIES ON ENDOTHELIAL FUNCTION

E. Piccinelli<sup>1,2</sup>, A. Maloberti<sup>1,2</sup>, J. Zannoni<sup>2</sup>, S. Castelnuovo<sup>3</sup>, P. Vallerio<sup>1</sup>, I. Bassi<sup>2</sup>, G. Pansera<sup>2</sup>, L. Occhi<sup>1</sup>, M. Varrenti<sup>4</sup>, G. Masciocco<sup>4</sup>, E. Perna<sup>4</sup>, M. Cipriani<sup>4</sup>, M. Frigerio<sup>4</sup> and C. Giannattasio<sup>1,2</sup>

<sup>1</sup>4th Section of Cardiology, De Gasperis Cardio Center, Niguarda Hospital, Milan, Italy, <sup>2</sup>School of Medicine and Surgery, Milan-

Bicocca University, Milan, Italy, <sup>3</sup>Dyslipidemia Center, Niguarda Hospital, Milan, Italy, <sup>4</sup>2nd Section of Cardiology, De Gasperis Cardio Center, Niguarda Hospital, Milan, Italy

**Introduction:** Endothelial dysfunction (ED) of peripheral arteries in chronic heart failure (CHF) subjects has been demonstrated. We assessed endothelial function in subjects undergoing unconventional treatments for CHF, namely heart transplantation (HTX), continuous-flow left ventricular assist device implantation (LVAD), and repeated levosimendan infusions (r-LEVO).

**Methods:** Twenty HTX recipients (median time from HTX 21 months), 20 patients supported with LVAD (median time from implant 39 months), and 20 patients receiving monthly Levosimendan infusions (median time on treatment 28 months) were enrolled and compared to a group of 20 healthy subjects. ED was evaluated with ultrasound assessment of the diameter before and after ischemic stress at the brachial artery level. The difference between the two diameters normalized for the baseline value (flow mediated dilation-FMD) has been used for the analysis. All the patients were stable at the time of FMD assessment, with those on r-LEVO being evaluated prior to infusion.

**Results:** FMD was significantly lower in HTX and LVAD groups with respect to controls ( $9.8 \pm 7.4$ ,  $9.3 \pm 5.7$ , and  $15.6 \pm 6.4\%$  respectively,  $p = 0.01$ ), but not in r-LEVO group ( $12.5 \pm 6.9\%$ ). When patients were analysed according to time from the operation or on treatment, ( $< \textit{versus} \geq$  of the median value), no differences were seen in HTX and r-LEVO group, while in LVAD group FMD was borderline significantly higher in patients with longer follow-up ( $8.4 \pm 6.4\% \textit{versus} 10.2 \pm 5.2\%$ ,  $p = 0.05$ ).

**Conclusions:** Based on this preliminary data we can inference the following: 1- FMD is abnormal in HTX recipients, despite their good functional status, probably due to factors unrelated to CHF (e.g. hypertension, renal insufficiency, denervation, and drug effects); 2- LVAD patients also show ED, with possible better adaptation in very long-term survivors; 3- Near-normal FMD values in CHF patients who remain stable with r-LEVO suggest that pulsed treatment may obtain favourable effects at peripheral level, persisting after clearance of the drug and its metabolites.

### RELATIONSHIP BETWEEN UNATTENDED AND ATTENDED BP VALUES AND VASCULAR HYPERTENSIVE TARGET ORGAN DAMAGE

C. Aggiusti, A. Painsi, M. Salvetti, F. Bertacchini, D. Stassaldi, S. Capellini, G. Saccà, L. Verzeri, E. Agabiti-Rosei, M.L. Muiesan

Medicina Interna and 2<sup>a</sup> Medicina, Università di Brescia and ASST Spedali Civili di Brescia, Brescia, Italy

**Introduction:** It has been suggested that measurement of “unattended” or “automated oscillatory(AOBP)” blood pressure values may provide advantages over conventional BP measurement and some hypertension guidelines now suggest this approach as the preferred one for measuring office BP. Data on the relationship between AOBP and cardiovascular events are much less solid as compared to those obtained with the standard BP measurement; conflicting data are available on the relationship between hypertensive organ damage and “attended” and “unattended” BP.

**Aim:** To evaluate the relationship between “attended” or “unattended” BP values and vascular hypertensive target organ damage in 396 subjects attending the outpatient clinic of an ESH Excellence Centre.

**Methods:** Both “unattended” BP (patient alone in the room, an oscillometric device programmed to perform 3 BP measurements, at 1 min intervals, after 5 min) and “attended” BP were measured with

the same device, on the same day of arterial stiffness assessment, in random order.

**Results:** Patient's mean age was  $61 \pm 14$  yrs, mean BMI  $26 \pm 4$ , 59% were male, 78% had a previous diagnosis of hypertension (66% treated). Systolic unattended BP was lower as compared to attended SBP ( $128.3 \pm 15.4$  vs  $134.8 \pm 16.9$  mmHg). Carotid MeanMaxIMT, CBMaxIMT and Tmax were significantly and similarly correlated with both attended ( $r = 0.206$ ,  $r = 0.222$  and  $r = 0.207$ ;  $P < 0.0001$ ) and unattended BP values ( $r = 0.194$ ,  $r = 0.208$  and  $r = 0.189$ ;  $P < 0.0001$ ). Similar correlations were also observed with attended ( $r = 0.422$ ,  $r = 0.429$  and  $r = 0.383$ ;  $P < 0.0001$ ) and unattended pulse pressure ( $r = 0.429$ ;  $r = 0.434$  and  $r = 0.388$ ,  $P < 0.0001$ ). The differences between correlations were not statistically significant (Steiger's Z test). No significant difference was observed between the ROC curves of attended or unattended SBP for the presence of carotid plaque (AUC 0.561 vs. AUC 0.555,  $p$  for the comparison = ns).

**Conclusions:** measurement of BP "attended" or "unattended" provides different values, being unattended BP lower as compared to attended BP. Our results suggest that attended and unattended BP values are similarly related with vascular hypertensive target organ damage.

## RELATIONSHIP BETWEEN UNATTENDED AND ATTENDED BP VALUES AND ARTERIAL STIFFNESS DAMAGE

A. Paini, M. Salvetti, C. Aggiusti, F. Bertacchini, D. Stassaldi, S. Capellini, G. Saccà, C. Arnoldi, E. Agabiti-Rosei, M.L. Muiesan

*Medicina Interna and 2<sup>a</sup> Medicina, Università di Brescia and ASST Spedali Civili di Brescia, Brescia, Italy*

**Introduction:** It has been suggested that measurement of "unattended" or "automated oscillatory (AOBP)" blood pressure values may provide advantages over conventional BP measurement and some hypertension guidelines now suggest this approach as the preferred one for measuring office BP. Data on the relationship between AOBP and cardiovascular events are much less solid as compared to those obtained with the standard BP measurement; conflicting data are available on the relationship between hypertensive organ damage and "attended" and "unattended" BP.

**Aim:** To evaluate the relationship between "attended" or "unattended" BP values and arterial stiffness in 248 subjects undergoing a visit and assessment of arterial stiffness at an ESH Excellence Centre.

**Methods:** Both "unattended" BP (patient alone in the room, an oscillometric device programmed to perform 3 BP measurements, at 1 min intervals, after 5 min) and "attended" BP were measured with the same device, on the same day of arterial stiffness assessment, in random order.

**Results:** Patient's mean age was  $62.5 \pm 14$  yrs, mean BMI  $26 \pm 4$ , 54% male, 75.4% had hypertension (74% treated). Systolic unattended BP was lower as compared to attended SBP ( $124.7 \pm 14.4$  vs  $131.0 \pm 16.4$  mmHg). PWV was similarly correlated with systolic unattended BP and with attended SBP ( $r = 0.432$  and  $r = 0.448$ ,  $p < 0.0001$ ) and with mean unattended and attended BP ( $r = 0.211$  and  $r = 0.224$ ,  $p < 0.0001$ ). Similar correlations were also observed between PWV and unattended and attended pulse pressure ( $r = 0.484$  and  $r = 0.488$ ,  $p < 0.0001$ ). The differences between correlations were not statistically significant (Steiger's Z test). No significant difference was observed between the ROC curves of attended or unattended SBP for the presence of increased arterial stiffness (AUC 0.674 vs. AUC 0.665,  $p$  for the comparison = ns).

**Conclusions:** Measurement of BP "attended" or "unattended" provides different values, being unattended BP lower as compared to

attended BP. Our results suggest that attended and unattended BP values are similarly correlated with the gold standard measure of arterial stiffness.

## PROGNOSTIC ROLE OF ASCENDING AORTIC REMODELING IN HYPERTENSIVE PATIENTS

D. Leone, L. Airale, S. Bernardi, M. Cesareo, G. Mingrone, A. Astarita, I. Maffei, M. Bollati, F. Veglio, A. Milan

*Centro Ipertensione Arteriosa, Torino, Italy*

**Introduction:** the latest ESC/ESH guidelines underlined the association between arterial hypertension and proximal aortic aneurysm. Studies which analyzed the relationship between cardiovascular events (CVE) and aortic dilatation have been performed only considering aortic diameter at Sinuses of Valsalva (SoV) level, while publications on the possible role of ascending aorta (ASC) are missing.

**Aim:** To evaluate the possible prognostic value (in terms of death, acute aortic syndrome, heart failure, myocardial infarction, arrhythmic events) of ASC dilatation in a population of essential hypertensive subjects.

**Methods:** 438 patients underwent two-dimensional transthoracic echocardiography from 2007 to 2013, and then they were recalled by phone on November 2018. Aortic dilatation has been defined as in previous study using absolute diameters: 36 mm in female, 41 mm in male.

**Results:** dilatation of the ASC was associated with CVE (HR = 2.218,  $p = 0.004$ ) independently of age, systolic blood pressure and sex. Patients with dilatation of ASC without left ventricular hypertrophy (LVH) (ASC+/LVH-) were at higher risk of CVE than those without dilatation or LVH (ASC-/LVH-) regardless of common confounders (HR = 2.005,  $p = 0.039$ ). People with ASC dilatation and LVH (ASC+/LVH+) showed a higher CV risk than those with LVH but no ASC dilatation (ASC-/LVH+; HR = 2.772,  $p = 0.043$ ).

**Conclusions:** ASC dilatation seems to be associated with a greater risk of CV events, regardless of the main confounders. In perspective, ASC dilatation could be considered to better stratify the CV risk of the hypertensive patient.

## EFFECT OF AGEING ON THE HEART RATE DEPENDENCE OF PULSE PRESSURE AMPLIFICATION

G. Pucci<sup>1</sup>, F. Battista<sup>2</sup>, R. Sgariglia<sup>1</sup>, A. Cerasari<sup>1</sup>, I. Dominioni<sup>1</sup>, F. Barsotti<sup>1</sup>, G. Vaudo<sup>1</sup>

<sup>1</sup>*Department of Medicine, University of Perugia-Unit of Internal Medicine, Terni University Hospital, Terni, Italy,* <sup>2</sup>*Sport and Exercise Medicine Division, Department of Medicine, University of Padova, Padova, Italy*

**Introduction:** Pulse pressure amplification (PPA) is considered a non-dimensional marker of early vascular ageing, and is inversely and independently associated to future CV events. It is acknowledged that PPA is influenced by heart rate (HR) and its related changes.

**Aim:** We aimed at evaluating the effect of ageing on the HR dependence of PPA.

**Methods:** In a cohort of 675 never-treated hypertensives (age range 18-89 years, mean age  $47 \pm 11$  years, 56% men), at low-to-intermediate CV risk and without signs of hypertension-mediated organ damage, PPA and simultaneous HR were calculated from radial

tonometry and estimated aortic pressure waveform through a radial-to-aortic generalized transfer function (SphygmoCor). The significance of the interaction term “age (young = below mean, old = above mean) × HR” as an independent predictor of PPA, was tested in a linear multivariate regression model after accounting for the non-linearity of the relationship between age and PPA, and the effect of other confounders (sex, height, carotid-femoral PWV).

**Results:** Mean PPA was  $1.28 \pm 0.15$ , mean HR  $66 \pm 11$  bpm. HR was positively and strongly correlated to PPA ( $p < 0.01$ ), explaining one fifth of its variance. The curvilinear relationship between age and PPA was best described by an inverse logarithmic equation ( $p$  for R change vs linear = 0.04). The interaction term “age × HR” was positively related to PPA after adjusting for multiple confounders ( $p < 0.01$ ). The slope of the relationship between HR and PPA was steeper in old vs young individuals (7.4% vs 5.3% each 10 bpm increase,  $p$  for slope difference = 0.02).

**Conclusions:** In our cohort, age is a significant effect-modifier of the relationship between HR and PPA. Ageing could be associated to more pronounced changes in PPA in response to HR changes. This may suggest a higher central hemodynamic load during low output states (e.g. during night or under the effect of HR-lowering drugs) in old vs young subjects.

## AORTIC STRAIN DECREASES IN HYPERTENSIVE PATIENTS WITH ASCENDING AORTA DILATATION

Marco Cesareo, Luca Sabia, Eleonora Avenatti, Dario Leone, Francesco Tosello, Anna Astarita, Giulia Mingrone, Iaria Maffei, Gaia Zocaro, Lorenzo Airale, Franco Veglio, Alberto Milan

*Internal and Hypertension Division, Department of Medical Sciences, AOU Città della Salute e Scienza, University of Turin, Torino, Italy*

**Introduction:** Ascending aorta (aA) dilatation is the main risk factor for aortic dissection, and it is found in 13% of hypertensive patients. aA dilatation is associated with increased global stiffness of the arterial tree (pulse wave velocity–PWV).

**Aim:** To assess local aA stiffness by strain analysis in hypertensive patients with different severity of aA dilatation compared to a control group.

**Methods:** 104 subjects (mean age  $66 \pm 9$  years, 71% male) underwent transthoracic echocardiography (TTE) and PWV assessment. Strain analysis was performed with speckle-tracking technique: maximal cross-sectional deformation was measured as Peak ascending Aorta Strain (PaAS, %). Stiffness Index was defined as  $100 \times \ln(\text{systolic pressure}/\text{diastolic pressure})/\text{PaAS}$ .

**Results:** PaAS significantly correlated with aA diameter ( $r = -0.50$ ,  $p < 0.001$ ), age ( $r = -0.20$ ,  $p = 0.048$ ), systolic pressure ( $r = -0.27$ ,  $p = 0.006$ ), left ventricular mass ( $r = -0.23$ ,  $p = 0.023$ ) and PWV ( $r = -0.25$ ,  $p = 0.015$ ). PaAS tends to progressively decrease according to severity of aA dilatation ( $p < 0.05$ ). In multivariate analysis, aA diameter was the only variable significantly associated with PaAS. Stiffness index, that takes into account hemodynamic status, rises exponentially with increasing aA dimensions, with dramatic change with aA diameter  $\geq 45$  mm ( $p < 0.05$ ).

**Conclusions:** aA dilatation in hypertensive subjects is associated with increased local aortic stiffness, assessable with strain analysis. Ascending aorta strain analysis can be a useful tool for functional addition to morphological data in hypertensive patients.

## EVALUATION OF ARTERIAL STIFFNESS IN PATIENTS WITH PRIMARY HYPERALDOSTERONISM

L. Petramala<sup>1</sup>, M. Mezzadri<sup>1</sup>, A. Concistrè<sup>1</sup>, V. Bisogni<sup>1</sup>, F. Olmati<sup>1</sup>, V. Saracino<sup>1</sup>, G. Iannucci<sup>2</sup>, C. Letizia<sup>1</sup>

*<sup>1</sup>Dpt of Translational and Precision Medicine, University of Rome “Sapienza”, Italy, <sup>2</sup>Dpt of Internal Medicine and Medical Specialties, University of Rome “Sapienza”, ITALY*

**Introduction:** Primary hyperaldosteronism (PA) represents a frequent cause of arterial hypertension, acting negatively on metabolic and cardiovascular complications; arterial stiffness evaluated by non-invasive method of the Pulse Wave Velocity may detect an early vascular damage in asymptomatic hypertensive patients.

**Methods:** we consecutively enrolled the parameters of arterial stiffness in 91 hypertensive subjects, 44 men (mean age  $50.9 \pm 13.3$  years) and 47 women (mean age  $50.5 \pm 14.8$  years), distinguished in 60 patients with essential arterial hypertension (EH), 22 patients with PA [5 with aldosterone-secreting adrenal adenoma (APA), 17 with idiopathic primary hyperaldosteronism (IHA)] and 9 subjects with non-secretory adrenal mass (INC); all patients were matched for anthropometric and hemodynamic parameters; as control group we enrolled 37 normotensive subjects (SN).

**Results:** The APA group showed a significant increase in the arterial stiffness index ( $11.7 \pm 4.8$  m/s;  $p < 0.02$ ) compared with IHA ( $8.8 \pm 2.3$  m/s), EH ( $8.3 \pm 3$  m/s), INC ( $8 \pm 2.2$  m/s) and normal subjects ( $7.2 \pm 1.7$  m/s). Furthermore, in APA group we found significantly reduced values of subendocardial variability ratio ( $104.8 \pm 25.7\%$ ) and delayed reflected waves ( $83.8 \pm 28.3$  ms) respect to EH ( $120.5 \pm 22$ , 4%,  $112.9 \pm 38.1$  ms, respectively;  $p < 0.05$ ), INC ( $118 \pm 20.2\%$ ,  $115.8 \pm 29$  ms, respectively;  $p < 0.05$ ) and SN ( $119.8 \pm 12\%$ ,  $131.2 \pm 32$  ms, respectively;  $p < 0.05$ ). PA group showed higher percentage of subjects with higher vascular age than chronological age (60%) compared to EH and SN (38% and 37% respectively;  $p < 0.05$ ). Regarding this parameter, APA group showed higher percentage compared to IHA group (80% vs 53%;  $p < 0.01$ ).

**Conclusions:** our study shows that non-invasive analysis of arterial stiffness is useful in the identification of early subclinical vascular remodeling in hypertensive patients, and that PA patients show high prevalence of subclinical organ damage compared to EH subjects.

## REDUCED SLEEP TIME AND THE RISK FOR OBSTRUCTIVE SLEEP APNEA REPRESENT INDEPENDENT PREDICTIVE FACTORS FOR PERIPHERAL VASCULAR DAMAGE

P. Nazzaro, A. Nardecchia, G. Schirosi, M. Contini, F. Caradonna Moscatelli, L. De Benedittis, G. Aceto, M. F Decaro, A.M. Papagni

*Dept of Neurosciences, Hypertension Unit “AM. Pirrelli”, University of Bari “Aldo Moro”, Bari, Italy*

**Introduction:** Many studies highlighted the cardiovascular risk due to sleep apnea syndrome (SAs). On the other hand, very few investigated the ability of predictive tests of SAs in subjects with different ascertained sleep time aiming to recognize how these sleep disturbances could be associated, in hypertensives treated with ARBs or ACEi, as monotherapy, to the micro- and macro-vascular damage.

**Methods:** After medical visit, 163 patients ( $136 \pm 11/82 \pm 12$ ), with similar age, metabolic and hypertensive state, underwent ABPM,

having placed an actigraphy device at the contralateral arm, to register the duration of physical activity (METs > 3:min), body position and, measuring the muscular tone, the duration of sleep (SleepT:min). Then, they also underwent tonometry, to measure arterial stiffness (PWVcf), videocapillaroscopy of the medial and distal phalanx of the 2nd, 3rd and 4th finger of the non-dominant hand during venous congestion (CVC) to determine structural capillary rarefaction, and assessment of cognitive impairment (CIS) by multiple choice (1–4) 18-item questionnaire investigating different neuropsychological functions. The aggregation of predictive factors of SAs (Lausanne) allowed to quantify the risk, low (LL) and high (HL), and to associate it in the patients with shorter (SS) or longer (LS) sleep time.

**Results:** The patients, divided in order of SleepT and Lausanne score, highlighted significant characteristics (m ± s.d.; \*:p < .05, \*\*:p < .01, \*\*\*:p < .001 vs LSHL; ^:p < .05, ^^:p < .01, ^^:p < .001 vs LSHL; °:p < .05, °°:p < .01, °°°:p < .001 vs SSSL).

pts/v ar	SleepT	Lausanne	METS> 3	PWV	CVC	CIS
LSLL	453±64	2.8±2.1	562±301	9.4±1.6	67.3±9.9	23.8±6.1
LSHL	440±57	11.1±2.8***	524±345	11.1±1.8**	62.9±6.1**	25.6±5.4
SSSL	301±53**** ^^	3.1±1.9^^^	575±361	11.2±3.1*	60.1±6.4***	29.4±7.1****
SSHL	257±65**** ^^	11.2±2.1*** °°°	529±313	11.5±3.1**	56.7±5.8**** A*	29.9±7.2**** ^^

Pearson test showed the association between Lausanne score and PWVcf (.324\*\*\*), CVC (- .319\*\*) e CIS (.207\*\*) e tra SleepT e PWVcf (- .269\*\*) e CVC (459\*\*\*) e CIS (- .298\*\*).

**Conclusions:** The findings showed that a restrained sleep time and the risk of SAs are independently associated to the vascular damage, microvascular in particular. Then, to investigate the quality of sleep and its disturbances should be a constitutive part of the examination in hypertensives, in particular if integrated with actigraphy and ABPM.

### THE INFLUENCE OF SIRT-1 ON OBESITY-RELATED ENDOTHELIAL DYSFUNCTION IS MEDIATED BY EPIGENETIC REGULATION OF P66SHC

Emiliano Duranti<sup>1</sup>, Martina Chiriaco<sup>1</sup>, Michele Lai<sup>1</sup>, Ilaria Puxeddu<sup>1</sup>, Monica Nannipieri<sup>1</sup>, Francesco Paneni<sup>2</sup>, Stefano Taddei<sup>1</sup>, Stefano Masi<sup>1</sup>, Agostino Viridis<sup>1</sup>

<sup>1</sup>Università di Pisa, Pisa, Italy, <sup>2</sup>Università di Zurigo, Zurigo, Switzerland

**Introduction:** Sirt-1 and p66Shc are involved in the regulation of cellular ageing through modulation of intracellular free radical production, particularly of mitochondrial origin (mtROS). As experimental models suggest they might influence endothelial function, in this study we assessed the impact of the Sirt-1/p66Shc axis on obesity-related endothelial dysfunction.

**Methods:** Small resistance arteries isolated from subcutaneous fat tissue of 48 obese patients and 47 healthy controls (further stratified by their age above or below 40 years in young and old groups) were mounted on a pressure myograph to assess endothelial function by means of dose–response curves to acetylcholine alone or in combination with SRT1720 (Sirt-1 agonist), MitoTEMPO (mtROS scavenger), gp91ds-tat (NADPH-oxidase inhibitor) and L-NAME (eNOS inhibitor). Sirt-1 and p66Shc expression were assessed by qPCR, while the binding of Sirt-1 to the promoter region of p66Shc was

assessed by CHIP assay. Four arteries from healthy controls were transfected overnight with p66Shc, and their endothelial function was evaluated before and after Sirt-1 incubation and compared with the endothelial function recorded before transfection.

**Results:** In the obese group, the expression of Sirt-1 was reduced while that of p66Shc was increased compared to healthy controls. Sirt-1 stimulation restored endothelial function in the obese and old groups (p < 0.001 vs baseline), but this effect was blocked by co-incubation with L-NAME. MitoTEMPO induced a greater improvement of endothelial function than gp91ds-tat (p < 0.01), and to a similar extent than the incubation with SRT1720. Indeed, incubation with SRT1720 did not further increase endothelial function if arterioles were preincubated with MitoTEMPO. The binding of Sirt-1 to the promoter region of p66Shc was reduced (p < 0.001 vs controls). After transfection with p66Shc, endothelial function was reduced compared to baseline and recovered to baseline following incubation with SRT1720.

**Conclusions:** Sirt-1 influences mtROS through epigenetic regulation of p66Shc and the Sirt-1/p66Shc/mtROS axis contributes to the endothelial dysfunction observed in obesity

### POSSIBLE ROLE OF SPLEEN IN THE DEVELOPMENT OF HYPERTENSION IN HUMANS

De Ciuceis<sup>1</sup>, M. Nardin<sup>1</sup>, C. Rossini<sup>1</sup>, M.A. Coschignano<sup>1</sup>, V. Brami<sup>1</sup>, C. Agabiti Rosei<sup>1</sup>, M. Salvetti<sup>1</sup>, A. Painei<sup>1</sup>, A. Petelca<sup>1</sup>, E. Porteri<sup>1</sup>, G. Chiarini<sup>1</sup>, G. Rossi<sup>2</sup>, G.A.M. Tiberio<sup>3</sup>, M.L. Muiesan<sup>1</sup>, D. Rizzoni<sup>1,4</sup>

<sup>1</sup>Clinica Medica, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, <sup>2</sup>Division of Haematology, ASST Spedali Civili of Brescia, Brescia, Italy, <sup>3</sup>Clinica Chirurgica, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, <sup>4</sup>Istituto Clinico Città di Brescia, Division of Medicine, Brescia, Italy

**Introduction:** Immune system (in particular T lymphocytes) is involved in the pathogenesis of arterial hypertension and microvascular remodelling. It has also been recently suggested a crucial role for spleen in the development and onset of hypertension, through a neuroimmune mechanism mediated by a splenic factor, the Placental growth factor (PIGF), in different models of experimental hypertension. However, to date no data are present in humans.

**Methods:** We therefore investigated 29 patients, who were previously splenectomized for idiopathic thrombocytopenic purpura or marginal lymphoma (clinical conditions associated with good survival) and 10 patients underwent an elective surgical intervention (cholecystectomy) in the same period, well matched for ages, sex and cardiovascular risk factors. In all patients clinical and 24-h blood pressure (BP) were recorded. Wall to lumen ratio of retinal arterioles (WLR) was obtained by Adaptive Optics as index of microvascular damage. Functional (basal) and structural (total) capillary density were studied by capillaroscopy before and after venous congestion.

**Results:** The groups did not present statistically significant differences for clinical or 24-h BP values (clinical BP 126.94 ± 8.20/72.38 ± 13.7 mmHg in splenectomized patients vs 125.56 ± 12.9/76.67 ± 5.59 mmHg in the cholecystectomized patients, p = NS; 24-h BP: 119.7 ± 13.8/66.4 ± 6.60 vs 119.20 ± 8.76/69.10 ± 7.53 mmHg respectively, p = NS). No differences in central BP and Augmentation index were observed between the groups. Retinal arteriole morphology and capillary density did not differ between the groups. However, WLR was slightly higher, albeit not

---

significant, in cholecystectomized than in splenectomized patients (Table).

	Splenectomized patients (n = 19)	Cholecystectomized patients (n = 10)	<i>p</i> value
WLR	0.27 ± 0.40	0.30 ± 0.38	0.10
Internal diameter (mm)	95.03 ± 13.06	89.57 ± 12.07	0.29
External diameter (mm)	121.41 ± 16.21	116.85 ± 15.55	0.48
Wall thickness (mm)	13.19 ± 2.38	13.64 ± 2.22	0.64
WCSA (mm <sup>2</sup> )	4553.5 ± 1254.70	4492 ± 1205.3	0.90

**Conclusions:** Our preliminary data do not confirm in humans the hypothesis of a difference in blood pressure values and indices of microvascular damage in splenectomized patients compared to cholecystectomized patients. However, a statistically not significant trend towards a greater WLR was observed in cholecystectomized patients. For a definitive conclusion about the involvement of the spleen in the genesis of hypertension also in humans it is necessary to extend the evaluation to a larger population.