Design and methods: We enrolled 10 patients suffering from metastatic renal and two from thyroid cancer, age 61±10 years (mean±SD). We measured blood pressure (BP),and cardiac and vascular parameters (standard transthoracic echocardiography complete of total longitudinal strain-tLS and carotid-femoral pulse wave velocity or PWV) before (baseline,B) and after 2 weeks of treatment (T). Data were analysed with non parametric tests for paired comparisons(T vs B)

Results: At B patients showed a normal BP (mean±SD:114±8/75±6mmHg,systolic/diastolic), PWV (10.8±2.2m/sec) and cardiac systo-diastolic function (EF: 59%, E/A: 0.77±0.12, decT 239±43msec, tLS -17.9±1.2).Measurements could not be repeated in 2 patients. In the remaining patients we observed a significant increase in systolic BP (133±18.5mmHg (p=0.003),a significant decrease in strain (-16.4±2.1, p=0.03)and a non significant increase of PWV to 12.2±2.5m/sec(p=0.09) . EF and the other parameters did not change.

Conclusions: Our results show that after two weeks of treatment with anti-VEGF drugs, systolic BP rises without a variation in cardiac function as assessed with EF. There is, however, at cardiac level an impaired longitudinal strain deformation and at vascular level a trend to an augmented arterial stiffness, which suggest that, in addition to a pressor effect, these drugs may unfavourably affect cardiovascular functions. This should be further tested by larger and longer-termed studies.

7B.09 THE PROGNOSTIC SIGNIFICANCE OF DIASTOLIC BLOOD PRESSURE DEPENDS ON AORTIC DAMAGES BUT NOT ON AGE

P. Courand[1,2], F. Khettab[1], G. Bricca[2], J. Fauvel[2], H. Milon[1], P. Lantelme[1,2,3].
[1]Service de Cardiologie, Hôpital de la Croix-Rousse, CHU Lyon, Lyon, FRANCE, [2]EAM 4173, Génomique fonctionnelle de l hypertension artérielle, Université Claude Bernard, Lyon, FRANCE, [3]Service de cardiologie, Hôpital Nord Ouest, Villefranche-sur-Saône, FRANCE

Objectives: With aging, and for the same systolic (S) blood pressure (BP), a low diastolic (D) BP, i.e a high pulse pressure (PP), is associated with a poor prognosis. This association is usually ascribed to aortic stiffening associated with the aging process. However, PP, which is commonly used to address this issue, is both tightly linked with DBP and a surrogate for aortic stiffness precluding the identification of the respective impact of, age, DBP and aortic damages on outcomes. Thus, our study aimed at determining the interactions between the prognostic value of DBP, age and aortic atherosclerosis (ATS).

Design and methods: 938 hypertensive patients recruited in the seventies with an aortography available. A calcification score assessed ATS. All-cause and cardiovascular deaths were assessed after 20 years of follow-up. We performed a survival analysis with a Cox regression model and cubic splines (variation of adjusted hazard ratio for a continuous variable) adjusted for SBP, DBP, age and major cardiovascular risk factor.

Results: An increase of 10 mm Hg of DBP was related to a protective effect in presence of ATS: hazard ratios 0.84 [0.72-0.99] for cardiovascular and 0.88 [0.78-1.00] for all-cause death; conversely, DBP had no prognostic value in absence of ATS: hazard ratios 1.05 [0.89-1.23] for cardiovascular and 0.99 [0.88-1.11] for all-cause death (p for interaction 0.061 and 0.087 respectively). No interaction was found between SBP and ATS (p for interaction NS). The figure below depicts the continuous risk for all-cause mortality according to DBP or SBP and the presence/absence of ATS (ATS +/-) (cubic splines).

Conclusions: The prognostic significance of low DBP is modulated by aortic damage independently of age. In the absence of aortic damage, no prognostic value of low DBP can be demonstrated. Our result can help us reconciling some controversies about the J curve since for a given SBP, low DBP is not always hazardous; it is so only in the presence of a poor aortic condition.

7B.10 MIDDLE AORTIC SYNDROME IN CHILDREN - SINGLE CENTRE EXPERIENCE

J. Antoniewicz[1], G. Brzezinska-Rajszys[2], P. Kalicinski[3], A. Kosciesza[4], M. Pedich[4], J. Daszkowska[2], R. Grenda[1]. *[1]The Children's Memorial Health Institute, Department of Nephrology, Kidney Transplantation & Hypertension, Warsaw, POLAND, [2]The Children's Memorial Health Institute, Department of Cardiology, Warsaw, POLAND, [3]The Children's Memorial Health Institute, Department of Surgery, Warsaw, POLAND, [4]The Children's Memorial Health Institute, Department of Radiology, Warsaw, POLAND*

Introduction: Middle aortic syndrome (MAS) is an uncommon condition characterized by segmental narrowing of the distal thoracic and/or abdominal aorta, commonly involving the visceral and renal arteries, with poorly controlled arterial hypertension.

Objective: Course of disease and treatment efficacy assessment in children with middle aortic syndrome with abdominal aorta involvement.

Material and methods: 23 children (13 girls, 10 boys) aged from 3,5 to 14,8 (mean 9,5±3,6): 6 with neurofibromatosis, 3 with Williams syndrome, 3 with Takayasu disease, 1 with telangiectasis. Renal artery stenosis and visceral arteries stenosis were diagnosed in 22 and 14 patients respectively, in 2 cases thoracic aorta was also involved. All children were observed from 0,8 to 14,5 years (mean 4,9±3,6). 20 patients underwent individualised surgical treatment (vascular surgery, angioplasty, stenting), while 3 were treated conservatively. Final outcome assessment was based on blood pressure index (BPi) analysis, control of target organ damage (left ventricular hypertrophy - LVH) and pharmacotherapy regimen.

Results: 12 children (52%) were accidentally diagnosed with hypertension. In 2 (9%) hypertensive emergencies occured. In all patients BP values were significantly reduced (systolic BPi 1,28 vs.1,1; p<0,05; diastolic BPi 0,96 vs.0,82; p<0,05) and in 12 (52%) finally normalised. In all cases LVH reduction was observed (left ventricular mass index deSimone: 51,4 vs. 34,2 g/m 2.7; p<0,05), although in 5 (22%) LVH persist. Drug intake was decreased from 3,3 in baseline to 3,1 (n.s.).

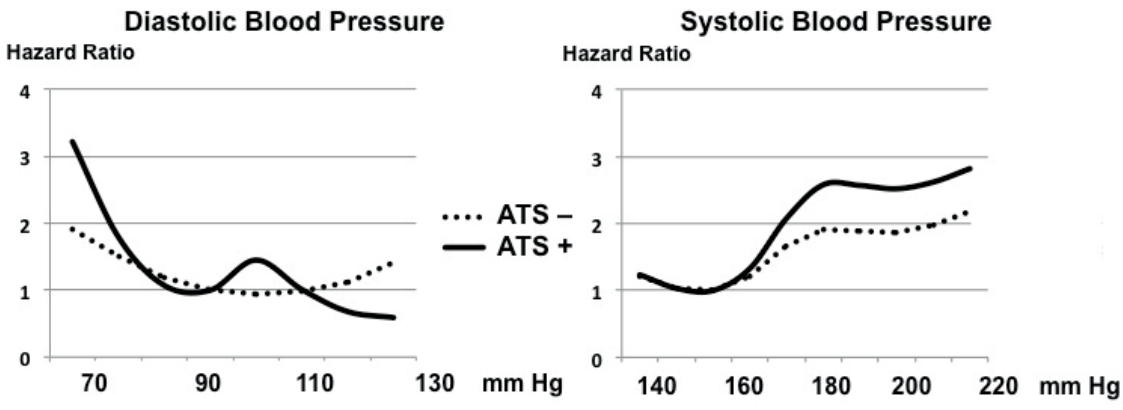
Conclusion: Complex treatment of MAS (surgery and pharmacotherapy) leads to successful clinical outcome.

7B.11 CHANGES IN ARTERIAL STIFFNESS DURING A FIVE-YEARS FOLLOW UP IN A GENERAL POPULATION: THE VOBARNO STUDY

A. Paini, M. Salvetti, C. Aggiusti, D. Stassaldi, F. Bertacchini, C. Agabiti Rosei, G. Rubagotti, G. Maruelli, R. Gatta, E. Agabiti Rosei, M.L. Muiesan.
Internal Medicine, University of Brescia, Brescia, ITALY

Background: Carotid-femoral pulse wave velocity (cfPWV) is an independent predictor of cardiovascular events and its measurement is recommended by cur-

Abstract 7B.09



rent hypertension guidelines. Very few data are available on the progression of PWV over time. The aim of the present longitudinal study was to compare the progression of aortic stiffness over a 5-year period in a general population in Northern Italy (Vobarno Study).

Methods: 227 subjects, 42% males (age 50±4 years and hypertension in 51% at baseline visit), underwent a baseline (BL) and a follow up (FU) visit, after 5.1±0.4 years. In all subjects laboratory examinations, measurement of clinic and 24 hours blood pressure (BP) and of PWV were performed at BL and at FU.

Results: In the overall population cfPWV increased from 8.28±1.27 at BL to 8.51±3.2 m/s at FU ($p<0.05$), change: 0.22±1.25. cfPWV significantly increased from BL to FU in hypertensive subjects (HT) (from 8.61±1.41 to 8.90±1.40, $p<0.01$) but not in normotensives (NT) (from 7.97±1.03 to 8.11±1.11, p n.s). The absolute change in cfPWV from BL to FU progressively increased from -0.052±0.108 in NT, to 0.480±0.163 in treated HT and to 0.483±0.138 in untreated HT (p for linear trend<0.01); after adjustment for possible confounders (age, gender, BMI, baseline cfPWV and change in mean BP from baseline) the difference remained statistically significant. At multivariate analysis the variables independently related to the progression of cfPWV were age (beta 0.18, $p<0.01$) and cfPWV, mean BP at BL (beta -0.55, $p<0.01$, and beta 0.18, $p<0.01$, respectively) and the change in mean BP during follow-up (beta 0.20, $p=0.001$).

Conclusions: In a general population sample in Northern Italy the main determinants of the increase in arterial stiffness during a 5 years FU were age, cfPWV and mean BP at BL and change in mean BP over time.

7B.12 AORTIC STIFFNESS MEASURED BY A NOVEL OSCILLOMETRIC METHOD INDEPENDENTLY PREDICTS CARDIOVASCULAR MORBIDITY AND MORTALITY: A STUDY OF 4146 SUBJECTS

T. Kahan[1], P. Boutouyrie[2], A. Cziráki[3], M. Illyés[3], S. Laurent[2], F.T. Molnár[4], G. Schillaci[5], M. Viigimaa[6]. *[1]Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Stockholm, SWEDEN, [2]Pharmacology Department and INSERM U 970, Hôpital Européen Georges Pompidou, Paris, FRANCE, [3]University of Pécs Medical School, Heart Institute, Pécs, HUNGARY, [4]Budapest University of Technology and Economics, Department of Hydrodynamic Systems, Budapest, HUNGARY, [5]Università degli Studi di Perugia, Unità di Medicina Interna, Terni, ITALY, [6]Tallinn University of Technology, Technomedicum, North Estonia Medical Centre, Tallinn, ESTONIA*

Objective: Carotid-femoral pulse wave velocity (PWV) assessed by applanation tonometry evaluates aortic stiffness and predicts cardiovascular morbidity and mortality independently of classical risk factors. We studied the prognostic information provided by a novel and simple oscillometric method, measuring aortic PWV from a single arm cuff.

Design and method: We studied 4146 subjects (51% women) aged 35-75 years, who attended voluntary health screening in Hungary. Oscillometric aortic PWV (Arteriograph, TensioMed Ltd, Budapest, Hungary) was assessed in addition to a medical history, physical examination, and laboratory tests. Cox regression analyses were used to identify predictive factors for the composite endpoint of all cause mortality, non-fatal myocardial infarction, and non-fatal stroke. All events were provided by the Hungarian National Health Insurance Fund, which performed an independent statistical analysis.

Results: Mean age was 53 years, brachial blood pressure 136/82 mm Hg, and total cholesterol 5.2 mM. There were 16% smokers, 48% patients on cardiovascular medications and 8% on antidiabetic drugs; 10% had a previous cardiovascular hospitalization. There were 241 events (100 deaths, 56 non-fatal myocardial infarctions, and 85 non-fatal strokes) during a mean follow-up of 5.5 years. By univariate analysis a 1.0 m/s increase in aortic PWV was associated with a 1.49 [1.34–1.65] ($P<0.001$; hazard ratio and 95% confidence interval) fold increased risk for the composite endpoint. Aortic PWV independently predicted the composite endpoint in the final model of multivariate analysis (1.14 [1.01–1.30]) adjusted for pulse pressure, ejection duration, male gender, age, concomitant cardiovascular disease and treatment with antiplatelet drugs (all $P<0.05$); body mass index, smoking, heart rate, blood pressure, augmentation index, diabetes, and cardiovascular drug therapy were all accounted for.

Conclusions: Aortic PWV assessed by a simple oscillometric method using an arm cuff only independently predicts all cause mortality and major cardiovascular events in a large cohort of subjects attending health screening. Using a simpler oscillometric cuff method for assessing aortic stiffness may facilitate risk assessment in clinical practice.

ORAL SESSION

ORAL SESSION 7C
RESISTANT HYPERTENSION

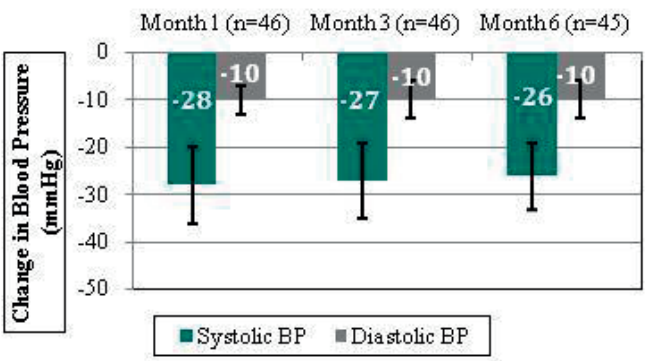
7C.01 SYMPATHETIC RENAL ARTERY DENERVATION WITH A MULTI-ELECTRODE CATHETER IN PATIENTS WITH DRUG-RESISTANT HYPERTENSION: 12 MONTH RESULTS OF THE ENLIGHTN I MULTI-CENTER TRIAL

C. Tsioufis[1], S.G. Worthley[2], M. Worthley[3], D. Chew[4], A. Sinhal[4], I. Meredith[5], Y. Malaiapan[6], V. Papademetriou[7]. *[1]First Cardiology Clinic, Univ. of Athens, Hippokration Hosp., Athens, GREECE, [2]Cardiovascular Res. Ctr., Royal Adelaide Hosp. and Dept. of Med., Univ. of Adelaide, Adelaide, AUSTRALIA, [3]Univ. of Adelaide, Adelaide, AUSTRALIA, [4]Flinders Univ., Flinders Medical Ctr., Adelaide, AUSTRALIA, [5]Monash Heart and Monash Cardiovascular Res. Ctr., Melbourne, AUSTRALIA, [6]Monash Medical Ctr., Monash Heart and Monash Cardiovascular Res. Ctr., Melbourne, AUSTRALIA, [7]VA Med. Ctr., Washington, DC, USA*

Objective: Sympathetic renal artery denervation is emerging as an approach for the treatment of patients with drug-resistant hypertension. Single-tip electrode radiofrequency ablation catheters have been used to achieve sympathetic fiber interruption through the renal artery wall. However,long-term results from multi-electrode systems have not been reported. We investigated the safety and efficacy of a multi-electrode catheter ablation system (EnligHTN) developed by St. Jude Medical.

Design and method: The EnligHTN renal denervation system has 4 electrodes attached on a basket mounted at the tip of the catheter. The basket is collapsed and expanded via an external mechanism. The electrodes are sequentially activated to achieve a predictable lesion pattern. The EnligHTN-I first-in-human study was designed to assess the safety and efficacy of this multi-electrode ablation system in patients with drug-resistant hypertension. A total of 46 patients (average age 60±10yrs, 33% female, taking an average of 4.1±0.6 medications) were enrolled in this study.Bilateral renal nerve ablation was performed using a percutaneous femoral approach. On average 7.7±0.8 lesions were created in the right renal artery and 7.4±1.4 in the left renal artery. The median procedure time was 34 minutes.

Results: Mean baseline office BP was 176/96 mmHg and mean 24h ambulatory BP was 150/83 mmHg. Average significant reductions (mmHg) of office BP ($p<0.001$) at each time point are shown below.



There was also a reduction in 24hr BP by 10/5, 10/5 and 10/6 mmHg($p<0.001$) respectively. At 6 months 33% had normalized BP(<140 mmHg systolicBP). The study utilized an independent Clinical Events Committee to adjudicate all adverse events. There were 3 device/procedure related serious adverse events reported to date which include: hypertensive renal disease progression, symptomatic hypotension and worsening of pre-existing renal artery stenosis. Twelve month efficacy and safety data will be presented at the meeting.

Conclusions: We conclude that data demonstrates that the EnligHTN ablation system continues to be safe and effective in the treatment of patients with drug-resistant hypertension.

7C.02 CREATION OF AN ILIOFEMORAL ARTERIOVENOUS FISTULA IN PATIENTS WITH SEVERE HYPERTENSION: A PROSPECTIVE OPEN LABEL MULTI-CENTER PILOT STUDY

S. Brouwers[1], E. Dolan[2], J. Galvin[3], A. Dupont[1], D. Schoors[1]. *[1]UZ Brussel, Brussels, BELGIUM, [2]Connolly Hospital Blanchardstown, Dublin, IRELAND, [3]Mater Private Hospital, Dublin, IRELAND*

Background: In patients with severe COPD the creation of an iliofemoral arteriovenous fistula (AVF) has been proven to increase functional exercise capacity. In a retrospective analysis of 24 subjects with end-stage COPD and concomitant hypertension, the creation of an iliofemoral fistula also decreased systolic office blood pressure significantly at 12 months by an average off -12.8+/-17.2mmHg.

Methods: An iliofemoral AVF was created using the ROX Anastomotic Coupler System in 8 patients with therapy-resistant hypertension. Office, home and ambulatory blood pressure, heart rate (HR), ECG and renal function (by estimated glomerular filtration rate and creatinine) were monitored at 0, 1, 3 and 6 months.

Results: The 5 males and 3 females (mean age 67.4+/-5.3 years, mean BMI 29.5 +/-4.2) were on an average of 4.0+/-0.8 different antihypertensive drugs. Office systolic blood pressure significantly decreased from 175.3+/-19.1 to 162.8+/-23.9 mmHg after 3 months, and to 157.5+/-26.1 mmHg after 6 months; office diastolic blood pressure decreased from 87.3+/-14.4 to 75.5+/-16.0 mmHg and 73.7+/-18.6 mmHg. Ambulatory systolic blood pressure significantly decreased from 151.8+/-16.7 to 146.2+/-20.7 mmHg after 3 months, and to 142.4+/-17.9 mmHg 6 months after the creation of the fistula; ambulatory diastolic blood pressure decreased from 82.0+/-15.2 to 72.0+/-15.6 mmHg and 69.0+/-14.1 mmHg. Home blood pressure significantly decreased over 6 months from 170+/-21 to 151+/-15 mmHg (systolic), and 95+/-15 to 70+/-8 mmHg (diastolic). HR did not change, no ECG changes were seen, and renal function remained stable throughout the study period. One patient developed mild lower leg edema, no other adverse events were seen.

Conclusions: In this prospective study in 8 patients with therapy-resistant hypertension the creation of an iliofemoral AVF decreased office, home and ambulatory blood pressure after 1, 3 and 6 months. There procedure has proven safety in larger studies in COPD patients. Further exploration of this technique as a possible new approach for treating pharmacotherapy resistant hypertensive patients might be warranted in a larger randomized trial.

7C.03 CAROTID BARORECEPTOR STIMULATION BLOOD PRESSURE RESPONSE MAPPED IN PATIENTS UNDERGOING ELECTIVE CAROTID SURGERY (C-MAP STUDY)

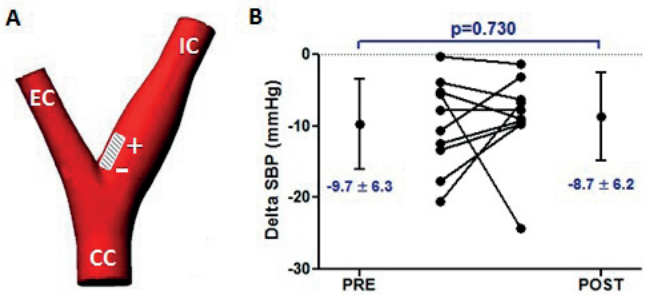
N. Kansal[1], D. Clair[2], D.A. Jaye[3], A. Scheiner[3]. *[1]University of California, San Diego, Department of Surgery, Division of Vascular and Endovascular Surgery, San Diego, CA, USA, [2]The Cleveland Clinic Foundation, Department of Vascular Surgery, Cleveland, OH, USA, [3]Medtronic Inc., Cardiac Rhythm Disease Management, Minneapolis, MN, USA*

Background: Device-based therapies which modulate the autonomic nervous system for the treatment of resistant hypertension and heart failure are under clinical evaluation. Continuous stimulation of the carotid baroreceptors has been shown to evoke a sustained systolic blood pressure (SBP) reduction of 35 mmHg in hypertensive subjects after a 1-year clinical study. However, no published report defines the optimum stimulation location. The Carotid Sinus Autonomic Response Mapping (C-Map) Study is a multicenter, prospective, non-randomized, acute feasibility study which aimed to characterize the dependence of reductions in blood pressure and heart rate (HR) on stimulation location and examine the acute effect of the endarterectomy on stimulation response. Successful baroreceptor stimulation (BRS) mapping may lead to the development of chronically implanted systems which are easier to implant and more effective than currently available systems.

Methods and results: Ten patients undergoing an elective carotid endarterectomy completed the study. Under general anesthesia, the carotid bifurcation was surgically exposed. Before and after plaque removal and vessel repair, multiple extravascular sites in the region of the carotid bifurcation were stimulated. The maximum SBP response to stimulation averaged -12.3±6.9 mmHg ($p<0.001$) with a corresponding HR change of -3.7±5.2 bpm ($p<0.05$) at an output level of 7.6±0.8V, 100Hz, and 0.510ms. The configuration that elicited the largest pressure reduction in 8 of 10 patients was with the electrodes arranged along the medial wall and longitudinal to the internal carotid artery (ICA) near the bifurcation (Figure A). There was no difference in average maximum response pre vs. post plaque removal (Figure B), with maximum response occurring prior to the endarterectomy in 5 of 10 patients, after in 4 of 10 patients, and unchanged in one.

Conclusion: Acute extravascular BRS mapping demonstrated that blood pressure reductions are dependent on electrode location and orientation. The largest SBP reductions were consistently elicited in the region of the medial wall of the ICA. This area can be targeted for future BRS lead design and implant.

Abstract 7C.03



7C.04 ENHANCED BLOOD PRESSURE RESPONSE TO RENAL DENERVATION IN RESISTANT HYPERTENSIVE PATIENTS TREATED WITH THE CENTRALLY ACTING SYMPATHOLYTIC AGENT MOXONIDINE

D. Hering[1,2], G. Lambert[1], P. Marusic[1], A. Walton[3], E. Lambert[1], H. Krum[4], M. Esler[1,3], M. Schlaich[1,3]. *[1]Neurovascular Hypertension & Kidney Disease Laboratory, Baker IDI Heart & Diabetes Institute, Melbourne, AUSTRALIA, [2]Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, POLAND, [3]Heart Centre Alfred Hospital, Melbourne, AUSTRALIA, [4]Monash Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health & Preventive Medicine, Melbourne, AUSTRALIA*

Objective: Renal denervation (RDN) is associated with a significant and sustained blood pressure (BP) reduction and inhibition of muscle sympathetic nerve activity (MSNA) in patients with resistant hypertension (RH). The magnitude of the BP response can vary considerably. We examined whether RH patients treated with the centrally acting sympatholytic agent moxonidine (RH+MOX) respond differently to RDN compared to patients not taking moxonidine (RH-MOX).

Design and methods: Office BP was obtained at baseline, 3, 6 months after RDN in 33 RH+MOX (age 61±2yrs; BMI 33±1kg/m^2) and 32 RH-MOX patients (age 61±1yrs; BMI 33±1kg/m^2, mean±SEM). MSNA was available from 18 RH+MOX and 13 RH-MOX at baseline, 3, 6 month follow-up.

Results: Baseline BP was 171/94±3/2mmHg in RH-MOX and 167/87±3/3 mmHg in RH+MOX (P=0.39 for difference in baseline BP). The change in SBP response to RDN was more pronounced in RH+MOX than in RH-MOX at 3 (comparison between groups:11.98±2.11 mmHg,$P<0.05$) and 6 month (19.24±3.11 mmHg,P=0.002) follow-up (group x visit interaction P=0.032). Baseline MSNA was similar between the two groups (47±3 RH+MOX vs. 46±3 RH-MOX bursts/min,P=0.69). There was a similar reduction in MSNA at 3 (-5±3 RH+MOX vs. -5±2 bursts/min RH-MOX) and 6 months (-5±3 RH+MOX vs. -4±3 bursts/min RH-MOX) with RDN (P=0.01 between visits; group x visit interaction P=0.95).

Conclusions: BP responses to RDN are enhanced in patients receiving the centrally acting sympatholytic agent moxonidine. Our observation of a similar baseline MSNA in both groups may be indicative of either "central moxonidine resistance" (i.e. no substantial effect of moxonidine on baseline central sympathetic outflow), or alternatively, exceedingly high central sympathetic outflow that was reduced to some extent by moxonidine to achieve current baseline levels. Either way, RH patients who display high MSNA despite treatment with the centrally acting sympatholytic agent moxonidine appear to experience a more pronounced BP response to RDN. Whether the sympathetic response to moxonidine could be used as a tool to predict the BP response to RDN merits further investigation.

7C.05 ORALLY ACTIVE AMINOPEPTIDASE A INHIBITORS REDUCE BLOOD PRESSURE BY BLOCKING THE ACTIVITY OF THE BRAIN RENIN-ANGIOTENSIN SYSTEM (RAS): A NEW STRATEGY FOR TREATING HYPERTENSION

Y. Marc[1], J. Gao[1], F. Balavoine[2], B. Roques[3], C. Llorens-Cortes[1]. *[1]INSERM U1050, Collège de France, Paris, FRANCE, [2]Quantum Genomics Society, Massy, FRANCE, [3]Université Paris-Descartes, Paris, FRANCE*

Objective: Overactivity of brain RAS has been implicated in development and maintenance of hypertension (HTA). We previously demonstrated that 1) aminopeptidase A (APA) is the enzyme generating brain angiotensin III (AngIII) and 2) AngIII is one of the main effector peptides of the brain RAS, exerting a tonic stimulatory control over blood pressure (BP) in hypertensive rats. APA thus represents a potential therapeutic target for HTA treatment. Our aim was to demonstrate the antihypertensive effect of RB150/QGC001, a prodrug of the specific and selective APA inhibitor, EC33, when administered orally in two experimental animal models of HTA.

Design and method: Male Wistar-Kyoto, DOCA-salt and spontaneously hypertensive rats (SHR) received oral saline, RB150 (0.3 to 150 mg/kg), enalapril (3 mg/kg), RB150 (100 mg/kg) plus enalapril (1 mg/kg), hexamethonium (20 mg/kg) alone or plus RB150 (150 mg/kg). We recorded invasive BP in conscious rats and measured brain APA enzymatic activity, plasma vasopressin (AVP) levels, diuresis, electrolyte output and renin activity. Toxicity, safety and pharmacokinetics studies were performed in Sprague-Dawley rats and Beagle dogs.

Results: RB150, given orally to DOCA-salt rats or SHRs crossed the intestinal, hepatic and blood brain barriers, entered the brain, generated EC33, which inhibited brain APA activity and dose-dependently decreased BP. BP decrease was due to 1) a reduced AVP release, increasing diuresis, thereby reducing blood volume and 2) a decreased sympathetic tone, reducing vascular resistances. RB150 treatment did not modify systemic RAS activity. In SHRs, concomitant RB150 oral administration with enalapril, a systemic RAS blocker, potentiated the RB150-induced BP decrease. Oral RB150 administration up to 1000 mg/kg to normotensive rats or dogs had no effect on behavior, BP, and respiratory parameters.

Conclusion: RB150 is the first orally active APA inhibitor, inhibiting brain RAS activity, reducing BP for several hours in hypertensive rats. RB150 may be the prototype of a new class of centrally acting antihypertensive agents that could be clinically tested as a novel additional treatment for hypertension.

7C.06 SUSTAINED BLOOD PRESSURE REDUCTION AND SYMPATHETIC INHIBITION ONE YEAR AFTER RENAL DENERVATION IN PATIENTS WITH RESISTANT HYPERTENSION

D. Hering[1,2], E. Lambert[1], P. Marusic[1], A. Walton[3], H. Krum[4], G. Lambert[1], M. Esler[1,3], M. Schlaich [1,3]. *[1]Neurovascular Hypertension & Kidney Disease Laboratory, Baker IDI Heart & Diabetes Institute, Melbourne, AUSTRALIA, [2]Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, POLAND, [3]Heart Centre Alfred Hospital, Melbourne, AUSTRALIA, [4]Monash Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health & Preventive Medicine, Melbourne, AUSTRALIA*

Objective: Renal denervation (RDN) reduces blood pressure (BP) and muscle sympathetic nerve activity (MSNA) in patients with resistant hypertension (RH). Whether the persistent BP lowering effect is accompanied by concurrent sympathetic inhibition following RDN is unknown. We therefore examined the long-term effect of RDN on BP and MSNA in patients with RH.

Design and methods: Office BP and multi-unit MSNA (microneurography) were obtained at baseline and at 3, 6 and 12 months following RDN in 25 patients (age 59±11 years, BMI 32±5 kg/m^2, mean±SD) with RH.

Results: Office BP averaged 171±22/94±16 mm Hg despite the use of an average of 4.6+2.0 antihypertensive drugs. Baseline MSNA was 50±11 bursts/min (79±17 bursts/100heartbeats), approximately 2-3 fold higher than the level typically observed in healthy control subjects. Mean systolic and diastolic office BP decreased significantly by -14.6/-7.3, -19.1/-10.3 and -25.0/-13.5 mmHg ($P<0.001$ for both SBP and DBP) with RDN at 3, 6 and 12 month follow-up, respectively. MSNA was reduced by -9±17, -9±17 and -12±18 bursts/100 heartbeats (P=0.005) at 3, 6 and 12 months follow-up. The reduc-

tion in MSNA was maintained despite a progressive fall in BP over time, following RDN.

Conclusions: These findings confirm previous reports on the favourable effects of RDN on elevated BP and demonstrate sustained inhibition of central sympathetic outflow up to one year follow up in patients with RH and high baseline MSNA. These observations are compatible with the hypothesis of a substantial contribution of afferent renal nerves to increased BP in patients with RH, which can be targeted therapeutically by RDN. Furthermore, our data indicate that occurrence of reinnervation, if any, is of negligible functional relevance.

7C.07 RENAL SYMPATHETIC DENERVATION IS NOT EFFECTIVE IN PATIENTS WITH CASUAL BLOOD PRESSURE LOWER THAN THE SIMPLICITY INCLUSION CRITERIA

S. Linnenweber[1], C. Veltmann[2], J. Menne[1], J. Widder[2], H. Osswald[2], J. Bauersachs[2], H. Haller[1], B. Schmidt[1]. *[1]Hannover Medical School, Department of Nephrology and Hypertension, Hannover, GERMANY, [2]Hannover Medical School, Department of Cardiology and Angiology, Hannover, GERMANY*

Renal sympathetic denervation is a new concept to treat resistant hypertension, which has gained wide distribution in Germany during a rather short time frame of about 2 years. Increasingly, patients are treated which do not fulfill the inclusion criteria of the Simplicity trails.

We examined factors, which might predict the success of renal denervation. This analysis compares patients which fulfill the blood pressure criteria of the Simplicity trials ("Classical criteria") with patients who did not (modified criteria). The latter group mainly consisted of patients who showed resistant hypertension in ambulatory blood pressure measurements but not in casual blood pressure measurements.

Casual blood pressure in patients with classical renal denervation criteria was 196±28 mmHg systolic and 99±23 mmHg diastolic before denervation. The respective values in patients with modified criteria were 131±12 mmHg systolic and 69±5 mmHg diastolic. After 6 months blood pressure had dropped to 164±48 mmHg systolic and 89±24 mmHg diastolic in patients denervated having classical inclusion criteria ($p<0.05$). In patients with modified criteria no change in blood pressure occurred (139±23 mmHg systolic and 79±17 mmHg diastolic, ns). The difference between both groups was statistically significant ($p<0.05$).

Our preliminary data point to the fact that only patients fulfilling the Simplicity criteria for renal denervation should be treated with this new promising method. Patients with lower casual blood pressure levels should not be treated until more evidence is available about the effectivity e.g. on lowering of ambulatory blood pressure or lowering the frequency of hypertensive crises in these patients.

7C.08 RENAL NERVE ABLATION DECREASES MEAN HEART RATE AND IMPROVES HEART RATE VARIABILITY AND ARRHYTHMIC BURDEN IN PATIENTS WITH RESISTANT HYPERTENSION

C. Tsioufis[1], V. Papademetriou[2], D. Tsiachris[1], K. Dimitriadis[1], C. Thomopoulos[1], A. Kasiakogias[1], A. Kordalis[1], A. Kefala[1], N. Koufakis[1], V. Antonakis[1], I. Anastasopoulos[1], I. Bafakis[1], D. Tousoulis[1], I. Kallikazaros[1], C. Stefanadis[1]. *[1]First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, GREECE, [2]Veterans Affairs and Georgetown University Medical Centers, Washington, DC, USA*

Background: Transluminal renal nerve ablation (RNA) reduces blood pressure (BP) in patients with treatment-resistant hypertension. We assessed the effect of RNA on heart rate, cardiac arrhythmias and indexes of heart rate variability (HRV) in patients with resistant hypertension.

Design and methods: Fourteen patients with resistant hypertension underwent ambulatory BP measurements and Holter monitoring at baseline and 1 month after RNA. Patients with grade II and above of the Lown-Wolf classification were considered to have complex ventricular arrhythmias while the presence of >or=3 consecutive premature supraventricular contractions was defined as paroxysmal atrial fibrillation (PAF). SyneScope analysis system calculated the recommended time- and frequency-domain parameters of HRV.

Results: RNA significantly reduced office and 24-hour BP (-38/14.1 mmHg, $p<0.001/0.003$ and -18/9.5 mmHg, $p<0.001/0.001$, respectively) but also office and ambulatory heart rate (by 7 bpm, $p=0.046$ and 5.5 bpm, $p=0.026$, respectively). One month after RNA, a significant decrease in average 24-hour heart rate (- 6.7 bpm, $p=0.022$) and in the number of premature ventricular and supraventricular contractions ($p<0.05$ for both) was noted. Complex ventricular arrhythmias and episodes of PAF were present in 5 patients at baseline and in 2 patients one month after RNA. A significant increase was observed in time and frequency domain indexes during the 24-hour Holter monitoring.

Conclusion: RNA in addition to BP lowering significantly reduces mean heart rate and arrhythmia burden while it restores autonomic balance in patients with resistant hypertension.

7C.09 HIGH INCIDENCE OF SECONDARY HYPERTENSION IN PATIENTS REFERRED FOR RENAL DENERVATION – THE COPENHAGEN EXPERIENCE

L.K. Olsen[1], A.L. Kamper[1], J.H. Svendsen[2], L.E. Bang[2], M. Frimodt-Møller[1], H. Kelbæk[2], M. Sander[2], B. Feldt-Rasmussen[1]. *[1]Rigshospitalet, Department of Nephrology, Copenhagen, DENMARK, [2]Rigshospitalet, Department of Cardiology, Copenhagen, DENMARK*

Objective: Renal denervation (RDN) is a promising new treatment option for patients with resistant hypertension. However, it is important to evaluate the initial experiences with patient selection in order to identify which patients are candidates for RDN. We therefore evaluated the entire population of patients referred for RDN at our tertiary centre.

Design and method: 100 patients were referred for RDN from March 2011 through September 2012. Clinical data were extracted from referral letters, documents from referring clinics and our own hospital. Data are given as mean (±SD) or percentage.

Results: Of the 100 patients 68 were men, with mean age 60 (±12) years. The mean number of antihypertensive agents was 3.9 (±1.6). The mean of clinic blood pressure (BP) was 176 (±28)/99 (±19) mmHg, and 24 h ambulatory BP 156(±20)/88(±13) mmHg. The majority (92%) of the patients were referred due to insufficient BP control, and the remaining due to unacceptable side effects. Referrals came from departments of cardiology (n=38), nephrology (n=20), private cardiology clinics (n=28) and general practitioners/other specialists (n=14). Overall 47 (47%) were candidates for RDN. RDN was rejected in 37 (37%) patients: 2 patients because of ineligible renal artery anatomy, 7 had severe systemic atherosclerosis or aortic disease, 3 had an adrenal tumor, 6 had renal artery stenoses, 5 had sufficient BP control without major pharmacological side effects, and 14 patients were rejected for other reasons such as severe co-morbidities. Furthermore 8 patients declined interest in RDN before completing clinical workup programme and as of now 8 patients were under clinical evaluation for RDN. Thus in total, 84 patients have been evaluated for RDN.

Conclusions: A large group of 11% (9 of 84) of the evaluated patients referred for RDN had secondary hypertension, and of these renal artery stenoses were most common. Secondary hypertension should be ruled out in all hypertension patients especially when insufficient response to therapy is observed.

7C.10 HETEROGENEOUS AND MODEST RESPONSE TO RENAL DENERVATION IN RESISTANT HYPERTENSION – A PROSPECTIVE CASE SERIES

K. Chan, F. Ng, M. Saxena, D. Collier, M. Matson, A. Jain, M. Caulfield, M. Lobo. *William Harvey Research Institute, Barts and The London NIHR Cardiovascular Biomedical Research Unit, QMUL, London, UNITED KINGDOM*

Objective: Renal denervation (RD) by radiofrequency ablation (Symplicity, Medtronic®) has been shown to reduce office blood pressure (OBP) by 32/12 mmHg at 6 months and this was sustained at 28/10 mmHg by 12 months in patients with resistant hypertension. We report the experience from our tertiary referral centre, and aim to identify potential predictors of response.

Method: Patients eligible for RD had baseline systolic blood pressure (SBP) >160 mmHg, with no secondary causes of hypertension or white-coat hypertension; lifestyle factors optimised and confirmed compliance with antihypertensive drugs.

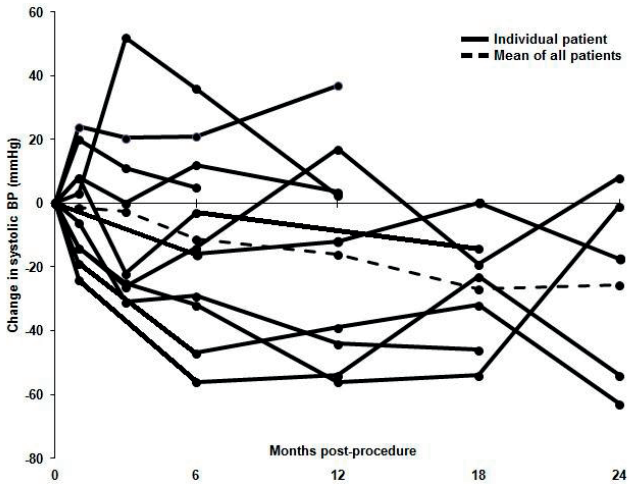
Results: 11 patients (5 men) mean age 59.5 ± 4.1 years with mean baseline OBP 183/103 mmHg underwent RD. On average, patients took 4.4 anti-hypertensives and had median 5 (range 3-7) ablations per renal artery. At 6 months, mean OBP fell by 11/10 mmHg (±9/4); daytime mean ambulatory blood pressure (ABP) reduction was 7/3 ± 6/4 mmHg, with 6 of 11 patients achieving >10 mmHg SBP reduction. One-year results showed modest further lowering compared to baseline: mean OBP fell by 16/9 mmHg (±11/7), and daytime ABP reduction was 9/5 ±3/2 mmHg. However, patients who didn't show >10 mmHg SBP reduction at 6 months continued to be non-responders at 12 months.

Early safety data demonstrates no procedure-related complications and no significant decline in renal function after one year. Pearson correlation analysis showed the following associations: number of radiofrequency ablations (with office SBP reduction; 6-month p=0.02, 12-month p=0.04); baseline daytime ABP pulse pressure (with systolic ABP reduction; 6-month p=0.006, 12-month p=0.001); and we observed some correlation of baseline eGFR with office diastolic BP (6-month p=0.097, 12-month p=0.062).

Conclusion: In our cohort we report markedly heterogeneous efficacy of renal denervation with much lower overall BP reduction than demonstrated in the Symplicity HTN2 cohort. Baseline pulse pressure and the number of RF ablations may be predictors of response to RD and warrant further exploration.

Figure: Change in office systolic BP post-renal denervation

Abstract 7C.10



7C.11 EVOLUTION OF AMBULATORY AND CENTRAL BLOOD PRESSURE AFTER SYMPATHETIC RENAL DENERVATION IN PATIENTS WITH RESISTANT ARTERIAL HYPERTENSION

C. Cerezo[1], A. Fontenla[2], F. Hernandez[2], F. Arribas[2], M. Praga[1], L.M. Ruilope[1], J. Segura[1]. *[1]Hypertension Unit. Department of Nephrology. Hospital 12 de Octubre, Madrid, SPAIN, [2]Unidad de Arritmias y Electrofisiología, Department of Cardiology, Hospital 12 de Octubre, Madrid, SPAIN*

Objective: To analyze the short-term results of the sympathetic renal denervation (RDN) over ambulatory and central blood pressure (BP) levels in patients with resistant hypertension (RH).

Methods: Clinical and analytical data were collected before RDN and after 1, 3 and 6 months. Ambulatory BP monitorization was performed before RDN and after 1, 3 and 6 months. In a subgroup of patients, ambulatory central BP predenervation and at 3 and 6 months of such procedure was measured.

Results: 17 patients with true RH were included, 7 (41.2%) male, mean age of 52.6±13.3 years with diabetes (41.2%), obesity (47.1%), sleep-apnea (35.3%) or previous cardiovascular disease (17.6%). Before RDN they presented a mean clinic systolic/diastolic BP (SBP/DBP) of 167±23/96±13 mmHg, a mean 24-hour ambulatory SBP/DBP of 152±11/90±11 mmHg, and a mean central SBP/DBP of 148±21/99±12 mmHg. The average use of antihypertensive drugs predenervation was 4.35±0.86.
After 1, 3 and 6 months post-procedure, mean clinic SBP/DBP values were 143±16/86±9 mmHg (p<0.001), 150±35/92±17 mmHg (p=0.248 and p=0.366), and 153±21/90±7 mmHg (p=0.015 and p=0.200), respectively. The number of antihypertensive drugs at 1, 3 and 6 months post-denervation was 4.0±0.84 (p=0.055), 3.5±1.0 (p=0.013) y 3.2±1.4 (p=0.043), respectively. After 1, 3 and 6 months post-denervation, mean 24-hour ambulatory SBP/DBP values were 134±16/81±10 mmHg (p=0.003 and p=0.001), 146±17/92±14 mmHg (p=0.542 and p=0696), and 143±25/80±7 mmHg (p=0.324 and p=0.225), respectively. The mean daytime and nighttime BP showed a similar behaviour throughout the treatment.
After 3 and 6 months of follow-up, ambulatory central SBP/DBP values were 151±25/102±12 mmHg (p=0.339 and 0.172), y 127±21/88±11 mmHg (p=0.586 and p=0.629), respectively, even though the number of patients with available central BP data is still low.

Conclusions: In patients with RH, sympathetic renal denervation produces a significant decrease in clinic and ambulatory BP at short-term as well as a reduction of the need for antiypertensive drugs. In clinical practice, such reductions of antihypertensive drugs should be done carefully to avoid an upturn of BP levels.

7C.12 POOR SLEEP QUALITY AND RESISTANT HYPERTENSION

R. Bruno[1], L. Palagini[2], A. Gemignani[2], L. Bontempelli[2], A. Di Giulio[3], A. Virdis[3], L. Ghiadoni[3], S. Taddei[3]. *[1]CNR - Institute of Clinical Physiology, Pisa, ITALY, [2]University of Pisa, Department of Neuroscience, Pisa, ITALY, [3]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, ITALY*

Objective: To determine the relationship between sleep quality and treatment resistant hypertension.

Design and methods: In this cross sectional, cohort study, 270 consecutive essential hypertensive patients were recruited at an Outpatient Hypertension Unit. Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI-Y2) were administered to all subjects. Resistant hypertension (RH) was defined as office blood pressure >140/90 mmHg with 3 or more antihypertensive drugs, or controlled blood pressure with 4 or more drugs. Poor sleep quality was defined as PSQI > 5, depressive symptoms as BDI > 10, and trait anxiety as STAI-Y2 > 40. Patients with other sleep disorders were excluded.

Results: Complete data were available for 222 patients (50.9% males, age 56.6 ± 12.5 years, RH 14.9%). Poor sleep quality had a prevalence of 38.2% in the overall population. RH was associated with poor sleep quality, increased sleep latency and reduced sleep efficiency. No significant relation have been found between RH and short sleep duration, depressive symptoms and trait anxiety. Poor sleep quality prevalence was higher in RH vs non-RH women (70.6%vs40.2 %, p=0.02), but not in RH vs non-RH men (43.8%vs 29.2% , p=0.24). In women, Poor sleep quality was an independent predictor of RH, even after adjustment for cardiovascular and psychiatric comorbidites (OR 5.3, CI 1.1-27.6), explaining 4.7% of its variance. In men, age, diabetes and obesity were the only variables associated with RH.

Conclusions: Poor sleep quality was significantly associated with RH in women, suggesting a new therapeutic target in this population.

ORAL SESSION

ORAL SESSION 7D
KIDNEY AND RENIN-ANGIOTENSIN SYSTEM

7D.01 EVIDENCE FOR FUNCTIONAL INTERACTION BETWEEN THE AT2-RECEPTOR AND THE RECEPTOR MAS

J. Leonhardt[1], K. Lucht[1], P. Namsolleck[2], M. Bader[3], D.C. Villela[1,4], R.A. Santos[4], T. Unger[2], U.M. Steckelings[1,5]. *[1]Center for Cardiovascular Research, Charité - Medical Faculty Berlin, Berlin, GERMANY, [2]Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, THE NETHERLANDS, [3]Max-Delbrück-Center for Molecular Medicine, Berlin, GERMANY, [4]Federal University of Minas Gerais, Belo Horizonte, BRAZIL, [5]IMM - Department of Cardiovascular and Renal Research, University of Southern Denmark, Odense, DENMARK*

Background: The receptor Mas (MasR) and the AT2-receptor (AT2R) are seven transmembrane, G-protein coupled receptors within the renin-angiotensin-system. Both receptors mediate tissue-protective actions in a very similar way. Moreover, various studies reported that effects of MasR-agonists could be abolished by AT2R-antagonists. Therefore a mutual interaction, e.g. dimerization, between the two receptors has been hypothesized.

Objective: The aim of this study was to investigate whether there is an interaction between MasR and AT2R in a sense that blockade or knockout of one receptor would have an impact on the function of the respective other receptor.

Design and methods: CX3CR1 mRNA expression was used as readout and measured by qRT-PCR in primary astrocytes in vitro. Astrocytes were isolated from wildtype (C57Bl-6), AT2R- or MasR-knockout mice and stimulated for 6 hours with the MasR agonist angiotensin-(1-7) (Ang1-7; 1μM), the AT2R-agonist Compound 21 (C21;1μM), TNFα (10ng/μl; served as technical control) or vehicle. Some cells were additionally pre-stimulated for 60 min with the AT2R-blocker PD123.319 (10μM) or the MasR-blocker A-779 (10μM).

Results: mRNA encoding the chemokine receptor CX3CR1 was significantly upregulated by both, stimulation of the AT2R and the MasR in primary murine astrocytes in vitro. Effects of Ang-(1-7) or C21 on CX3CR1 expression were completely absent when their respective receptor was either pharmacologically blocked or knocked out. Surprisingly, effects of Ang-(1-7) and C21 were also eliminated when the respective other receptor (AT2 in case of Ang-(1-7), MasR in case of C21) was blocked or deleted. Showing a significant modulation of CX3CR1 expression by stimulation with TNFα controlled for technical accuracy of the assays.

Conclusion: Our results suggest that in primary mouse astrocytes, there is a functional interaction/dependence between MasR and AT2R. This data are supported by recent data from our group showing AT2R-MasR-dimerisation by FRET.

7D.02 RENIN INHIBITION VERSUS ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKADE IN ANEURYSMAL FIBULIN-4 MICE: UNRAVELING THE IMPORTANCE OF ANGIOTENSIN II TYPE 2 RECEPTOR STIMULATION

L. Te Riet[1], E. Moltzer[2], E.D. Van Deel[3], L. Speelman[4], P.M. Van Heijningen[3], J.N. Van Vliet[3], M. Vermeij[5], I. Van Der Pluijm[1], E.V. Rouwet[1], A.H.J. Danser[2], J. Essers[3]. *[1]Vascular Surgery, Erasmus MC, Rotterdam, THE NETHERLANDS, [2]Internal Medicine, Erasmus MC, Rotterdam, THE NETHERLANDS, [3]Cell Biology & Genetics, Erasmus MC, Rotterdam, THE NETHERLANDS, [4]Biomedical Engineering, Erasmus MC, Rotterdam, THE NETHERLANDS, [5]Pathology, Erasmus MC, Rotterdam, THE NETHERLANDS*

Objective: Increasing evidence supports a role for the angiotensin (Ang) II-Ang II type 1 receptor (AT1R)-TGFβ axis in aneurysm development. Counteracting this axis, e.g., by stimulating Ang II type 2 (AT2) R (which antagonize AT1R-mediated effects) may thus be beneficial. Such stimulation will occur during treatment with an AT1R blocker, since the elevated Ang II levels that accompany such blockade can only bind to the non-blocked AT2R. It will not occur during renin or ACE inhibition.

Methods: To study the importance of AT2R stimulation, we treated aneurysmal homozygous Fibulin-4R/R mice with the AT1R blocker losartan or the renin inhibitor aliskiren (60 and 62.5 mg/kg p.o. per day, resp.). These mice display a 4-fold reduced fibulin-4 expression, which results in cystic media degeneration, aortic regurgitation, left ventricular dilation, a reduced ejection fraction, and fractional shortening. Treatment started pre- or postnatally (on day E14.5 and 60), and lasted up to E19.5 and >160 days.

Results: Prenatal losartan exposure blunted the enhanced TGFβ signalling (evidenced by immunostaining for pSmad2, an intracellular TGFβ mediator), in addition to its blood pressure-lowering effect. It also prevented elastic fiber fragmentation in the aortic media of newborn Fibulin-4R/R mice. Postnatal treatment with losartan or aliskiren similarly reduced hemodynamic stress, and increased the lifespan of Fibulin-4R/R mice (which normally die at ~120 days) to >160 days. Elastic fiber fragmentation was not rescued in established aneurysms by either drug, although aliskiren reduced aneurysmal size in adult mice. Postnatal treatment with losartan or aliskiren marginally affected cardiac structure, but dramatically improved cardiac function with increased ejection fraction of 2-fold.

Conclusion: In established aortic aneurysms neither losartan nor aliskiren prevents aortic media degeneration, although aliskiren did reduce aneurysm size. Both drugs identically lowered blood pressure, and improved cardiac function and survival. These data support suppression of the Ang II-AT1R-TGFβ axis rather than AT2R stimulation as the main reason for the beneficial effects of RAS blockade in aneurysm development.

7D.03 ANGIOTENSIN II RECEPTOR–INTERACTING MOLECULE, ATRAP, EXERTS A SELECTIVE INHIBITORY MODULATION ON PATHOLOGICAL ACTIVATION OF TISSUE ANGIOTENSIN II RECEPTOR SIGNALING IN HYPERTENSION

K. Tamura[1], H. Wakui[1], A. Maeda[1], M. Ohsawa[1], T. Dejima[2], K. Azushima[1], T. Kanaoka[1], K. Uneda[1], R. Kobayashi[1], S. Haku[1], K. Azuma[3], Y. Toya[1], A. Yamashita[4], S. Umemura[1]. *[1]Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, Yokohama, JAPAN, [2]Department of Cardiology, International Goodwill Hospital, Yokohama, JAPAN, [3]Department of Nephrology and Hypertension, Yokohama Dai-ichi Hospital, Yokohama, JAPAN, [4]Department of Molecular Biology, Yokohama City University Graduate School of Medicine, Yokohama, JAPAN*

The ATRAP/Agtrap was identified as an interacting molecule with the cytoplasmic carboxyl-terminal domain of Ang II type 1 receptor (AT1R), and previous in vitro and in vivo studies showed that ATRAP promotes constitutive internalization of the AT1R so as to specifically inhibit the pathological activation of its downstream signaling, such as p38MAPK and calcineurin/NFAT pathways, but preserve baseline physiological signaling activity including ERK1/2 and JNK pathways.

Thus, the balance of the endogenous expression of ATRAP and AT1R in local tissues may be important in the regulation of RAS under pathological but not physiological condition, and ATRAP may exert a functionally selective inhibition on AT1R signaling pathways under pathological conditions. In Ang II-infused mice and genetically hypertensive rats, development of hypertension and organ injury such as cardiac hypertrophy and renal fibrosis was accompanied with a decrease in tissue ATRAP expression, but without change in tissue AT1R expression.

To examine hypothesis that a tissue-specific regulatory balancing of ATRAP and AT1R expression may be involved in modulation of pathological AT1R signaling in each tissue, we generated ATRAP transgenic mice (TGM) and knockout mice. In cardiac-specific ATRAP TGM, development of cardiac hypertrophy, activation of p38MAPK, and expression of hypertrophy-related genes in response to Ang II stimulation were abolished, in spite of no BP difference between TGM and control mice. In kidney-dominant ATRAP TGM, development of hypertension in response to high-salt loading was suppressed, concomitant with an increase in urinary sodium excretion through down-regulation of epithelial sodium channels. Furthermore, targeted gene disruption of ATRAP promoted dietary high fat loading-mediated hypertension and adipose tissue inflammation, which were associated with insulin resistance.

These results suggest that ATRAP functions as an endogenous and functionally selective inhibitor of tissue AT1R, which is able to block pathological receptor signaling but preserve physiological receptor signaling in hypertension and metabolic disorders.

7D.04 P2Y2 RECEPTOR DEFICIENCY AGGRAVATES PROGRESSION OF CHRONIC KIDNEY DISEASE

S. Potthoff, J. Stegbauer, J. Wagenhaeuser, B. Duvnjak, L.C. Rump, O. Vonend.
Medical Faculty, Department of Nephrology, University Düsseldorf, Düsseldorf, GERMANY

Purinergic signaling is involved in various pathophysiological states. Nucleotides, predominantly ATP and UTP, are the main agonists for P2Y receptors. In chronic kidney disease(CKD), sympathetic overactivity, endothelial dysfunction and increase in shear stress contribute to a higher extracellular abundance of ATP. P2Y2 receptors play an important role in renal tubule function, inflammation and proliferation. Knockout mice (P2Y2R-KO) were used to investigate the impact of P2Y2-receptors in CKD.

Wildtype(WT) and P2Y2R-KO mice underwent subtotal nephrectomy (SNX; follow-up of 56±2 days). Survival, kidney function, kidney size, blood pressure (BP), glomerulosclereosis-index were assessed. Profibrotic and pro-inflammatory pathways were assessed via qPCR. A [3H]-thyimidine-based proliferation assay was performed to examine the effect of extracellular ATP on glomerular epithelium cells(GEC).

Survival was inferior in P2Y2R-KO mice after SNX compared to WT (63.1% vs. 88.9%). Increase in serum-creatinine and serum-urea with a significant decrease in creatinine-clearance was present in each group. However, decline in creatinine-clearance was significantly more pronounced in P2Y2R-KO mice (day56, P2Y2R-KO vs. WT: 53.9±7.7 vs. 84.3±8.7 μl/min;p<0.05). BP increased to a higher extent in P2Y2R-KO compared to WT-mice (day56, P2Y2R-KO vs. WT: 177±2 vs. 156±7 mmHg;p<0.05). Glomerulosclerosis-index was not significantly different. However, P2Y2R-KO showed a 2.5-fold higher urinary albumin-creatinine-ratio (UACR) compared to WT (day 56;p<0.05). Also, WT-kidneys showed a significant increase in remnant kidney weight (RKW) whereas hypertrophy was abolished in P2Y2R-KO mice (RKW compared to day0: P2Y2R-KO vs. WT: 113±6 vs. 150±6 %;p<0.05).At day 56, qPCR data indicated a significant increase the profibrotic TGF-β1 (2.2; S.E.: 1.0–4.5) and PAI1 (4.3; S.E.: 1.4–22.2) and the proinflammatory MCP1 (4.1; S.E.: 1.1–32.7) in P2Y2R-KO vs. WT mice. In GEC, ATP induced a significant, dose dependent increase in DNA-synthesis up to 180.1 ± 20.5 %.

In summary, P2Y2R-KO compared WT mice show a worse outcome after SNX. Higher BP, increased UACR and absence of compensatory hypertrophy are the main contributing factors. Hence, P2Y2 receptor is crucial for BP regulation and tissue adaptation in CKD.

7D.05 HYPERTENSIVE NORMOFILTERERS WITH FORMER GLOMERULAR HYPERFILTRATION HAVE INCREASED SYMPATHETIC ACTIVITY AND HIGHER RISK OF RENAL DAMAGE

E. Benetti[1], F. Saladini[1], R. De Toni[1], C. Fania[1], L. Mos[2], P. Ballerini[3], A. Bortolazzi[4], G. Zanata[5], A. Mazzer[3], P. Palatini[1]. *[1]University of Padova, Padua, ITALY, [2]Town Hospital, San Daniele del Friuli, ITALY, [3]Town Hospital, Vittorio Veneto, ITALY, [4]Town Hospital, Rovigo, ITALY, [5]Town Hospital, Pordenone, ITALY*

Objective: In the majority of hypertensive subjects normofiltration represents a state of preserved renal function. However, previous research has shown that some normofilterers may represent a group of former hyperfilterers with increased risk of microalbuminuria. We did a prospective study to investigate whether in hypertensive normofilterers with former glomerular hyperfiltration, clinical characteristics differ from those of true normofilterers.

Design and methods: Creatinine clearance (CrCl) and albumin excretion rate (AER) were measured at entry and after 8.5 years of follow-up, in 534 young-to-middle-age stage 1 hypertensive subjects from the HARVEST (mean age 34.6±8.3 years, 69% men). All subjects remained untreated throughout the study. Glomerular hyperfiltration was defined as a CrCl>=150 ml/min/1.73m2. Baseline ambulatory BP, 24h urinary epinephrine, echocardiographic data, and routine blood tests were also obtained.

Results: At follow-up end, 442 participants were normofilterers. Of these, 395 had normal CrCl at baseline (true normofilterers, Group 1) whereas 47 subjects had a baseline CrCl >=150 ml/min/1.73m2 (former hyperfilterers, Group 2). Participants of Group 2 had higher age-and-sex-adjusted systolic blood pressure (p=.007) than those of Group 1. In addition, 24h urinary epinephrine (p<.001), heart rate (p=.05), ambulatory night-time BP fall (p=.004), and left ventricular end-systolic stress (p=.01) were higher in Group 2. During the follow-up, subjects of Group 2 had a greater baseline-adjusted increase in glucose than those of Group 1 (p=.03) and a tendency to the impairment in the other metabolic data. At follow-up end, microalbuminuria was 5.3% in subjects of Group 1 and was 36.2% in those of Group 2 (p<0.0001). This difference held true in a multivariable logistic regression in which several confounders, ambulatory blood pressure, baseline AER, and other risk factors were taken into account (p<0.0001).

Conclusions: These data show that young-to-middle-age hypertensive normofilterers with former hyperfiltration are a distinct subgroup characterized by higher sympatho-adrenergic activity and poorer metabolic profile. These patients are at increased risk of renal damage and should be treated earlier for hypertension.

7D.06 ACTIVATION OF ANGIOTENSIN II TYPE 1 RECEPTOR-ASSOCIATED PROTEIN SUPPRESSES VASCULAR HYPERTROPHY AND OXIDATIVE STRESS IN ANGIOTENSIN II MEDIATED HYPERTENSION

T. Dejima[1], K. Tamura[2], H. Wakui[2], A. Maeda[2], M. Ohsawa[2], K. Uneda[2], T. Kanaoka[2], K. Azushima[2], K. Azuma[3], A. Yamashita[4], S. Umemura[2].
[1]Department of Cardiology, International Goodwill Hospital, Yokohama, JAPAN, [2]Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, Yokohama, JAPAN, [3]Department of Nephrology and Hypertension, Yokohama Dai-ichi Hospital, Yokohama, JAPAN, [4]Department of Molecular Biology, Yokohama City University Graduate School of Medicine, Yokohama, JAPAN

Backgrounds: We previously cloned a molecule interacting with Ang II type 1 receptor, which we named ATRAP (for Ang II type 1 receptor-associated protein). Previous in vitro studies showed that ATRAP promotes constitutive internalization of the Ang II type 1 receptor and further attenuates Ang II-mediated hypertrophic responses in cardiovascular cells. Increased reactive oxygen species (ROS) are implicated in several vascular pathological states associated with vascular hypertrophy.

Objective: The present study was designed to investigate the putative functional role of ATRAP in vascular hypertrophy and oxidative stress in hypertension in vivo.

Methods and results: We first examined the effect of Ang II infusion on aortic hypertrophy and NADPH oxidase components expression in the aorta of C57BL/6J wild-type mice. The Ang II treatment promoted vascular hypertrophy in aorta, with a concomitant and significant increase in the expression of aortic NADPH oxidase components. We next generated transgenic mice expressing ATRAP in tissues including aorta under control of the β-actin promoter. Systolic blood pressure did not differ between wild-type mice and ATRAP transgenic mice at baseline and comparably and significantly increased both in wild-type mice and in ATRAP transgenic mice in response to Ang II infusion. However, in the aorta of ATRAP transgenic mice, the Ang II hypertension-mediated development of vascular hypertrophy and activation of NADPH oxidase components were significantly suppressed.

Conclusion: These results demonstrate that activation of ATRAP at local tissue sites including aorta efficiently inhibits the vascular hypertrophy and oxidative stress provoked by Ang II-mediated hypertension, thereby suggesting ATRAP to be a novel therapeutic target in vascular disease.

7D.07 INHIBITION OF PHOSPHODIESTERASE 5 ATTENUATES ANGIOTENSIN II-DEPENDENT HYPERTENSION AND VASCULAR FUNCTION IN WILD TYPE BUT NOT IN ENOS-KO MICE

S. Potthoff, S. Sivritas, M. Hoffman, S. Stramer, L.C. Rump, J. Stegbauer.
Medical Faculty, Department of Nephrology, University Düsseldorf, Düsseldorf, GERMANY

In the regulation of vascular tone, the vasoconstrictor response of angiotensin II (AngII) is balanced by the NO/cGMP pathway. Inhibition of phosphodiesterase 5 (PDE5) via sildenafil reduces the degradation of cyclic GMP (cGMP) and thereby increases nitric oxide (NO) dependent vasorelaxation. Elevated AngII levels cause hypertension and reduce endothelium-dependent relaxation by decreasing NO-bioavailability. To examine the role of the NO/cGMP pathway in AngII-induced hypertension, AngII was administered via osmotic minipumps (500ng/kg/min; 14 days) in wild type mice and eNOS-KO mice, a model for endothelium dependent dysfunction. At day 14, vascular function was tested in isolated perfused kidneys.

During AngII treatment, systolic blood pressure was significantly higher in eNOS-KO compared to WT-mice (174±23 vs. 156±4mmHg; P<0.01). Due to the incapacity of NO-synthesis, urinary and renal cGMP levels were significant lower in AngII treated eNOS-KO mice. In isolated perfused kidneys, NO-dependent vasorelaxation was significantly impaired in AngII treated WT mice. In contrast, AngII treatment did not affect NO-dependent vasorelaxation in eNOS-KO mice. To elucidate the role of PDE5 in AngII-dependent vascular dysfunction and hypertension, WT and eNOS-KO mice were treated either with or without sildenafil (100mg/kg/d) in addition to AngII-treatment. Interestingly, sildenafil treatment significantly reduced systolic blood pressure elevation in WT mice (with vs. without sildenafil: 156±4 vs. 139±7; p<0.05) but not in eNOS-KO mice (with vs. without sildenafil: 174±23 vs. 169±11; p=NS). Accordingly, sildenafil-treatment improved NO-dependent vasorelaxation in kidneys of AngII treated WT but not eNOS-KO mice.

In WT mice, chronic sildenafil treatment ameliorates AngII-dependent hypertension and endothelium dependent dysfunction through the inhibition of cGMP degradation. These findings are absent in eNOS-KO mice due to the lack of NO-dependent cGMP production in these mice.

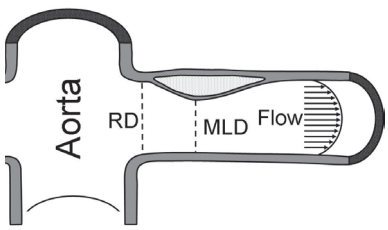
In conclusion, this study reveals new evidence for the pivotal role of PDE5 in the pathogenesis of AngII-induced hypertension.

7D.08 MINIMAL RENAL ARTERY DIAMETER AND CARDIOVASCULAR EVENTS IN SUBJECTS WITH ISCHEMIC HEART DISEASE AND NON-SIGNIFICANT RENAL ARTERY STENOSYS

L. Zanoli[1], S. Rastelli[1], C. Marcantoni[2], J. Blanco[1], D. Capodanno[3], I. Torrisi[1], C. Tamburino[3], P. Boutouyrie[4], S. Laurent[4], P. Castellino[1]. *[1]Internal Medicine, University of Catania, Catania, ITALY, [2]Nephrology Department, Cannizzaro Hospital, Catania, ITALY, [3]Cardiology, University of Catania, Catania, ITALY, [4]Pharmacology, INSERM U960, AP-HP, HEGP, Paris, FRANCE*

Recently, our group reported for the first time that small renal arteries, defined by a low reference diameter(RD<5.2mm) or minimal luminal diameter (MLD<2.9mm) (Fig.1), are independently associated with low GFR and resistant hypertension, independent of the degree of stenosis and major confounders. In the present study we took advantage of the RAS-CAD cohort to test whether the renal artery diameter (either RD<5.2mm or MLD<2.9mm) could impact the prognosis of patients with coronary artery disease (CAD) and non-significant renal artery stenosis (RAS 10-70%) independent of major confounders.

Fig.1



Methods: We used proportional hazards models to analyze the first-onset of major cardiovascular (CV) events (myocardial infarction, heart failure, stroke or cardiovascular death) in relation to MLD and RD in 185 participants with RAS 10-70% (mean age, 67 years; 32% women).

Results: During a median follow-up of 4.5 (range, 0.1 to 5) years, 64 of 185 participants (34.6%) experienced a major CV event. Subjects with MLD<2.9mm are associated with higher risk of cardiovascular events. The RR for MLD<2.9mm to be associated with major CV event was 2.04 (95% CI: 1.17- 3.57; P=0.01), in multivariable models adjusted for age, sex, smoking, and presence of dyslipidemia, hypertension, diabetes mellitus, chronic kidney disease and 2-3 coronary stenoses >70%. When MLD was added to a standard risk factor model, integrated discrimination improvement was 2.3% (from 71.3% to 73.6%).

Conclusions: In patients with CAD and non-significant renal artery stenosis (RAS 10-70%), MLD<2.9mm is associated with increased risk for a first cardiovascular event. MLD improves risk prediction when added to standard risk factors and may represent a valuable biomarker of cardiovascular disease risk in patients with ischemic heart disease and non-significant renal artery stenosis.

7D.09 PLASMA SOLUBLE (PRO)RENIN RECEPTOR IS NOT RELATED TO PLASMA RENIN OR PRORENIN IN PATIENTS WITH VARIOUS DEGREES OF RENIN ANGIOTENSIN SYSTEM ACTIVATION

A. Blanchard[1], D. Bergerot[1], Y. Chambon[1], M. Monge[1], E. Curris[1], M. Azizi[1], G. Nguyen[2]. *[1]Assistance Publique des Hôpitaux de Paris, Center for Clinical Investigation, European Hospital Georges Pompidou, Paris, FRANCE, [2]UMR CNRS7241/InsermU1050 and College de France, Paris, FRANCE*

Objective: To investigate the impact of various degrees of renin angiotensin system (RAS) activation on plasma concentration of the soluble form of the (pro)renin receptor (sPRRc).

Design and method: We studied 40 patients (pts) with type-2 diabetes (with or without microangiopapthy, Db+/Db-), 44 patients with hypertension (with or without RAS blockers, HTN+/HTN-), 10 pts with primary aldosteronism (PA), 11 pts with Gitelman's syndrome (GS), 1 pt with a renin tumor (RT) and 131 healthy subjects (HS). sPRRc (ELISA), renin (PRC), prorenin (proR, IRMA) and aldosterone (PAC, RIA) concentrations were measured on ad libitum sodium (Na) diet at 09:00 after 1-h rest in the supine position.

Results: sPRRc was 1000- and 100-fold higher than PRC and proR in HS, respectively. Db+ or Db- pts did not have higher sPRRc than HS in spite of higher PRC and proR. sPRRc was significantly higher in HTN+ pts than in HS but this was not the case in HTN- pts. sPRRc was similar in PA and GS pts and significantly higher than in HS even though they had very contrasted PRC and proR. Despite a very high PRC and proR, RT pt had a low sPRRc.

Conclusion: sPRRc is higher in HTN+, PA and GS pts than in HS without any correlation with PRC and proR suggesting that sPRR and RAS regulation are independent.

	sPRR (ng/mL)	PRC (mUI/L)	ProR (mUI/L)	PAC (pg/mL)
HS (n=131)	23.2±4.7	19 (17;21)	192 (178;207)	40 (35;44)
Db- (n=20)	24.8±5.9	35 (20;63)†	235 (137;403)	27 (19;37)
Db+ (n=20)	24.8±5.3	42 (23;77)†	644 (437;950)‡	27 (19;40)
HTN- (n=23)	25.4±5.6	12 (9;17)*	139 (101;190)	47 (38;59)
HTN+ (n=21)	27.2±4.6*	54 (42;69)‡	328 (262;411)‡	32 (25;43)
PA (n=10)	27.6±5.5*	7 (3.6;14)‡	99 (55;178)‡	211 (92;481)‡
GS (n=11)	26.7±6.3*	127 (68;237)‡	690 (398;1197)‡	114 (57;229)‡
RT (n=1)	15.6	308	3064	256

Data are mean±SD or geometric mean (95%CI). * p<0.05, † p<0.01 and ‡ p<0.001 vs. HS

7D.10 PREVALENCE AND FACTORS ASSOCIATED WITH 'WHITE-COAT' HYPERTENSION AND MASKED HYPERTENSION IN 5,693 HYPERTENSIVE PATIENTS WITH KIDNEY DISEASE

M. Gorostidi[1], P. Sarafidis[2], A. de la Sierra[3], J. Segura[4], J.J. De La Cruz[5], J.R. Banegas[5], L.M. Ruilope[4]. *[1]Hospital Universitario Central de Asturias, Oviedo, SPAIN, [2]AHEPA University Hospital, Athens, GREECE, [3]Hospital Mutua Terrassa, Barcelona, SPAIN, [4]Hospital Universitario 12 de Octubre, Madrid, SPAIN, [5]Universidad Autonoma, Madrid, SPAIN*

Objective: To assess the prevalence and determinants of 'white-coat' hypertension (WCH) and masked hypertension (MH) in hypertensive patients with kidney disease.

Methods: Cross-sectional analysis from the Spanish ABPM Registry. Within a 14,382-patient sample, we identified 5,693 patients (39.6%) with kidney disease as defined by the 2013 KDIGO guidelines. Estimated glomerular filtration rate (eGFR) was calculated by the CKD-EPI equation. WCH was diagnosed when office BP = or >140/90 and 24-h BP <130/80 mmHg and MH when office BP <140/90 mmHg and 24-h BP = or <130/80 mmHg. Two separate logistic regression models were used to assess related factors. Tested variables were age, gender, duration of hypertension, body mass index (BMI), wais circumference, eGFR, albuminuria, diabetes, target organ damage other than kidney damage, and cardiovascular disease.

Results: Mean age was 61.0±13.9 years and 52.6% of patients were male. Only 21.7% had office BP <140/90 mmHg whereas 43.5% had mean 24-h BP <130/80 mmHg. The prevalence of WCH in patients with uncontrolled office BP was 36.8% (95% CI 35.7-37.9). In univariate analyses female gender, older age, increase in BMI, waist circumference, and albuminuria, and the

presence of diabetes, organ damage, and cardiovascular disease were associated with WCH. In multivariate analyses, only female gender, older age, organ damage, increased BMI, and albuminuria remained as independent associations. In patients with office BP <140/90 mmHg, prevalence of MH was 32.1% (95% CI 30.9-33.3). In univariate and multivariate analyses only older age, and increased BMI were associated with MH.

Conclusions: One of three hypertensive patients with kidney disease showed WCH. This condition was associated with age, female sex, obesity, and a more advanced cardiorenal disease. One of three renal patients with controlled office BP showed MH. This condition was less predictable than WCH. The burden of misclassification of BP control at the office calls for a wider use of ABPM in hypertensive patients with kidney disease.

7D.11 DIRECT ANGIOTENSIN TYPE 2 RECEPTOR STIMULATION INHIBITS T-LYMPHOCYTE RECRUITMENT TO THE CENTRAL NERVOUS SYSTEM AND MODULATES T-CELL DIFFERENTIATION

V. Valero-Esquitino[1], D. Cirera-Salinas[2], T. Stubbe[3], K. Lucht[1], A. Pascual[2], C. Curato[2], J. Arkink[1], C. Brandt[4], P. Namsolleck[5], T. Unger[5], U.M. Steckelings[1,6].
[1]Center for Cardiovascular Research, Charité-Universitätsmedizin Berlin, Berlin, GERMANY, [2]NeuroCure Exzellenzcluster, Charité-Universitätsmedizin Berlin, Berlin, GERMANY, [3]Center for Anatomy, Institute of Cell Biology and Neurobiology, Charité-Universitätsmedizin Berlin, Berlin, GERMANY, [4]Institute of Medical Immunology, Charité-Universitätsmedizin, Berlin, GERMANY, [5]CARIM, University of Maastricht, Maastricht, THE NETHERLANDS, [6]Department of Cardiovascular and Renal Research, University of Southern Denmark, Odense, DENMARK

The angiotensin type 2 receptor (AT2R) acts anti-inflammatory in models of neuronal injury. Here we identifed the impact of direct AT2R stimulation by the selective non-peptide agonist C21 on T-cell infiltration into the central nervous system (CNS) during myelin oligodendrocyte glycoprotein (MOG) induced experimental autoimmune encephalomyelitis (MOG-EAE), a mouse model of multiple sclerosis. Furthermore, we examined the effects of AT2R-stimulation on T-cell differentiation in vitro.

C57BL/6 mice were immunized with the MOG35-55 fragment and treated from day 3 before immunization until day 18 post-immunization (p.i.) with C21 (0.3 mg/kg bw i.p.) or vehicle. Leukocytes were isolated from the lumbar part of the spinal cord on day 18 p.i. and T-cell subsets identified and quantified by flow cytometry using anti-CD45, anti-CD11b, anti-TCR, anti-CD4 and anti-CD8 antibodies. To test whether AT2R stimulation modulates T helper (Th) cell differentiation, naive T-cells were isolated from spleen and lymph nodes of C57BL/6 mice, sorted, polarized in vitro under Th0, Th1, Th17 and Treg conditions and simultaneously treated with C21 (1μM) or vehicle for 4 days. 24 hours after the last treatment, mRNA expression of cytokines characteristic for pro-inflammatory Th1 cells (IFNγ), Th17 cells (IL-17), or anti-inflammatory Treg (FoxP3) were determined in order to see whether AT2R stimulation modifies T-cell differentiation.

Treatment with the AT2R agonist C21 resulted in a significant decrease in the absolute number of infiltrating T-cells and CD4+ T-cells during the acute phase of EAE when compared to vehicle treated mice ($p<0.01$). Furthermore, quantitative RT-PCR analysis showed a significant decrease of IFNγ or IL-17 expression in C21-treated Th1 or Th17 polarized T-cells, respectively, whereas an upregulation of FoxP3 in Treg polarized T-cells was observed after AT2R-stimulation.

We conclude that AT2R stimulation attenuates T cell infiltration and inhibits differentiation of naive T-cells into pro-inflammatory Th1 and Th17 T-cell subsets while differentiation into anti-inflammatory Treg is promoted. Our findings identify AT2R stimulation as a potential new therapeutic concept in autoimmune diseases.

7D.12 ON THE ORIGIN OF URINARY RENIN

L. Roksnoer[1], B. Heijnen[2], H. J. Struijker-Boudier[2], A.H.J. Danser[1].
[1]Erasmus MC, Rotterdam, THE NETHERLANDS, [2]Maastricht University, Maastricht, THE NETHERLANDS

Objective: Urinary renin (R), unlike angiotensinogen (Aog), is unrelated to urinary albumin, and may be released from renal tissue (e.g. the collecting duct, where Ang II stimulates renin release) or could represent activated filtered plasma prorenin (PR). Indole-3-carbinole (I3C) dose-dependently increases PR and blood pressure (BP) in Cyp1A1-Ren2 transgenic rats (TGR). We used these rats to establish the consequences of circulating PR/Ang II elevation on urinary R.

Design and methods: Young (4-weeks old) TGR were administered I3C for 4 weeks, followed by a 4-week washout period. Animals were either treated with placebo, the AT1 receptor antagonist losartan or hydralazine during I3C exposure. For comparison, wildtype (WT) rats were also treated with placebo or losartan for 4 weeks. Blood and 24-hr urine were collected at the end of each period to measure R, PR, Aog, albumin and creatinine.

Results: In TGR, I3C increased plasma PR >300-fold and raised systolic BP to >200 mm Hg. Plasma R increased >20-fold, whereas plasma Aog was unaltered. Losartan normalized BP in IC3-treated TGR, without altering plasma PR. It increased plasma R even further and lowered plasma Aog. Hydralazine lowered (but did not normalize) BP. In WT rats, losartan increased plasma R >15-fold and lowered plasma Aog, without affecting plasma PR. All changes in plasma were reversible after washout. I3C increased urinary R, Aog and albumin (but not creatinine), and losartan prevented this, whereas hydralazine reduced/normalized the increases in urinary Aog and albumin, without affecting urinary R. After I3C washout, urinary albumin remained elevated in placebo-treated animals. Losartan did not alter any urinary parameter in WT rats. PR was detectable only in urine of TGR during IC3 + placebo.

Conclusion: Lowering BP in IC3-treated TGR with hydralazine reduced albumin, PR and Aog (but not R) excretion, whereas additional AT1 receptor blockade was required to also suppress urinary R. This suggests urinary R is released from kidney sites and depends on AT1 receptor stimulation by Ang II.

ORAL SESSION

ORAL SESSION 7E
THERAPEUTIC ASPECTS

7E.01 EFFECTS OF COMBINATION OF PERINDOPRIL, INDAPAMIDE AND CALCIUM CHANNEL BLOCKERS ON DEATH AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES IN THE ADVANCE TRIAL

J. Chalmers[1], H. Arima[1], M. Woodward[1], N.R. Poulter[2], G. Mancia[3].
[1]The George Institute for Global Health, The University of Sydney and the Royal Prince Alfred Hospital, Sydney, AUSTRALIA, [2]International Centre for Circulatory Health, Imperial College, London, UNITED KINGDOM, [3]University of Milan-Bicocca and San Gerardo Hospital, Milan, ITALY

Objective: To determine the effects of a fixed combination of perindopril and indapamide in combination with calcium channel blocker (CCB) on death and cardiovascular outcomes in patients with type 2 diabetes.

Design and method: The Action in Diabetes and Vascular disease: preterAx and diamicroN MR Controlled Evaluation (ADVANCE) trial was a multicentre, factorial randomized controlled trial. A total of 11140 patients with type 2 diabetes were randomly assigned to perindopril-indapamide (4 mg/1.25 mg) or placebo. Randomized treatment effects on all-cause death, cardiovascular death and major cardiovascular events were compared in subgroups defined by baseline use of CCB (3427 with and 7713 without CCB).

Results: Over mean follow-up of 4.3 years, 879 all-cause deaths, 468 cardiovascular deaths and 1000 major cardiovascular events were observed. The patients treated with CCB had higher risk profile and greater use of antihypertensive drugs at baseline. During follow-up, mean systolic blood pressure difference between randomized groups was 4.7 and 6.2 mm Hg for patients with and without CCB. Active treatment reduced the relative risk of death by 28% (95% CI 10 to 43%) among patients with CCB compared to 5% (-12 to 20%) among those without CCB (p homogeneity=0.02) and 14% (2 to 25%) for the whole population. Similarly, the relative risk reduction (RRR) for cardiovascular death was 24% (-2 to 43%) vs 14% (-8 to 32%) for those with and without CCB and 18% (2 to 32%) for the whole population. The RRRs for major cardiovascular events for those with and without CCB and for the whole population were 12% (-8 to 28%), 6% (-10 to 19%) and 8% (-4 to 19%) respectively.

Conclusions: The combination of perindopril and indapamide with CCB appears to provide further protection against death and cardiovascular outcomes in patients with type 2 diabetes.

7E.02 4 YEARS OUTCOME OF AMLODIPINE PLUS TELMISARTAN OR AMLODIPINE PLUS DIURETICS REGIMEN ON CARDIOVASCULAR EVENTS IN HYPERTENSIVE PATIENTS 13542: FINAL RESULTS OF CHIEF TRIAL

W. Wang[1], L.Y. Ma[1], Y.Q. Zhang[1], M.B. Liu[1], Q. Deng[1], D.L. Zhu[2], S.P. Ma[3], F.H. Lu[4], X.H. Tang[5], J. Huang[6], S.L. Chu[2], L.Q. Zhang[7], L.Y. Zhao[8], X.F. Zhou[9], Y.X. Wang[10], C.B. Lei[11], J.G. Wang[2], L.Y. Chen[12], W. Li[1], L.S. Liu[1]. *[1]National Center for Cardiovascular Disease, Fu Wai Hospital, Peking Union Medical College, Beijing, CHINA, [2]Shanghai Hypertension Institute, Ruijin Hospital, Shanghai, CHINA, [3]Hebei Province People Hospital, Shijiazhuang, CHINA, [4]Shandong Province Medical Academy, Jinan, CHINA, [5]Zhejiang Province Hospital, Hangzhou, CHINA, [6]1st Hospital of Nanjing Medical University, Nanjing, CHINA, [7]Shanxi Province People Hospital, Taiyuan, CHINA, [8]Tangdu Hospital, Xian Shanxi, CHINA, [9]Sichuan Province Hospital, Chendu, Sichuan, CHINA, [10]Liaoning Province Stroke Association, Liaoning, CHINA, [11]Datong Kuangwuju Hospital, Datong, Shanxi, CHINA, [12]Guangdong Province People Hospital, Guangzhou, CHINA.*

Objective: To evaluate the effects of amlodipine-based antihypertensive combination regimen on blood pressure control and impact on cardiovascular events.

Methods: From Oct. 2007 to Oct. 2008, a total of 13 542 hypertensive patients from 180 centers in China were included in this multi-centre randomized, controlled, blind-endpoint assessment clinical trial. Inclusion criteria were: essential hypertension, 50 - 79 years of age with at least one cardiovascular risk factor and signed consent forms. Patients were randomly assigned to receive low-dose amlodipine + diuretics (group A) or low-dose amlodipine + telmisartan (group T). The primary endpoints are composite of non-fatal stroke/myocardial infarction and cardiovascular death. Study patients will be followed-up for 4 years. Dec 31,2011 all completed clinical study treatment. We plan to public final results Jun 2013.

Results: The characteristics of patients between the two groups were similar: mean age (61.5 +/- 7.7) Yrs with 19% history of cerebrovascular diseases, 12% coronary diseases, 18% diabetes, 42% dyslipidemia, mean initial blood pressure 157/93 mm Hg. After 156-week treatment, mean blood pressure in group A and B were reduced to (130.4 +/- 11.0)/(78.1 +/- 7.6) mm Hg, (130.3 +/- 11.6)/(77.9 +/- 7.9) mm Hg respectively. Blood pressure control rates reached 86.6% and 87.1% in group A and T, respectively. The cardiovascular events will be analysis.

Conclusion: Amlodipine-based antihypertensive combination regimens achieved satisfactory blood pressure control rate in patients with hypertension. The composit cardiovascular events will be report June 2013.

7E.03 DOES HYPERTENSIVE PATIENT FENOTYPE INFLUENCE WHEN SELECTING THE BEST COMBINATION OF ANTIHYPERTENSIVE DRUGS?

C. Cerezo, A. Sevillano, L. Guerrero, L. Fernandez, M. Praga, L.M. Ruilope, J. Segura. *Hypertension Unit. Department of Nephrology, Hospital 12 de Octubre, Madrid, SPAIN*

Objective: To investigate in clinical practice if differences exist in the clinical and biochemical initial characteristics in hypertensive patients receiving two common antihypertensive drug combinations: renin-angiotensin-aldosterone suppressors (RAAS) plus thiazide diuretics (DIU) or RAAS plus calcium-channel blockers (CCB). The appearance of new cases of diabetes in both groups was also analyzed.

Design and method: A cross-sectional analysis included hypertensive patients treated in the last year in our Hypertension Unit. Clinical and analytical data were collected as the number and type of antihypertensive drug taken both at the beginning of the follow up and the last available visit.

Results: 2398 patients were included, mean age 61.3±14.7 years, mean follow-up 6.4±3.6 years. The distribution of patients according to the number of antihypertensive drugs was: 0 drugs, 145 (6.0%) patients; 1 drug, 505 (21.1%); 2 drugs, 552 (23.0%); and 3 or more drugs, 1196 (49.9%) patients. Among the patients receiving two drugs we identify 3 groups: RAAS+DIU, with 228 patients (41.3%), RAAS+CCB, 228 patients (41.3%) and other double combinations in 96 patients (17.4%). No significant differences were detected between both groups in the initial levels of blood pressure, body mass index, abdominal circumference, fasting glucose, serun creatinine, estimated glomerular filtration rate, serum uric acid and potassium, and lipid profile. At the end of the follow-up, observed blood pressure reductions were similar in both groups. No analytical differences were detected, except for higher levels of serum uric acid and lower of potassium in the RAAS+DIU group. The percentage of patients diagnosed with type 2 diabetes increased 8.3% in the RAAS+DIU group and 5.7% in the RAAS+CCB group ($p<0.001$).

Conclusions: In daily practice, most hypertensive patients require drug combinations. We have not detected clinical or analytical differences at the time of selecting between a combination of a RAAS with DIU or with CCB. The use of a RAAS+DIU combination is accompanied by a larger number of new-onset diabetes in comparison to the combination with BSRA+CA.

7E.04 LACK OF DIFFERENCE BETWEEN NEBIVOLOL/HYDROCHLOROTHIAZIDE AND METOPROLOL/HYDROCHLOROTHIAZIDE ON CENTRAL WAVE AUGMENTATION AND BLOOD PRESSURE

D. Eeftinck Schattenkerk[1], B. Van Den Bogaard[1], M. Cammenga[1], B. Westerhof[2], E. Stroes[1], B. Van Den Born[1]. *[1]Academic Medical Center, Amsterdam, THE NETHERLANDS, [2]Bmeye b.v., Amsterdam, THE NETHERLANDS*

Background: Third generation, vasodilating beta-blockers such as nebivolol offer potential benefit on central wave augmentation and central blood pressure (cBP) compared to older non-vasodilation beta-blockers by attenuation of wave reflection, be it alone or in combination with other BP lowering drugs such as hydrochlorothiazide (HCTZ). We compared the effect of nebivolol/HCTZ and. metoprolol/HCZT on wave augmentation and cBP.

Methods: We used a randomized double blind crossover design to compare nebivolol/HCTZ 5/12.5 mg and metoprolol/HCTZ 100/12.5 mg once daily in subjects with an untreated office blood pressure (BP) of 140-179/90-109 mmHg. Measurements were performed at baseline and after four weeks of treatment with either nebivolol/HCTZ or metoprolol/HCTZ. After a washout-period of four weeks patients crossed over to the alternative treatment arm. The central wave augmentation index (AIx) and cBP were obtained by radial applanation tonometry using a validated general transfer function. AIx was corrected for a heart rate (HR) of 75 beats.min-1 (AIx@hr75). Hemodynamics were assessed by non-invasive continuous finger arterial BP measurement.

Results: We analyzed data of 22 subjects (17 male), aged 59.9±6.4 years, office BP 155±16/93±10 mmHg. At baseline AIx was 30.3±6.8 %, AIx@hr75 was 23.7±5.8, cBP was 145±18/93±10 mmHg and HR was 61±7 beats.min-1. Neither nebivolol/HCTZ nor metoprolol/HCTZ affected central wave augmentation significantly. AIx was 31.4±9.5 % for nebivolol/HCTZ and 32.7±9.6 % for metoprolol/HCTZ. AIx@hr75 was 20.9±8.3 % for nebivolol/HCTZ and 21.9±8.5 % for metoprolol/HCTZ. Nebivolol/HCTZ lowered cBP by 16±15/10±8 mmHg and metoprolol/HCTZ by 13±12/9±7 mmHg (both p<0.001). Nebivolol/HCTZ lowered HR by 8.1±5.4 beats.min-1 and metoprolol/HCTZ by 8.6±4.9 beats.min-1. Nebivolol/HCTZ and metoprolol/HCTZ equally lowered cardiac output and left ventricular contractility, while total peripheral resistance and stroke volume did not change. There was no significant difference in effect between nebivolol/HCTZ and metoprolol/HCTZ in respect to central wave augmentation, cBP, or hemodynamics.

Conclusion: Treatment with the third-generation, vasodilating beta-blocker nebivolol was not superior to second generation beta-blocker metoprolol in reducing aortic wave augmentation and central BP when combined with hydrochlorothiazide.

7E.05 3-YEAR EVENT RATES IN PATIENTS WITH HYPERTENSION AND DIABETES MELLITUS OR HEART FAILURE AT BASELINE TREATED WITH DIFFERENT ANTIHYPERTENSIVE REGIMENS. RESULTS OF THE 3A REGISTRY

U. Zeymer[1], R. Dechend[2], T. Riemer[1], I. Hagedorn[3], R.E. Schmieder[4]. *[1]Klinikum Ludwigshafen, Ludwigshafen, GERMANY, [2]Helios Klinikum Berlin Buch, Berlin, GERMANY, [3]Novartis Pharma, Nuremberg, GERMANY, [4]University Hospital Erlangen, Erlangen, GERMANY*

Background: Little is known about the long-term event rate in stable outpatients with hypertension in real life. Therefore we evaluated the 3-year event rates in high risk patients with hypertension anfd diabestes mellitus and/or heart failure.

Methods: The non-interventional 3A Registry included outpatients in whom the physican had decided to initiate or modify antihypertensive therapy in patients not achieving blood pressure control or where a modification was required for other reasons (e.g. adverse events or drug intolerance). Patients were recruited into 3 groups: treatment with the direct renin inhibitor aliskiren, an ACE-inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) or antihypertensive agents not blocking the renin-angiotensin system (RAS), alone or on top of existing antihypertensive regimens. The subgroups of atients with diabestes and/or heart failure at baseline were prospectively followed for three years.

	Aliskiren (n=804)	Aliskiren + ACE-I or ARB (n=907)	ACE-I or ARB (n=411)	Non-RAS (n=285)
Relative reduction in systolic blood pressure	13.3 %	13.0 %	10.7 %	11.3 %
Absolute reduction in systolic blood pressure	20.9 mmHg	20.9 mmHg	15.4 mmHg	16.1 mmHg
Improvement in GFR	14.8 %	11.0 %	11.7 %	7.6 %
3-year clinical events				
Death	7.1 %	7.2 %	7.8 %	7.0 %
Myocardial infarction	1.5 %	1.9 %	2.0 %	1.4 %
Stroke	1.7 %	1.4 %	0.2 %	1.8 %

Results: Overall patients (68 % with aliskiren, 18% with ACE-I/ARB, 14% without RAS-blockade) recruited by 899 physicans in Germany in 2008 and 2009 had 2-year follow-up. Patients with the aliskiren based regimen had significantly higher baseline blood pressure, more cardiovascular co-morbidities, a higher prevalence of diabetes and renal disease and were treated with more antihypertensive drugs at baseline (median 3.1 vs. 2.5 vs. 1.5). The cumulative 3-year event rates and improvements in blood pressure and renal function are given in the table.

Conclusion: In this real life experience in patients with hypertension and diabetes and/or heart failure aliskiren alone or in combination with ACE-I/ARBs is associated with an improvement in blood pressure and no increase in clinical events.

7E.06 TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE

H. Beaussier[1], M. Frank[2], F. Coudore[3], M. Briet[2], S. Peyrard[4], M. Azizi[2], P. Plouin[5], S. Laurent[6], P. Boutouyrie[6], G. Bobrie[5]. *[1]CRC GHPSJ, INSERM U970 PARCC HEGP, Paris, FRANCE, [2]CIC, HEGP, Paris, FRANCE, [3]Service de Pharmacologie Clinique HEGP, Paris, FRANCE, [4]URC HEGP, Paris, FRANCE, [5]Service de Médecine Vasculaire, Unité d'Hypertension Artérielle HEGP, Paris, FRANCE, [6]Service de Pharmacologie Clinique, INSERM U970 PARCC HEGP, Paris, FRANCE*

Objective: We previously showed (Bobrie et al. J Hypertens 2012) that sequential-nephron blockade (SNB) was more effective than combined renin angiotensin system blockade (RB) for controlling BP in patients with resistant hypertension (RH). In this post-hoc analysis, we assessed medication adherence (MA) and its influence on the antihypertensive response to SNB/RB with a new combined scoring system.

Method: Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) >135 and/or 85 mmHg, despite 4 week-treatment with irbesartan 300 mg+HCTZ 12.5 mg+amlodipine 5 mg, were randomised either to SNB (i.e.+spironolactone 25 mg, then +furosemide 20-40 mg, then +amiloride 5 mg, n=82) or RB (ramipril 5-10 mg, then bisoprolol 5-10 mg, RB group, n=82) for 12 weeks. MA was scored according to 4 criteria: (i) trough/peak plasma irbesartan (Irb) concentration (HPLC); (ii) urinary AcSDKP/creatinine ratio (UR) to evaluate ramipril intake; (iii) delay of last medication intake before visit (LMI); and (iv) pill counting (PC, %). One point of MA score was attributed to trough Irb >20ng/ml, UR >4nmol/mmol, LMI <24h and PC >80%. MA was defined as low (LMA, score <2), intermediate (IMA, score=3), and optimal (OMA, score=4).

Results: 82 pts among 164 had OMA (46 SNB and 36 RB); 52 pts had IMA (23 SNB and 29 RB); and 30 pts had LMA (13 SNB and 17 RB) (inter-groups difference: NS). LMA pts were younger than SMA pts (50±11 vs. 56±10 yrs, p<0.011). In OMA pts, the difference in dASBP/dADBP between SNB vs RB was significant (-11 [-17 ;-6]/-6 [-9 ;-2] mmHg, p<0.0001/p=0.0025), favoring SNB, whereas in LMA pts the difference between the two groups did not reach significance (-6 [-19 ;7]/-1 [-10 ;7] mmHg, p=0.352/p=0.7096).

Conclusion: The major BP lowering effect of SNB vs. RB observed in pts with OMA is lost in pts LMA. Combined methods for assessing MA allow determining the true efficacy of antihypertensive strategies in patients with RH. Reinforcement of MA in RH pts is deemed necessary.

7E.07 NIFEDIPINE GITS/CANDESARTAN CILEXETIL COMBINATION - BENEFICIAL EFFECTS ON VASODILATORY HEADACHE AND ANKLE OEDEMA BEYOND BLOOD PRESSURE CONTROL

S.E. Kjeldsen[1], H. Haller[2], P. Harvey[3], B. Gil-Extremera[4], G. Villa[5], F. Heyvaert[6], G. Mancia[7]. *[1]Oslo University Hospital Ullevaal, Oslo, NORWAY, [2]Hannover Medical School, Hannover, GERMANY, [3]The Crouch Oak Family Practice, Surrey, UNITED KINGDOM, [4]Hospital Universitario San Cecilio, Granada, SPAIN, [5]Fondazione S. Maugeri, IRCCS, Pavia, ITALY, [6]Huisartsenpraktijk De Regenboog, Deurne, BELGIUM, [7]University of Milano-Bicocca, Milan, ITALY*

Objective: The DISTINCT I (reDefining Intervention with Studies Testing Innovative Nifedipine GITS – Candesartan Therapy I) study aimed to determine the efficacy and safety of nifedipine GITS/candesartan cilexetil (NC) combinations compared with respective monotherapies and placebo.

Design and methods: This was a multicentre, double-blind, multifactorial study in which patients aged >18 years with diastolic blood pressure [DBP] between 95 to 110 mmHg were randomized to placebo, monotherapy or combination therapy with N20, 30 or 60 mg and C4, 8, 16 or 32 mg for 8 weeks. Primary endpoints were change from baseline in DBP at Week 8 (response surface model [RSM]); this analysis was repeated for systolic blood pressure (SBP), and safety. Secondary efficacy variables included least-square (LS) mean change in BP, control and response rates.

Results: Overall, 1381 patients were randomized. Mean (SD) baseline SBP/DBP was 156.5 (11.3)/99.6 (3.5) mmHg. N and C in combination both contributed significantly to SBP/DBP reductions (P<0.0001 [RSM]). Control (<140/90 mmHg) and response rates for all NC combinations were significantly higher than placebo (P<0.05) and most respective monotherapies. Median time to achieve first BP control was quicker for combination than monotherapy (12 vs. 15 days). Treatment-emergent adverse events (AEs) were reported by 16.2% of all patients; most were mild-moderate. NC combination had a lower incidence of treatment-emergent AEs than N monotherapy (18.3% vs. 20.5%), and a lower incidence of vasodilatory AEs (18.3% vs. 23.6%), including headache (5.5% vs. 11.0%; P=0.003) and new-onset peripheral oedema (3.6% vs. 5.8%). Discontinuation rate was low (7.6% [NC combination] vs. 6.8% [placebo] and 10.5% [monotherapy]). Only 4 non–dose-dependent hypotensive events were reported.

Δ LS mean SBP/DBP, mmHg	C0	C4	C8	C16	C32
N0	-5.3/-6.7	-11.8/-9.4*	-13.5/-10.7*	-13.5/-9.4*	-16.5/-12.8*
N20	-11.9/-9.9*	-18.7/-13.7*,†	-20.2/-14.4*,†	-20.8/-14.6*,†	----
N30	-13.6/-10.1*	----	-20.4/-14.7*,†	-19.7/-14.2*,†	-22.1/-16.1*,†
N60	-16.8/-12.0*	----	----	-21.6/-15.9*,†	-23.8/-16.5*,†

*P<0.05 vs. placebo; †vs. respective monotherapies (ANCOVA, FAS population [n=1362]).

Conclusions: Both nifedipine GITS and candesartan cilexetil contributed significantly to the blood pressure reduction of the combination. A positive dose response was demonstrated within the doses investigated. Nifedipine/candesartan combinations were well-tolerated and reduced vasodilatory side-effects by 22%, including headache (by 50%) and peripheral oedema (by 40%) compared with nifedipine monotherapy. N30-60/C8-32 is, therefore, an optimal dose range.

7E.08 EFFECTS OF NIFEDIPINE AND VALSARTAN VERSUS HIGH DOSE MONOTHERAPY ON CENTRAL HEMODYNAMICS IN PATIENTS WITH INADEQUATELY CONTROLLED HYPERTENSION: FOCUS STUDY

J. Park[1], J. Ha[2], H. Jung[3], M. Rhee[4]. *[1]Cheil General Hospital, Kwandong University College of Medicine, Seoul, SOUTH KOREA, [2]Severance Hospital, Yonsei University College of Medicine, Seoul, SOUTH KOREA, [3]The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, SOUTH KOREA, [4]Dongguk University Hospital, Goyang-si, SOUTH KOREA*

Objectives: This study investigated whether the low-dose combination of nifedipine GITS and valsartan is more effective in reducing central blood pressure (BP) than high-dose monotherapy with either agent in essential hypertension inadequately controlled by low-dose monotherapy.

Background: Measures of central BP and arterial stiffness hold prognostic information beyond conventional peripheral BP. Calcium channel or renin-angiotensin system blockers have shown better efficacy in improving central hemodynamics among antihypertensives, but there are currently no direct comparisons.

Methods: This is a prospective, open-label, randomized, active-controlled study, including 203 patients with uncontrolled hypertension. Patients were randomized to receive 30 mg nifedipine GITS plus 80 mg valsartan (N30+V80), 60 mg nifedipine GITS (N60), or 160 mg valsartan (V160) for 8 weeks. Central hemodynamics were measured by applanation.

Results: The primary efficacy variable, central systolic BP, compared to baseline at 8 weeks was significantly reduced by 27.21±14.70 mm Hg in the N30+V80 group and by 27.08±16.48 mm Hg with N60 group compared to 14.36±16.61 mm Hg with V160 group. There were no significant differences between N30+V80 and N60 groups. The change in augmentation index (AIx) was -5.39±9.21% in the N30+V80 group, -4.45±8.17% with N60, and -2.43±8.56% with V160. The decrease in the N60 group was statistically significant compared to V160 alone (P=0.0464). Pulse pressure (PP) amplification was significantly increased from 1.26±0.14 to 1.37±0.21 (P<0.001) in the N30+V80 group, but not in N60 or V160 group. But compared to V160 group, the change of PP amplification was significantly higher in combination (P=0.041) and N60 (P=0.017) groups. By multivariate regression analysis, changes in central systolic BP are determined by baseline pressure and drugs used (P<0.001).

Conclusions: Low-dose combinations of nifedipine GITS plus valsartan or high-dose nifedipine were more effective in improving central hemodynamics than high-dose valsartan in patients with hypertension.

7E.09 AZILSARTAN MEDOXOMIL/CHLORTHALIDONE FIXED-DOSE COMBINATION: EFFICACY BY BASELINE HYPERTENSION SEVERITY IN THREE COMPARATOR-CONTROLLED TRIALS

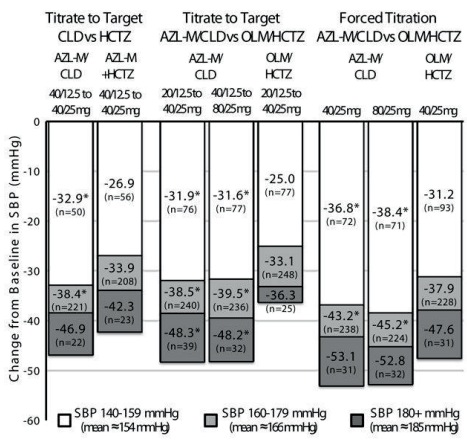
W. Cushman[1], D. Sica[2], G. Bakris[3], W. White[4], M. Weber[5], E. Lloyd[6], A. Roberts[6], S. Kupfer[6]. *[1]University of Tennessee College of Medicine, Memphis, TN, USA, [2]Virginia Commonwealth University, Richmond, VA, USA, [3]University of Chicago Medicine, Chicago, IL, USA, [4]University of Connecticut School of Medicine, Farmington, CT, USA, [5]Downstate Medical Center, Brooklyn, NY, USA, [6]Takeda Global Research and Development Center, Inc., Deerfield, IL, USA*

Objective: We evaluated a fixed-dose combination (FDC) of the angiotensin II receptor blocker azilsartan medoxomil (AZL-M) and chlorthalidone (CLD) in 3 trials: 1 study of AZL-M/CLD FDC vs coadministration of AZL-M with HCTZ and 2 studies of AZL-M/CLD vs an olmesartan (OLM)/HCTZ FDC (NCT00818883, NCT00846365, NCT01033071). We examined systolic blood pressure (SBP) response by baseline hypertension (HTN) severity (SBP 140-159, 160-179, and 180+ mmHg) in these studies.

Design and method: Drug was forced-titrated (FT) to the highest dose in all patients in one OLM/HCTZ comparator trial (12 wks). The other OLM/HCTZ comparator trial (8 wks) and the AZL M+HCTZ comparator trial (10 wks) were titrate-to-target (TtT) studies; ie, patients received a higher dose only when target BP (140/90 mmHg) was not achieved at a lower dose. Analysis of covariance (treatment as factor, baseline clinic SBP as covariate) was used for subgroup analyses.

Results: Patients had mean age of 55-57 y, slightly higher (60) in patients with SBP 180+ mmHg in the FT study. Approximately 70% had baseline clinic SBP 160-179 mmHg. In the full population of each trial, AZL-M/CLD led to statistically significantly greater clinic SBP reduction than comparator. Analyses by baseline SBP levels showed statistically significantly greater clinic SBP reductions with AZL-M/CLD vs comparator in the 140-159 and 160-179 mmHg subgroups in all studies and the 180+ subgroups in the TtT OLM/HCTZ comparator study; nonsignificant differences were seen in the 180+ subgroups in the other 2 studies (Figure). AZL/CLD also resulted in consistently greater decreases vs comparators in ambulatory SBP. The tolerability of AZL-M/CLD when titrated to target up to 40/25 mg was similar to comparators. The 80/25 mg AZL-M/CLD dose or forced titration reduced tolerability.

Conclusions: AZL-M/CLD decreased SBP more than AZL-M+HCTZ or OLM/HCTZ regardless of baseline HTN severity.



AZL-M=azilsartan medoxomil; CLD=chlorthalidone; HCTZ=hydrochlorothiazide; OLM=olmesartan
* Significant difference vs comparator at 0.05 level

7E.10 SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF QGC001, A CENTRALLY ACTIVE AMINOPEPTIDASE A INHIBITOR, IN HEALTHY VOLUNTEERS

F. Balavoine[1], P. Kousignian[2], D. Bergerot[3], N. De Mota[4], D. Chassard[2], L. Ségard[1], B.P. Roques[5], C. Llorens-Cortès[4], M. Azizi[3]. *[1]Quantum Genomics, Massy, FRANCE, [2]Biotrial, Rueil-Malmaison, FRANCE, [3]Clinical Investigation Centre, Hôpital Européen Georges-Pompidou, Université Paris-Descartes, Paris, FRANCE, [4]INSERM U1050, Collège de France, Paris, FRANCE, [5]Université Paris-Descartes, Paris, FRANCE*

Objective: Inhibition of brain aminopeptidase A (APA) which converts angiotensin II (AngII) into AngIII has emerged as a novel antihypertensive treatment, as demonstrated in several experimental animal models. QGC001/RB150 is an inactive prodrug able of releasing in the brain its active metabolite EC33, a selective inhibitor of human APA (Ki=300 nM). The aim of the present study was to evaluate in human the safety, the pharmacokinetics and the pharmacodynamic effects of QGC001.

Design and method: 48 healthy male volunteers were randomly assigned to receive in double-blind and fasted conditions, single oral doses of 125, 250, 500, 750, 1000 and 1250 mg of QGC001 (n=6/dose) or placebo (n=2/dose). We measured plasma and urine levels of both QGC001 and EC33 by LC/MS/MS, plasma renin concentrations (PRC), plasma and free urine aldosterone (PAldo and UAldo), plasma copeptin (PCop), and plasma and urine cortisol (PCort and UCort) concentrations, and supine SBP, DBP and HR at various time points.

Results: All doses of QGC001 were well clinically and biologically tolerated. Plasma peak concentrations of QGC001 increased linearly with the dose, with a median tmax of 1.5 h for QGC001 and 3.0 h for EC33. The median plasma t1/2 of QGC001 was 1.6 h consistent throughout doses. Urinary excretion of QGC001 and EC33 was below 4% of the administered dose. When compared to placebo, QGC001 did not significantly change PRC, PAldo, UAldo, PCop, PCort or UCort. No significant change was observed for supine HR, SBP and DBP in any treatment group.

Conclusion: Single oral administration of QGC001 up to 1250 mg in healthy volunteers is well-tolerated. Following oral administration, QGC001 is absorbed via the gastrointestinal tract and converted partially into its active metabolite EC33 in plasma. Like in animal experiments, in normotensive subjects, QGC001 has no effect on the systemic renin-angiotensin-aldosterone parameters and on PCop levels, a marker of vasopressin release. In normotensive subjects, a single dose of QCG001 had no effect on BP or HR.

ORAL SESSION

ORAL SESSION 8A
CARDIOVASCULAR RISK FACTORS

8A.01 CAFFEINE BLOOD LEVELS APPEAR NEGATIVELY ASSOCIATED WITH SYSTOLIC BLOOD PRESSURE IN NON-SMOKERS

I. Guessous[1], M. Prujim[2], B. Ponte[3], D. Ackermann[4], G. Ehret[5], P. Vuistiner[6], F. Paccaud[6], M. Mohaupt[4], N. Ansermot[7], B. Vogt[4], A. Péchère-Bertschi[8], P. Martin[3], M. Burnier[2], C. Eap[7], M. Bochud[6]. *[1]Unit of Population Epidemiology, Geneva University Hospitals, Geneva, SWITZERLAND, [2]Service of Nephrology, Centre Hospitalier Universitaire Vaudois, Lausanne, SWITZERLAND, [3]Service of Nephrology, Geneva University Hospitals, Geneva, SWITZERLAND, [4]Service of Nephrology, University Hospital of Bern, Bern, SWITZERLAND, [5]Service of Cardiology, Geneva University Hospitals, Geneva, SWITZERLAND, [6]Institute of Social and Preventive Medicine, Lausanne, SWITZERLAND, [7]Unit of Pharmacogenetics and Clinical, Centre Hospitalier Universitaire Vaudois, Lausanne, SWITZERLAND, [8]Unit of Hypertension, Geneva University Hospitals, Geneva, SWITZERLAND*

Objective: Genome-wide association studies found the CYP1A1/A2 locus to be associated with blood pressure. CYP1A2 variants associated with higher self-reported caffeine intake were associated with lower risk of hypertension in non-smokers. We explored whether circulating caffeine levels were associated with blood pressure in a population-based family study, taking smoking status into account.

Design: Nuclear families were randomly selected from the general population in three Swiss cities. Five sitting office blood pressure measurements taken using a validated non-mercury auscultatory sphygmomanometer were averaged. Fasting circulating caffeine levels were measured using ultra-performance liquid chromatography-mass spectrometry/mass spectrometry. We used linear mixed models to explore the associations of caffeine levels with blood pressure, while adjusting for major confounders, antihypertensive treatment, and familial correlations. Caffeine levels were square-root transformed.

Results: The 291 men and 313 women had the following characteristics: mean age 47.3 and 48.9 years, mean BMI 26.0 and 24.2 Kg/m2 , mean systolic BP 122.6 and 116.4 mm Hg and diastolic BP 78.6 and 74.1 mm Hg, respectively. In 158 smokers and 446 non-smokers, median (IQR) caffeine levels were 406 (131;979) and 631 (261;1333) ng/ml, respectively. Square root transformed caffeine levels (ng/mL) were associated negatively with systolic (–0.09 [Std. error, 0.04], P= 0.036), but not with diastolic (–0.04 [0.03], P= 0.09) blood pressure in non-smokers. In smokers, a positive association was found with systolic (0.13 [0.06], P=0.026), but not with diastolic, blood pressure. Smoking modified the effect of circulating caffeine levels on systolic blood pressure (P for interaction with smoking = 0.009).

Conclusions: This study on caffeine blood levels suggests a negative association with systolic blood pressure in non-smokers, and a positive association in smokers.

8A.02 ASSESSING SALT-SENSITIVITY FROM 24H AMBULATORY BP MONITORING IN HYPERTENSIVE SUBJECTS DURING HABITUAL DIET. ROLE OF A NEW INDEX OF NOCTURNAL BLOOD PRESSURE FALL

P. Castiglioni[2], G. Parati[1], V. Brambilla[3], L. Brambilla[3], M. Gualerzi[3], M. Di Rienzo[2], P. Coruzzi[4]. *[1]Dept. Health Sciences, University of Milano-Bicocca and Dept. Cardiology, S. Luca Hospital, Istituto Auxologico Italiano, Milan, ITALY, [2]Fondazione Don C. Gnocchi, Milan, ITALY, [3]Fondazione Don C. Gnocchi, Parma, ITALY, [4]Dept. Clinical and Experimental Medicine/ University of Parma, Parma, ITALY*

Objective: We showed that a nocturnal nondipping pattern in BP with high 24H heart rate as observed from 24H ABPM during habitual diet may identify a condition of sodium sensitivity [1]. We also showed that nocturnal Pulse Pressure (PP) changes identify nondipping patterns associated to sodium sensitivity better than mean arterial pressure (MAP) changes [2]. Aim of this work is to evaluate whether other ABPM indexes of nocturnal nondipping behaviour may improve the prediction of sodium sensitivity, and whether gender influences this prediction.

Methods: 24H ABPM was performed in 30 male (M) and 16 female (F) hypertensive subjects. Night falls of MAP and PP (MAPNF, PPNF) were calculated, in % of daytime levels. A new index of "total BP night fall", TOTNF, was also calculated combining the night fall of BP mean level and of BP pulsatile component: TOTNF= MAPNF+PPNF. All subjects underwent a traditional sodium sensitivity test to be classified as salt-sensitive (SS) or salt-resistant (SR). Gaussianity was checked and significances of the factors "salt-sensitivity" and "gender" were assessed by 2-factor ANOVA (p=0.05) separately for MAPNF, PPNF, and TOTNF. Values were expressed as mean ±sd.

Results: TOTNF was lower in SS (15.7±8.3) than in SR (24.0±10.3) patients. Moreover salt-sensitivity was a factor statistically more significant for TOTNF (p=0.02) than for PPNF (SS=3.2±5.5, SR=8.6±7.4, p=0.05) or MAPNF (SS=12.5±5.2, SR=15.5±5.6, p=0.12). This makes TOTNF better predictor of salt sensitivity than MAPNF or PPNF. Furthermore, the factors "gender" and "salt sensitivity" did not interact significantly for TOTNF (p>0.80). However, the factor "gender" was close to the statistical significance, with TOTNF lower in F (15.8±7.7) than in M (23.1±10.1, p=0.07) subjects.

Conclusions: In uncomplicated essential hypertensives, the proposed index of BP night fall may more easily identify a condition of risk associated to salt sensitivity during habitual diet, simply by evaluating whether TOTNF is lower than a given threshold. This approach appears feasible in both M and F, but gender differences should be considered for selecting classification thresholds in the two sexes.

8A.03 LEFT VENTRICULAR MASS VERSUS PULSE WAVE VELOCITY AS DETERMINANTS OF CORONARY ARTERY DISEASE IN PATIENTS WITH ESSENTIAL HYPERTENSION: DATA FROM A GREEK 6-YEAR-FOLLOW-UP STUDY

A. Kordalis, C. Tsioufis, K. Dimitriadis, D. Tsiachris, P. Valenti, D. Ntarahani, V. Bouralexis, D. Aragiannis, A. Kefala, A. Milkas, C. Stefanadis. *First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, GREECE*

Objective: The aim of the present study was to compare the predictive role of arterial stiffness and augmented left ventricular mass index (LVMI) for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients.

Design and method: We followed up 1128 essential hypertensives (mean age 56.1 years, 587 males, office blood pressure (BP)=144/91 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and at baseline underwent complete echocardiographic study for estimation of LVMI, while arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior SP). The distribution of PWV was split by the median (8.1 m/sec) and accordingly subjects were classified into those with high (n=566) and low values (n=562). Moreover, CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.

Results: The incidence of CAD over the follow-up period was 2.83%. Hypertensives who developed CAD (n=32) compared to those without CAD (n=1096) had at baseline higher waist circumference (101.8±11.1 vs 97.2±11.9 cm, p=0.033), LVMI (123.7±22.9 vs 107±24.2 g/m^2, p=0.014) and prevalence of high PWV levels (69% vs 48%, p=0.019), while there was no difference regarding baseline office BP, serum creatinine and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that high baseline PWV levels predicted CAD (hazard ratio=2.657, p=0.008). However, in multivariate Cox regression model, waist circumference (hazard ratio=1.016, p=0.04) and LVMI (hazard ratio=1.023, p=0.018) but not high baseline PWV turned out to be independent predictors of CAD.

Conclusions: In essential hypertensive patients LVMI predicts future development of CAD, whereas high baseline PWV exhibits no independent prognostic

value. These findings support that LVMI constitutes a superior prognosticator of events than PWV and its estimation is essential in order to improve overall risk stratification in hypertension.

8A.04 INDIVIDUAL VISIT-TO-VISIT VARIATION OF BLOOD PRESSURE OVER 6 YEARS AND IMPACT ON ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN A GENERAL POPULATION: THE IPC COHORT

B. Pannier[1], F. Thomas[1], O. Hanon[2], S. Czernichow[3], C. Lemogne[4], T. Simon[5], J. Simon[6], K. Bean[1], N. Danchin[7]. *[1]Centre Ipc, Paris, FRANCE, [2]Service Geriatrie-Hopital Broca, Paris, FRANCE, [3]Service Nutrition-Hopital Ambroise Pare, Boullogne-Billancourt, FRANCE, [4]Service Psychiatrie-Hopital Egp, Paris, FRANCE, [5]Service Pharmacologie-Hopital Saint Antoine, Paris, FRANCE, [6]Service Oncologie-Ch La Pitie Salpetriere, Paris, FRANCE, [7]Service Cardiologie-Hegp, Paris, FRANCE*

Objectives: Blood pressure (BP) visit-to-visit variability is deleterious in high risk treated hypertensives. The point remains controversial in treated hypertensives or in general normotensive population. We assessed the risk of death and of cardiovascular mortality according to BP visit-to-visit variation in a general primary care French population.

Design and method: 40,926 normotensives and 14,283 untreated high blood pressure patients, were twice examined (time interval: 5.8±2.2 years) for a health check-up. BP was the average of the last two measurements from three consecutive 10-minute resting supine recordings. All cause and cardio-vascular (CV) mortality were followed-up for 6.1±3.2 years on average: 1131 people died, whom 114 from CV causes. Absolute visit-to-visit variation of systolic BP was assessed by tertiles and relationship with mortality analyzed through multivariate cox models (Hazard Ratio, 95% CI) by considering the first (V1) then the second visit (V2) parameters.

Results: Visit-to-visit high SBP variation (higher tertile of SBP variation) was associated with an increased risk of All-cause and cardiovascular mortality, respectively 1.14 (1.01-1.30) and 1.95 (1.25-3.05), after adjustments on V1 variables in the entire population. Among baseline hypertensives, risks of All cause and cardiovascular mortality were respectively 1.39 (1.16-1.67) and 1.87 (1.12-3.13). No association between visit-to-visit high SBP variation and mortality was observed among normotensives subjects.

Conclusions: In this large primary care population, we confirm that the individual visit-to-visit variation of BP in true life is an independent bad prognosis factor among hypertensives. But visit-to-visit variation is no longer a prognosis marker in normotensives. The impact of underlining cardiovascular structural and functional alterations associated with hypertension appeared one of the main factors for this relationship.

8A.05 RELATIONSHIP BETWEEN SERUM URIC ACID AND AORTIC STIFFNESS IN UNTREATED HYPERTENSIVE SUBJECTS

G. Mulè, P. Cusimano, A. Castiglia, T. Viola, A.C. Foraci, G.B. Rini, G. Cerasola, S. Cottone. *Dipartimento di Medicina Interna e Specialistica, Università di Palermo, Palermo, ITALY*

Recent studies have reported an association between serum uric acid (SUA) and reduced arterial elasticity. However, in these studies arterial elastic properties have been assessed chiefly by measuring brachial-ankle pulse wave velocity (PWV) or peripheral PWV and only sometimes by using aortic PWV. Moreover, the relationships between SUA and arterial stiffness have never been statistically adjusted for albuminuria. Furthermore, the studies exploring the influence of uric acid on aortic distensibility in subjects with arterial hypertension yielded conflicting results. The aim of our study was to evaluate the relationships between SUA and aortic stiffness in a group of essential hypertensive patients, attending our Hypertension Centre.

We enrolled 222 untreated hypertensive patients (mean age: 44 ± 10 years; 60 % males), without cardiovascular complications and without severe renal insufficiency. In all subjects routine blood chemistry, including SUA determination (by uricase/peroxidase method) and albumin excretion rate (AER) assay were obtained. Moreover, measurement of carotid-femoral pulse wave velocity (c-f PWV), by an automatic computerised method (Complior) and 24-h ambulatory blood pressure (BP) monitoring were performed

Patients with c-f PWV > 12 m/sec (n = 44) showed SUA levels significantly higher than those with lower values of PWV (5.9 ± 1.2 vs 5.3 ± 1.1 m/sec; p = 0.002). This difference held after correction by ANCOVA for age, gender, mean arterial pressure (MAP), body mass index, and serum creatinine (p = 0.02), but not after further adjustment for AER. Univariate analysis of correlation disclosed a significant association of SUA with c-f PWV (r = 0.23; p = 0.001). This correlation lost statistical significance when AER was added in a multiple regression model including, as covariates, age, gender, MAP, serum creatinine, metabolic syndrome and SUA.

The results of our study show that, in essential hypertensive subjects, a positive relationship between SUA and aortic stiffness exists This association may be mediated by endothelial dysfunction, as suggested by the loss of its statistical significance, after adjustment for albumin excretion rate.

8A.06 HYPOKALEMIA AS A POTENTIAL CAUSE OF CARDIOVASCULAR COMPLICATIONS IN HYPERTENSIVE BUT OTHERWISE APPARENTLY HEALTHY MIDDLE-AGED AND ELDERLY SUBJECTS

N. Mattsson, P. Kumarathurai, O.W. Nielsen, A. Sajadieh. *Department of Cardiology, Bispebjerg University Hospital, Copenhagen, DENMARK*

Purpose: Potassium has important functions in the body including specific cellular functions and interactions in the Renin-Angiotension-Aldosterone System. Less is known about the prognostic impact of mild hypokalemia in an apparently healthy population. We hypothesized that incidental mild hypokalaemia in middle aged and elderly subjects with hypertension is associated with increased rate of stroke and mortality.

Methods: Apparently healthy middle-aged and elderly (55-75 year old) subjects from the cohort of the "Copenhagen Holter Study" (N: 671) were studied. The study population was divided into two groups: a mild hypokalemic group, p-potassium < 3.7 mM, (mean: 3.4 mM, range 2.7-3.6) versus a normokalemic group (mean: 4.0 mM, range 3.7-5.4). The primary end-point was combined death or stroke and the secondary end-point was stroke. In the Cox models adjustments were performed for relevant covariables and variables with known association to death or stroke.

Results: Subjects with mild hypokalemia were older (67.0 years (6.94) vs. 64.0 years (6.66) p<0.0001) had higher systolic blood pressure (165.1 mmHg (26.1) vs. 154.6 mmHg (23.5) p<0.0001). The groups were not significant different in terms of gender, body mass index, smoking status, diabetes, p-creatinin and p-cholesterol. The incidence of combined death or stroke was significantly higher in the hypokalemic group (HR 2.42, CI 95% 1.58-3.70) and multivariate adjustment for conventional risk factors did not change significance. Stroke as isolated events was also significantly higher in the hypokalemic group (HR 2.40, CI 95% 1.51-3.82). In 453 hypertensive subjects hypokalemia was a predictor of death or stroke both in an univariate model and after multivariate adjustment for conventional risk factors (HR 1.7, 95%CI 1.04-2.83), but in normotensive subjects the association was weak and disappeared after adjustment for conventional risk factors.

Conclusions: Apparently mild hypokalemia carry a poor prognosis in hypertensive middle-aged and elderly subjects.

8A.07 CARDIAC FUNCTION OF HYPERTENSIVE MEN DURING MODERATE SHORT-TERM COLD EXPOSURE

H. Hintsala[1], T. Kenttä[2,3], H.V. Huikuri[2,3], J.J.K. Jaakkola[1,4], T.M. Ikäheimo[1,4]. *[1]Center for Environmental and Respiratory Health Research, University of Oulu, Oulu, FINLAND, [2]Institute of Clinical Medicine, University of Oulu, Oulu, FINLAND, [3]Oulu University Hospital, Oulu, FINLAND, [4]Institute of Health Sciences, University of Oulu, Oulu, FINLAND*

Objective: Intense cold exposure involving whole-body cooling is known to produce electrocardiographic changes such as J (Osborn) waves, interval prolongation, and arrhythmias, which could contribute to increased cardiovascular morbidity and mortality during winter. However, the effects of habitual short-term cold exposure on cardiac function are not known. In addition, the pathophysiological effects of hypertension may further affect cardiac function in cold. The aim of our study was to assess cardiac function among untreated borderline hypertensive and normotensive men during moderate short-term cold exposure simulating common outdoors condition during the winter.

Design and method: We conducted a population-based recruitment of 51 hypertensive and 32 normotensive men (age 55-65 years) who underwent exposures to control (18°C, 15 min) and whole-body cold exposure (-10°C, wind 3m/s, winter clothes, 15min). 12-lead ECG recordings were performed. ECG descriptors were derived from lead V5 and II.

Results: Moderate short-term cold exposure increased the mean T-peak to T-end (TpTe) interval among both hypertensive and normotensive men (lead II 67±14

vs. 72±16, p<0.05 and 71±8 vs. 75±8 ms, p<0.05, respectively). Similarly, the mean T-wave amplitude increased during cold exposure (lead V5 0.22±0.11 vs. 0.29±0.12, p<0.001 and 0.31±0.10 vs. 0.38±0.12 mV, p<0.001, respectively). The T-wave amplitude differed significantly between the two groups (p<0.001). However, the TpTe interval did not show any significant differences between hypertensive and normotensive men. Neither QT, PR, and QRS intervals, arrhythmias nor Osborn waves were altered during cold exposure.

Conclusions: Short-term cold exposure typical in subarctic countries in winter induced changes in T-wave morphology among middle-aged hypertensive and normotensive men, which could indicate increased repolarization heterogeneity that has been associated with increased risk of ventricular arrhythmias. Borderline hypertension was not associated with altered cardiac function in the cold.

ORAL SESSION

ORAL SESSION 8B
HEART AND HAEMODYNAMICS

8B.01 ASSOCIATION BETWEEN LEFT ATRIAL VOLUME, ARTERIAL STIFFNESS AND CLINIC AND 24 HOURS BLOOD PRESSURE IN A GENERAL POPULATION IN NORTHERN ITALY. THE VOBARNO STUDY

M. Salvetti[1], A. Paini[1], D. Stassaldi[1], F. Bertacchini[1], G. Rubagotti[1], C. Agabiti Rosei[1], C. Aggiusti[1], R. Gatta[1], E. Agabiti Rosei[1], M.L. Muiesan[1].
Internal Medicine, University of Brescia, Brescia, ITALY

Background: Left atrial (LA) dilatation is associated to an increased risk of cardiovascular complications. Assessment of LA volume, but not of linear dimensions, may improve the accuracy in the detection of LA dilatation. The relationship between clinic and 24 hours blood pressure (BP) values, arterial stiffness and LA volume have not been extensively evaluated. Aim of our study was to assess the relationship between LA volume, evaluated by 2-dimensional echocardiography, arterial stiffness and different measures of BP load (clinic and 24 hours BP) in a general population sample in a town in Northern Italy.

Design and methods: 250 subjects (mean age 56±4 years, BMI 26±5, 57% males) participating in our ongoing population study (Vobarno study) underwent standard laboratory examinations and clinic and 24 hours systolic (SBP) and diastolic (DBP) blood pressure measurement (Spacelabs 90207). Left ventricular (LV) structure was assessed by ultrasound and carotid-femoral PWV was measured using Complior SP (Artech, Pantin, France). Left atrial volume was measured by the area-length method using the apical 4-chamber and 2-chamber views, as suggested by the ESC imaging Guidelines.

Results: At univariate analysis LA volume was significantly correlated with BMI (r=0.34, p<0.001), systolic BP: clinic r=0.21, 24 hours r=0.26 (all p<0.01); diastolic BP: clinic r=0.16, 24 hours r=0.20 (all p<0.05); pulse pressure (PP): clinic r=0.16, 24 hours r=0.20 (all p<0.05), uric acid r=0.20 (p<0.01), plasma glucose r=0.13 (p<0.05) and left ventricular mass index (LVMI) (r=0.547, p<0.001). At multivariate analysis LA volume was independently correlated to BMI (beta= 0.36, p<0.001), male gender (beta=0.31, p<0.001), 24 hours heart rate (beta= -0.24, p<0.01), 24 hours systolic BP (beta= 0.14, p<0.05), and PWV (beta= 0.12, p<0.05). When LVMI was added to the model the variables independently related to LA volume were LVMI (beta=0.358, p<0.001), BMI (beta= 0.206, p<0.001), male gender (beta=0.275, p<0.001), 24 hours heart rate (beta= -0.170, p<0.01) and uric acid (beta 0.121, p<0.05).

Conclusions: In a general population sample in Northern Italy left atrial volume is more strictly related to 24 hours BP values than to clinic BP, and to the increase in LV mass.

8B.02 AN INVESTIGATION INTO THE EFFECT OF PHARMACOLOGICALLY ALTERED ARTERIAL LOAD ON VENTRICULAR-ARTERIAL INTERACTION USING SPECKLE TRACKING ECHOCARDIOGRAPHY AND PULSE WAVE ANALYSIS

M. Kearney[1], B. McDonnell[1], J. Coulson[2], M. Munnery[3], J. Thompson[1], A. Nio[1], E. Stohr[1], Z. Yousef[2], J. Cockcroft[3], K. Backx[1], R. Shave[1].
[1]Cardiff Metropolitan University, Cardiff, UNITED KINGDOM, [2]University Hospital Wales, Cardiff, UNITED KINGDOM, [3]Wales Heart Research Institute, Cardiff, UNITED KINGDOM

Objective: Ventricular-arterial interaction (VAI) can be quantified using the ratio of arterial (Ea) and ventricular (Ees) elastances. However, Ea does not consider arterial wave reflections and Ees is a global measure of LV function. Speckle tracking echocardiography (STE) quantifies regional LV mechanics and pulse wave analysis (PWA) describes the arterial pressure waveform. The purpose of this study was to pharmacologically modify wave reflection, and thus arterial load, to determine the effect on VAI using Ea/Ees, STE and PWA.

Design and method: 11 participants (46±7 years) underwent simultaneous STE and PWA during consecutive administration of glyceryl trinitrate (GTN) and phenylephrine (PE).

Results: GTN reduced end systolic pressure (ESP) and AIx while PE elevated both. Neither GTN nor PE affected heart rate (HR) or mean arterial pressure (MAP). Whilst GTN decreased Ea/Ees, Ea and Ees were individually unaltered. However, there was a decrease in the timing of the peak of the reflected wave and an increase in the time to peak (TTP) of both longitudinal strain and apical systolic circumferential strain rate. PE did not alter Ea/Ees or LV mechanics.

Conclusions: Changes in LV strain and wave reflections due to acute alterations in arterial load may reflect adjustments to VAI otherwise undetected by Ea/Ees.

8B.03 HYPERTENSION TREATMENT BASED ON NON-INVASIVE BIOIMPEDANCE (HOTMAN®)

D. Màrquez[1], C. Cerezo[2], C. Romero[3], L. Fernandez[2], L. Guerrero[2], L.M. Ruilope[2], J. Segura[2]. *[1]Hospital Dr. Arturo Oñativia, Unidad de Prevención Cardionefrometabólica, Salta, ARGENTINA, [2]Hospital Universitario 12 de Octubre, Unidad de Hipertensión Arterial, Madrid, SPAIN, [3]Hospital Privado, Departamento de Clínica Médica, Córdoba, ARGENTINA*

Objectives: 1) Compare Blood pressure (BP) control in patients treated based on HOTMAN. 2) Compare the hemodynamic differences between groups pre and posthotman. 3) Compare the cases where the treatment suggested by the specialist was similar from the treatment based on HOTMAN.

Abstract 8B.02

Variable / Condition: mean (SD)	Baseline 1	GTN	Baseline 2	PE
HR	49 (6)	49 (5)	48 (5)	47 (4)
MAP	81 (5)	82 (6)	82 (6)	83 (7)
ESP	94 (12)	88 (12)**	93 (13)	95 (13)*
E_a (mmHg/ml)	1.15 (0.31)	1.10 (0.25)	1.17 (0.27)	1.22 (0.27)
E_{es} (mmHg/ml)	1.91 (0.46)	1.98 (0.42)	1.91 (0.58)	1.86 (0.41)
E_a/E_{es} (mmHg/ml)	0.61 (0.12)	0.56 (0.10)*	0.64 (0.13)	0.66 (0.07)
AIx (%)	23 (14)	9 (13)**	21 (15)	23 (13)*
TTP reflected wave (ms)	242.09 (27.79)	227.73 (19.84)*	244.00 (27.71)	246.55 (24.65)
TTP longitudinal strain (ms)	381.29 (36.45)	400.67 (39.50)*	418.99 (46.90)	424.70 (56.11)
TTP apical systolic circumferential strain rate (ms)	178.10 (26.26)	201.78 (28.22)*	188.84 (23.62)	191.55 (25.12)

*p<0.05; **p<0.001

Methods: Interventional study. Inclution: 50 to 75 y/o with 2 or more drugs and poor office BP control. A 24h ABPM study and bioimpedance (HOTMAN) were done. This system provides hemodynamical information such as Cardiac Index (CI), SI (Stroke Index), HR (heart rate), SSVRI (Stroke Systemic Vascular Resistance Index) and TFC (Thoracic Fluids Conductivity). Patients were divided in: control group (office BP >140/90 and 24h ABPM <130/80) and case group (office BP >140/90, and 24h ABPM >130/80). Only case group received treatment based on ABPM + HOTMAN, and returned 4 weeks later to repeat the studies. One of the specialists suggested an empirical treatment based on ABPM to compared his choice with hotman study.

Results: Thirty one patients were included, 10 controls and 21 cases. Mean age was 65,7 ± 8,3. The 24h systolic blood pressure was 121,2 ± 9,8 vs 143,6 ± 7,5 (control vs case group pretreatment p:<0,001). Postreatment BP decreased to 130,6 ± 18,4 (pre vs postreatment p:<0,001). Similar results were found for daytime and nightime SBP. The number of antihypertensive drugs was 3,2 ± 1 in control group vs 2,9 ±1 in case group pretreatment (NS), and 3,4 ± 1,1 postreatment (table 1). We found differences in hemodynamics patterns for SSVRI (control group vs postreatment 229,8 ± 78,5 vs 175,6 ± 55 p:0,04, and pre and postreatment 210,4 ± 80,3 vs 175,6 ± 55 p:0,04). The treatment suggested by the specialist vs HOTMAN study was similar in 6 of 21 cases (28,5%).

Conclusion: Hypertension treatment based on HOTMAN study helped our terapheutical decision and improved BP control. Further studies are needed to evaluate strong end points.

8B.04 PREVALENCE OF ECHOCARDIOGRAPHIC LEFT ATRIAL ENLARGEMENT IN HYPERTENSION: A SYSTEMATIC REVIEW OF RECENT CLINICAL STUDIES

C. Cuspidi[1], M. Rescaldani[2], C. Sala[2]. [1]*Department of Health Science, University of Milano-Bicocca and Istituto Auxologico Italiano, Milan, ITALY,* [2]*Department of Clinical Sciences and Community Health, University of Milano and Fondazione Policlinico, Milan, ITALY*

Aim: Left atrial enlargement (LAE) is a marker of hypertensive heart disease associated with increased cardiovascular risk. We reviewed recent literature about the prevalence of LAE, as assessed by echocardiography, in order to update our information about the clinical relevance of this cardiac phenotype in human hypertension.

Design: A MEDLINE search using the key words "left atrial enlargement", "left atrial dilatation", "left atrial size", "hypertension", "echocardiography", "atrial fibrillation" was performed in order to identify relevant papers. Full articles published in English language from January 1st 2000 to July 1st 2012 reporting studies in adult individuals were considered.

Results: A total of 15 studies, including 10,141 untreated and treated subjects were considered. LAE was defined by 11 different criteria (4 studies applied two or more criteria, range 2-3) and its prevalence consistently varied among studies (16.0-83.0%); in the pooled population LAE prevalence was 32%. According to a gender-based analysis of 9 studies (8,588 patients) LAE prevalence was similar in women as in men (OR 1.23, 95% CI, 0.83-1.83, p=0.30). Data provided by 10 studies (n=9,354 patients) showed that prevalence of left ventricular hypertrophy was significantly higher in patients with LAE (68.2%) than in their counterparts (41.8%) (OR 2.97, 95% CI : 2.68-3.29, p <0.01).

Conclusions: Our analysis shows that LAE is present in a relevant fraction of the hypertensive population. As LAE is an independent predictor of cardiovascular events, the accurate detection of this phenotype may improve risk evaluation in hypertensive patients.

8B.05 RIGHT VENTRICULAR MORPHO-FUNCTIONAL REMODELING IN NEVER TREATED MILD HYPERTENSIVES: ROLE OF AORTIC PRESSURE AND BIVENTRICULAR PARAMETERS

C. Mongiardi, A.M. Maresca, C. Marchesi, V. Ferrari, F. Annoni, L. Merletti, V. Vacirca, C. Gadaleta, A. Bertolini, L. Guasti, A.M. Grandi. *Department of Clinical and Experimental Medicine, University of Insubria, Varese, ITALY*

Objective: Previous studies have shown an increased right ventricle's (RV) morpho-functional remodeling in hypertensives. No evidence is available about a relationship between Aortic Pressure (AP) and RV morpho-functional remodeling. Aim of our study was to investigate relationship between RV and left ventricular (LV) morpho-functional parameters and AP in mild hypertensives;

Design and method: We enrolled consecutively 107 patients without cardiovascular diseases or diabetes, never treated with anti-hypertensive drugs. We identified 74 hypertensives (24h-BP >125/80mmHg), 33 normotensives matched for age (46±6 vs 44±6years), gender and body mass index (26±3 vs 26.2±4kg/m2). All underwent blood tests, pulse wave analysis/velocity (PWA/PWV) and echocardiography according with LV-RV ASE/EAE guidelines.

Results: 24h-BP was higher in hypertensives (132±9/85±7 vs 116±6/74±4mmHg, P<0.001). WBC, neutrophil count, triglycerides, fasting glucose, HDL, LDL cholesterol were similar in two groups. Systolic-AP and PWV were higher in hypertensives (124±11mmHg vs 116±16 P=0.013; 7.1±2 vs 6.2±1m/s P=0.04). LV, RV diameters and systolic function were normal in all and similar in the groups. LV mass index (36±8 vs 31±6g/m2.7 P<0.001) and relative wall thickness (0.42±0.05 vs 0.37±0.05 P<0.001) were higher in hypertensives. RV wall thickness was higher in hypertensives too (5.3±0.1 vs 4.6±0.1mm P=0.02). Hypertensives showed lower LV lateral/septal E' and higher E/E'; they showed also lower RV-E' (13.8±3 vs 15.1±3cm/s P=0.03) but similar E'/A' and E/E' values; Univariate analysis showed an association between RV thickness and inter-ventricular septum (IVS), systolic-AP, RV-E' and E'A' but a regression analysis assessed that only IVS was significantly associated (β=0.39 P=0.001). A regression analysis showed that RV-E' was significantly related to IVS and LV-E' (β=-0.31 P=0.001, β=0.27 P=0.004). A further regression analysis revealed a stronger association of RV thickness and E' to systolic-AP than to 24h-systolic-BP (respectively r=0.22 p=0.026, r=0.28 p=0.003 vs r=-0.17 p=0.07, r=-0.29 p=0.002).

Conclusions: We found that RV morpho-functional remodeling appears to be mainly related to IVS thickness. Also in this study aortic pressure was associated to RV parameters as far as 24h-BP.

Abstract 8B.03

Table1.- Baseline Characteristics and treatment by bioimpedance

Variable	Control Group(a)	Case Group Pre-hotman(b)	Case Group Post-hotman(c)	*a vs b*	*b vs c*	*a vs c*
n	10	21	18			
Age	68,9±6,6	62,8±8,9	63,4±8,9			
Male	40%	42%				
BMI	28,9±2,8	27,1±4,2	27,1±4,2			
Drugs *n*	3,2±1	2,9±1	3,4±1,1	ns	<0,001	ns
24hSBP	121,2±9,8	143,6 ±7,5	130,6±18,4	<0,001	<0,001	ns
24hDBP	74,7±9,5	82,9±11,9	77,4±11,3	<0,001	< 0,01	ns
CI	2±0,7	2,8±0,8	2,9±0,7	0,4	0,3	0,2
SI	44±28,2	46,4±15,6	46,8±14,2	0,7	0,9	0,7
SSVRI	229,8±78,5	210,4±80,3	175,6±55	0,5	0,04	0,04

Abreviations: BMI (body mass index), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), CI (cardiac Index), SSVRI (Stroke Systemic Vascular Resistance Index).

8B.06 HAEMODYNAMICS ARE ASSOCIATED WITH VARIANTS OF THE OBESITY ASSOCIATED (FTO) GENE IN AN OMANI ARAB PEDIGREE

M. Hassan[1], S. Al-Sinani[1], S. Vorgantii[2], S. Albarwani[1], S. Al-Yahyaee[1], T. Comuzzie [2], R. Bayoumi [1]. *[1]Departments of Physiology and Biochemstry,College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, OMAN, [2]Departemnt of Genetics, Texas Biomedical Institute, San Antonio, TX, USA*

Objective: We aimed to study the association between haemodynamics, blood pressure and type 2 diabetes with the obesity-associated FTO SNPs rs9939609 and rs8050136.

Design and method: The study was conducted in one, large, extended, isolated and highly consanguineous Omani Arab pedigree of 232 individuals aged 16 - 80 years. Ambulatory blood pressure was recorded (Schiller BR102) and haemodynamic indices (corrected for body surface area) were measured using impedance cardiography during 10 minutes of rest, 3 minutes of mental stress and 3 minutes cold pressor test using the Task Force Monitor (CNSystems, Austria). Body mass index (BMI), Waist circumference, fat percentage, fasting, postprandial glucose and insulin, insulin resistance and HbA1C were measured using standard methods. Measured genotype analysis was used as a family-based association method as implemented in the SOLAR program (San Antonio, Texas). For multiple testing Bonferroni correction was applied and the level of significance was calculated to be P = 0.004.

Results: The rs8050136 and rs9939609 SNPs were significantly associated with the resting haemodynamic indices: Total peripheral resistance index (P = 0.001 and 0.005), cardiac index (P = 0.0008 and 0.007, cardiac contractility (P = 0.001 and 0.003) and acceleration index (P = 0.001 and 0.0005), respectively. However stroke index (P = 0.02), end-diastolic index (P = 0.01) did not reach significances levels. Of the ABPM parameters only sleep BP dip was associated with rs8050136 (P = 0.05) but did not reach significance levels. Similarly the rs8050136 SNP was associated with BMI (P = 0.027) and T2D (P = 0.041) but not with fat percentage and other T2D parameters.

Conclusion: In this isolated pure Arab population variants of the obesity associated FTO gene were significantly associated with resting haemodynamic parameters that make up blood pressure. Dissecting BP into its primary and intermediate phenotypes my help in the understanding of the genetic link between blood pressure, obesity and T2D.

8B.07 PREVALENCE AND CLINICAL PROFILE OF PATIENTS WITH TAKO-TSUBO CARDIOMYOPATHY AND HISTORY OF SYSTEMIC HYPERTENSION

R. Citro[1], P. Predotti[1], A. Silverio[2], M. Di Maio[2], R. Giudice[2], C. Prota[2], L. Soriente[1], R. Ascoli[1], B. Palumbo[1], R. Pietrofeso[1], F. Silvestri[1], F. Piscione[2]. *[1]Heart Departement, A.O.U. San Giovanni e Ruggi, Salerno, ITALY, [2]Medical-Surgical Departement, University of Salerno, Salerno, ITALY*

Background: Tako-Tsubo cardiomyopathy (TTC) is an acute condition characterized by transient and reversible left ventricular myocardial systolic dysfunction and distinctive contraction pattern despite the absence of significant obstructive coronary artery disease (CAD). The clinical presentation of TTC resembles that of an acute coronary syndrome. However the impact of the factors generally considered at risk for CAD on clinical course of TTC patients is not well elucidated.

Aim: To establish the prevalence and clinical profile of patients with TTC and history of systemic hypertension.

Methods: The study population consisted of 51 patients (mean age 63.59 ± 14.07 years; female 94.1%) enrolled according to the Mayo Clinic diagnostic criteria for TTC. Data collection included information on patient demographics (sex, age, heart rate, systolic and diastolic blood pressure), signs and symptoms at presentation, medical history, trigger events, electrocardiographic ST-segment changes and presence of prolonged QTc interval on admission, clinical observations during hospitalization (including major cardiovascular events) and echocardiographic findings.

Results: Patients with (27; female= 92%; mean age= 66.0±10.9 years) and without (24; female= 96%; mean age= 59.5±16.4 years; p= 0.11) history of systemic hypertension were compared. Among hypertensive patients thirteen were pretreated with betablockers. No significant differences about presenting symptoms, electrocardiographic features at admission, left ventricular morphology, incidence of in-hospital complications and length of hospitalization were observed. Systolic (135.00±19.68 vs 115.60±30.01; p = 0.009) and diastolic blood pressure (79.81±10.14 vs 67.79±14.17; p= 0.001) were significantly higher in patients with history of hypertension, conversely heart rate at admission was significantly lower in this cohort (82.88±15.92 vs 95.42±23.78; p= 0.032). Moreover, there is a trend for a lower incidence of physical trigger events in hypertensive patients (7.7% vs 28.0%; p= 0.075).

Conclusions: History of systemic hypertension is commonly reported in patients with TTC. However, it seems do not influence the clinical course and the occurrence of complications. Of note, the pretreatment with a beta-blocker does not prevent TTC onset.

ORAL SESSION

ORAL SESSION 8C
EXPERIMENTAL PHARMACOLOGY AND HYPERTENSION

8C.01 ANGIOTENSIN-(1-7) MODULATES RENAL VASCULAR RESISTANCE THROUGH INHIBITION OF MITOGEN-ACTIVATED PROTEIN KINASE P38 IN APOLIPOPROTEIN E DEFICIENT MICE

S. Potthoff[1], M. Fähling[2], T. Clasen[1], Y. Mori[1], S. Sivritas[1], A. Patzak[2], L.C. Rump[1], S. Stegbauer[1]. *[1]Medical Faculty, Department of Nephrology, University Düsseldorf, Düsseldorf, GERMANY, [2]Institute of Vegetative Physiology, Charité Berlin, Berlin, GERMANY*

ApoE-KO mice are characterized by endothelial dysfunction and increased vasoconstrictor response. Previously, we have shown that chronic Ang-(1-7)-treatment ameliorates endothelial dysfunction in apoE-KO. However, the impact of Ang-(1-7) on vasoconstrictor response to AngiotensinII (AngII) is unknown.

To examine the role of Ang-(1-7) in vascular resistance in atherosclerosis, apoE-KO and wild type (WT) mice fed on western diet were treated via osmitic-minipumps either with Ang-(1-7) (82µg/kg/hr) or saline (6 weeks). Vascular resistance was tested in isolated perfused kidneys. AngII induced renal pressor-response was significantly increased in apoE-KO and chronic Ang-(1-7) treatment attenuated AngII induced pressor-response in apoE-KO compared to WT mice.

Accordingly, in apoE-KO, phospho-MLC20, a marker of enhanced contractility was increased in preglomerular vessels compared to WT and reduced after Ang-(1-7) treatment. To examine the underlying cause, we measured reactive oxygen species (ROS) production and changes in NADP(H)-oxidase expression levels. In apoE-KO mice, p47phox was increased (1.5-fold;P<0.05) and reduced after chronic Ang-(1-7) treatment compared to WT. Concordantly, urinary isoprostane-8 excretion and H2O2 generation were significantly decreased in Ang-(1-7) treated apoE-KO mice. ROS is known to activate MAPK-p38 which itself modulates pressor response. To test the role of p38, we measured p38-activity and renal pressor-response to AngII in the presence of SB203580, a p38-inhibitor: In preglomerular vessels of apoE-KO, the phospho-p38/p38-ratio was increased compared to WT. Chronic Ang-(1-7) treatment restored this ratio almost to WT levels (2.8±0.5 vs. 1.0±0.1 vs. 1.3±0.2;P<0.05). Administration of SB203580 (5µmol/L) reduced renal pressor-response to AngII in apoE-KO but not in Ang-(1-7) treated mice. Hence, chronic inhibition of p38 with BIRB796 (30mg/kg) attenuated the increased pressor-response to AngII in apoE-KO mice.

In summary, p38 plays a crucial role in regulating renal vascular resistance in apoE-KO mice. Moreover, Ang-(1-7) attenuates pressor-response to AngII by reducing p38 activity. This study revealed a new pathway how Ang-(1-7) modulates vascular function.

8C.02 GENETICALLY HIGH PLASMA ANGIOTENSINOGEN LEVELS POTENTIATE L-NAME INDUCED BLOOD PRESSURE ELEVATION AND CAUSE EARLY INCREASED END-ORGAN DAMAGE IN TRANSGENIC RATS

J. Bohlender, B. Gudo.
University of Bern, Institue of Cell Biology, Bern, SWITZERLAND

Objective: Genetically elevated plasma angiotensinogen (Ang-N) levels have been associated with increased plasma and tissue angiotensin (Ang) II levels and increased blood pressure in humans and animal models. This may increase the sensitivity to additional blood pressure (BP) stressors and induce greater BP changes and greater end-organ damage compared to normal plasma Ang-N levels. We tested this hypothesis in our newly established transgenic rat strain (TGR) with high transgenic plasma (Val5)-Ang-N concentrations treated by L-nitroarginine methyl ester (L-NAME) to decrease endogenous NO production and thus its antihypertensive effect.

Methods: Heterozygous male TGR and nontransgenic Sprague-Dawley control rats (CTR) aged 10 weeks received 30 mg/kg body weight L-NAME or vehicle (drinking water, n=8 per group) for 3 weeks. Blood pressure (BP, tail cuff) was measured before and at the end of the experiment when heart weight (HW), body weight (BW), plasma Ang-N and aldosterone (radioimmunoassay) and urinary (u) Na, K, creatinine and protein concentrations were determined. Kidney mRNA expression (RT-PCR) was quantified for endothelin-1 (ET), renin (REN), non-transgenic AGT, AT1-receptor, fibronectin (FIB), collagen-1, collagen-4, transforming-growth-factor beta, NADPH-oxidase subunits phox47 and phox91, and cardiac collagen-4 and Ang-converting-enzyme.

Results: Plasma total Ang-N was ~7 times higher in TGR. Baseline BP was +24 mmHg, u-protein 6.9-times, uNa and uNa/creatinin 1,8-times, HW/BW 1,2-times, kidney ET-mRNA 1.8-times (p<0.05 all) and plasma aldosterone 1,5-times (p=NS) higher, and uK 0.6-times (p=NS) and REN-mRNA expresion 0.35-times lower in TGR vs. CTR without differences for the other genes (p=NS). L-NAME increased BP by 36% vs. 25% (p<0.05), HW/BW 16% vs. 1.5% (p<0.05), plasma aldosterone 51% vs. -13% (p<0.05) in TGR vs. CTR. It decreased TGR uNa and uNa/creatinin (~40%), CTR kidney REN-mRNA expression (-42%, p<0.05) and increased CTR u-protein (10,3-times) and TGR kidney FIB- and phox47-mRNA (+55%, +26%, p<0.05) without significant other differences or treatment effects (p=NS).

Conclusion: Genetically high plasma Ang-N levels augment the L-NAME-induced hypertensive response and cause early increased cardiac and renal end-organ damage compared to normal plasma Ang-N levels.

8C.03 IMPACT OF SELECTIVE SOLUBLE ADENYLYL CYCLASE INHIBITION ON GENES AFFECTING ENDOTHELIAL STIFFNESS

J. Nedele[1], M. Herrmann[1], A. Salomon[2], K. Guske[1], B. Schmitz[1,2], S. Brand[2], E. Brand[1]. *[1]University Hospital Münster, Internal Medicine D, Nephrology, Hypertension and Rheumatology, Muenster, GERMANY, [2]University Hospital Münster, Institute for Sports Medicine, Molecular Genetics of Cardiovascular Disease, Muenster, GERMANY*

Objective: Components of the Renin-Angiotensin-Aldosterone-System (RAAS) are expressed in vascular endothelial cells. In particular, epithelial Na+-channels (ENaC), the mineralocorticoid receptor, and the Na+/K+-ATPase have been reported to regulate the endothelial stiffness in response to serum Na+. The soluble adenylyl cyclase (sAC) activates the Na+/K+-ATPase in renal epithelial collecting duct cells. Nuclear sAC constitutes a functional complex with cAMP response element binding protein (CREB), suggesting a general role of sAC in overall gene regulation. We determined the chromatin binding capacities of sAC at CRE sequences. The effects of sAC inhibition and aldosterone application on the expression of genes affecting endothelial stiffness and sAC itself were analyzed.

Design and methods: We performed Chromatin Immunoprecipitation (ChIP) assay with antibodies against sAC and CREB in vascular endothelial (EA.hy926) and human kidney cells (IHKE). CRE luciferase reporter vector was transfected and subsequently incubated with sAC inhibitor KH7 and/or cAMP in both cell lines. The impact of KH7 and cAMP on CREB and phosphorylated CREB expression was analyzed using Western Blot. Total RNA of KH7- and aldosterone-treated EA.hy926 cells was isolated to analyze expression of genes involved in aldosterone signaling by real-time PCR.

Results: We detected binding of sAC at CRE motifs in endothelial and kidney cells. Specific pharmacological inhibition of sAC by KH7 significantly decreased transcriptional activity of the CRE control vector, whereas cAMP stimulation could not overcome reducing effects of KH7 in both cell lines. In addition, phosphorylated CREB was significantly reduced after KH7 treatment, while unphosphorylated CREB remained unaffected. Inhibition of sAC and aldosterone application significantly altered expression of downstream targets of aldosterone signaling, e.g. mineralocorticoid receptor and Na+/K+-ATPase alpha1 and beta1.

Conclusion: Since sAC interacts with CRE sites, it harbours transcriptional trans-acting properties, thereby potentially influencing expression of genes involved in aldosterone signaling. Selective sAC inhibition significantly reduced CREB-mediated CRE control vector activity as well as CREB phosphorylation, which could not be restored by cAMP stimulation.

8C.04 IMPROVED VASCULAR REMODELING AND ENDOTHELIAL FUNCTION IN TRANSGLUTAMINASE 2 KNOCK-OUT MICE INFUSED WITH ANGIOTENSIN II

C. Savoia[1], E. Arrabito[1], L. Sada[1], S. Michelini[1], L. Pucci[1], M. Briani[1], T. Bucci[1], C. Nicoletti[2], E. Candi[3], E.L. Schiffrin[4], M. Volpe[1]. *[1]Clinical and Molecular Medicine Department, Sapienza University of Rome, Rome, ITALY, [2]DAHFMO-Unit of Histology and Med. Embr. Sapienza University of Rome, Rome, ITALY, [3]Department of Experimental Medicine and Surgery, Faculty of Medicine University of Rome Tor Vergata, Rome, ITALY, [4]Lady Davis Institute for Medical Research, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montreal, CANADA*

Objective: Transglutaminase 2 (TG2) induces cross-linking of proteins. This is potentially relevant for cell-matrix interactions. We previously demonstrated that angiotensin II (Ang II) positively regulated TG2 expression in vascular smooth muscle cells from SHR. Here we hypothesized that Ang II induces vascular remodeling in part through TG2.

Methods: TG2-knockout mice (TG2-K/O, 8 weeks old, 6 for each group) and age-matched wild type (WT) control mice were treated or not with Ang II (400 ng/kg/min) for 14 days. Blood pressure (BP) was measured by tail-cuff method. Endothelium -dependent and –independent relaxation were assessed by dose-response curves to acetylcholine (1 nM to 100 μM) ± L-NAME (100 μM) and sodium nitroprusside (10 nM to 1 mM) respectively, in mesenteric arteries pre-contracted with norepinephrine (10 μM). Media-to-lumen ratio (M/L) and cross sectional area (CSA) were evaluated on pressurized preparations.

Results: BP was increased in TG2-K/O mice as compared to WT (120.3±1.3 mmHg vs 88.3±1.9 mmHg, p<0.05), Ang II infusion significantly increased BP only in WT (+28% vs untreated WT, P<0.05), whereas BP was unchanged in TG2-K/O after Ang II infusion. Endothelium dependent relaxations were similarly preserved in untreated WT, TG2-K/O and Ang II-treated TG2-K/O. Ang II infusion impaired acetylcholine induced relaxation only in WT (-50% vs untreated WT, p<0.05). L-NAME blunted acetylcholine-induced relaxation in all the groups except for Ang II-treated WT, suggesting an impairment of NO production only in this group. Endothelium independent relaxation was similar in all the groups. TG2-K/O presented reduced M/L as compared to WT (4.8±0.3% vs 6.5±0.2%, p<0.05). Ang II infusion increased M/L only in WT (+13% vs untreated WT, p<0.05). M/L resulted unchanged in TG2-K/O after Ang II infusion. CSA was similar in all the groups.

Conclusions: TG2-K/O presented improved vascular remodelling despite the higher BP values as compared to WT. Ang II failed to increase M/L and impair endothelial function in TG2-K/O. Hence TG2 may play a role in Ang II-induced vascular structural and functional alterations.

8C.05 FUNCTIONAL CONSEQUENCES OF UMOD GENETIC VARIATION ON BLOOD PRESSURE CONTROL

L. Anderson[1], D. Graham[1], S. Padmanabhan[1], S. Kumar[2], J.M. Bates[2], H.S. Raffi[2], N.J. Fraser[1], N.R. Ferreri[3], S. Hoa[3], A.F. Dominiczak[1], M.W. McBride[1]. *[1]University of Glasgow, Glasgow, UNITED KINGDOM, [2]University of Oklahoma, Oklahoma, OK, USA, [3]New York Medical College, New York, NY, USA*

Objective: To functionally assess UMOD promoter SNPs and characterize the cardiovascular phenotype of the UMOD knock out mouse (THP-/-).

Design and methods: rs13333226 genotype was determined in renal cells; TK-10 (AA), 786-0 (AA) and ACHN (GG). 1 and 2kb promoter constructs were generated and promoter activity assessed and confirmed by site direct mutagenesis. Hemodynamic parameters of THP-/- and wild type (WT) mice were measured using radiotelemetry and tail cuff. Systolic blood pressure (SBP) and renal function (eGFR) were investigated ±2% NaCl. Mouse primary medullary thick ascending limb (mTAL) cells were used to investigate the relationship between UMOD expression and the Na+-K+-2Cl- cotransporter isoform A (NKCC2A).

Results: 2kb TK10 (AA) promoter construct, demonstrated a 17 fold increase of luciferase activity, compared with the contrasting genotypes (p<0.0001), implicating rs4997081 as the functional SNP and further verified by site directed mutagenesis. Radiotelemetry revealed lower SBP in THP-/- compared to WT (116.6±0.3 mmHg vs.136.2±0.4 mmHg, p<0.0001). SBP in THP-/-, measured by tail cuff, was not significantly affected by 2%NaCl whereas, WT mice showed increased SBP +2%NaCl loading (136.2±1.4 mmHg vs. 173.3±2.9 mmHg, WT control vs. WT +2%NaCl, p<0.0001). eGFR was also increased in THP-/-+2% NaCl compared with WT mice (28.8±0.36 ml/min/g vs. 21.1±0.3 ml/min/g, p<0.001). siRNA knockdown of UMOD in WT mTAL cells resulted in a reduction of NKCC2A mRNA expression (1± 0.03 vs. 0.26 ± 0.01, control vs. +siRNA, p<0.001).The addition of TNF-a significantly reduced NKCC2A mRNA expression (1±0.03 vs. 0.51±0.08, control vs. control +TNF-a, p<0.001, and furthermore in the absence of UMOD; 0.18± 0.05,+siRNA +TNF-a, p<0.0001). TNF-a stimulation increased UMOD expression (1±0.08 vs. 3.25±0.06; control vs. +TNF-a, p<0.0001). In contrast, knockdown of UMOD increased basal TNF production (3.54±0.8 vs. 1±0.1, siRNA vs. control, p<0.01).

Conclusions: We identified rs4997081 as a functional variant in the human UMOD promoter and showed that baseline blood pressure is reduced in UMOD knockout mice. Importantly, UMOD knockout mice did not exhibit an increase in SBP after ingesting 2% NaCl.

8C.06 PRESSURE, ECHOCARDIOGRAPHIC, HISTOLOGICAL AND MOLECULAR EFFECTS OF STENT IMPLANTATION IN THE AORTIC ISTHMUS IN A GROWING ANIMAL MODEL

G. Ceolotto[1], L. Semplicini[1], N. Maschietto[2], H. Poser[3], I. Iacopetti[3], E. Valerio[2], T. Pilla [3], G.M. De Benedictis[3], G. Gerardi[3], D. Bernardini[3], C. Basso[4], L. Aresu[3], O. Milanesi[2], A. Semplicini[1]. *[1]Dept. of Medicine, Padua, ITALY, [2]Dept. of Women's and Children's Health, Padua, ITALY, [3]Dept. of Animal Medicine, Production and Health, Padua, ITALY, [4]Dept. of Cardiological Sciences, Padua, ITALY*

Background: Stent implantation is a novel technique for the relief of aortic coarctation in adult and pediatric patients. A low treatment age is limited by the possibility of inserting a stent dilatable to adult dimensions. However, increased stiffness of the aortic wall from childhood to adulthood could favor recurrent arterial hypertension.

Aim: To study the pressure, echocardiographic, histological and molecular changes induced by aortic stenting in a developing animal.

Methods: Platinum-iridium stent was implanted in the aortic isthmus of 8 3-5 month old female sheep (STENT). Vascular catheterization and angiography were performed in 4 control sheep (SHAM). All had echocardiography, blood tests and ascending (AsAo) and descending (DsAo) blood pressure measurements every 90 days. Twelve months after intervention the animals were sacrificed after dobutamine stress test. SOD, NOS3, CASP3, MMP9, ICAM, E-selectin gene expression were quantified in AsAo ad DsAo.

Results: Diastolic blood pressure was significantly lower in DsAo than in AsAo both in SHAM and STENT with no difference between groups. Invasive blood pressure, basal and after dobutamine, echocardiography indices, blood tests and histology findings did not differ among groups. In AsAo SOD and MMP9 were higher (+50 and + 75%, respectively) and NOS3 lower (-22 %) in STENT than in SHAM (p<0.001), with no difference in DsAo. In STENT SOD and MMP9 were higher in AsAo than in DsAo (+ 200% and + 60%, respectively).

Conclusions: Aortic stent implantation in a developing animal model does not impact negatively on direct and indirect markers of pressure homeostasis. However, we have documented stent induced molecular aortic remodeling.

8C.07 EFFECTS OF HIGH GLUCOSE ON ANG II INDUCED JAK2/STAT3 TYR-PHOSPHORYLATION IN CARDIAC FIBROBLASTS

T. Fiaschi, F. Magherini, T. Gamberi, A. Modesti, P. Modesti. *Department of Biomedical, Experimental and Clinical Sciences, Florence, ITALY*

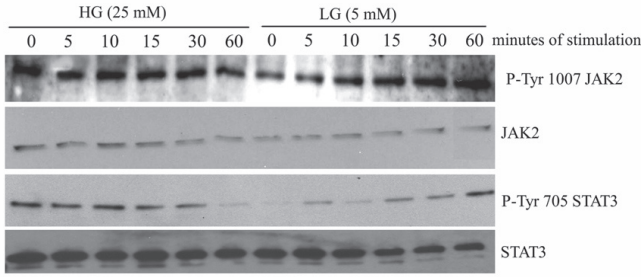
Objective: Cardiac fibroblasts significantly contribute to diabetes-induced structural and functional changes. Angiotensin (Ang) II activates Janus kinase signal transducers and activators of transcription (JAK-STAT) pathway. The activation of STAT3 during cardiac hypertrophy was recently reported to induce collagen synthesis. The objective of the present study was to determine the effects of glucose on Ang II induced JAK2/STAT3 Tyr-phosphorylation in cardiac fibroblasts.

Disegn and methods: Cultured rat ventricular fibroblasts (3rd passage, >99% purity) changed to serum free for 24 h, were stimulated with Ang II (100 nM) after 2h incubation with normal glucose (NG, 5mM), or high glucose (HG, 25 mM) buffer. JAK2 and STAT3 phosphorylation and SOD2 expression were then investigated by Western blot analysis using specific antibodies. Generation of reactive oxygen species was investigated using DCF-DA probe.

Results: Ang II enhances JAK2 and phospho-Tyr 705 STAT3 phosphorylation (60% and 90% vs buffer, respectively) after 60 minutes, in fibroblasts preincubated in NG. Conversely, in fibroblasts preincubated with HG, JAK2 and STAT3 phosphorylation were already significantly enhanced before Ang II stimulation (50%, and 110% respectively, p<0.05 for both). Ang II ROS generation was significantly enhanced in HG vs NG (+50%, p<0.05). However no further increase in JAK2 and phospho-Tyr 705 STAT3 phosphorylation was observed. Furthermore, enhanced phospho-Tyr 705 STAT3 nuclear migration and increased expression of SOD2was observed in HG condition.

Conclusions: Present findings indicates that HG concentration enhances in fibroblasts JAK2 and STAT3 phosphorylation, both implicated in cardiac hypertrophy and collagen deposition. Although Ang II stimulation cannot further enhance JAK2 and STAT3 phosphorylation, the participation of HG induced intracellular ANG II synthesis in cardiac fibroblasts cannot be excluded.

Abstract 8C.07



8C.08 A SUSTAINED RELEASE OF S-NITROSOGLUTATHIONE HAS A LONGER IMPACT ON PULSE THAN ON MEAN ARTERIAL PRESSURE

M. Parent, A. Boudier, P. Leroy, P. Maincent, I. Lartaud, F. Dupuis. *Université de Lorraine, EA 3452 CITHEFOR, Faculté de Pharmacie, Nancy, FRANCE*

Objective: Among NO-donors, S-nitrosoglutathione (GSNO) shows pleiotropic effects in the cardiovascular field especially vasodilation on both arteries (Dahboul, PLoS ONE, 2012) and veins (Sogo, Br. J. Pharmacol., 2000). While the former could lead to a reduction in mean arterial pressure (MAP), the latter could reduce pulse arterial pressure (PAP) via a decrease in preload and stroke volume (as NO-donors do not change aortic wall elasticity, Niederhoffer, Hypertension, 1997). However, the therapeutical use of free GSNO is limited by its lack of stability and short half-life (< 1 hour). We developed a new formulation of GSNO, i.e. in situ subcutaneous forming implants (ISI, biodegradable and biocompatible poly(lactide-co-glycolide) acid) and compared its impact on MAP and PAP after single administration in rats.

Design and method: Male Wistar rats (n=7) equipped with telemetric devices were injected with phosphate buffered saline (PBS), free GSNO or GSNO-loaded (30 mg/kg) ISI under transient isoflurane anesthesia to reduce stress. MAP and PAP were recorded continuously for 2 days in awake animals. Each rat served as its own control (2-week wash-out period). Graphs of the variations of MAP (δMAP) and PAP (δPAP) vs baseline were built and areas under the curve (AUC) calculated for each day (D) or night (N) period.

Results: Free GSNO decreased both MAP (-56±6 mmHg, 40 min) and PAP (-19±1 mmHg, 125 min). GSNO-loaded ISI significantly lowered MAP for 18h, with a longer effect on PAP (30h).

Values are mean ± s.e.m.*: P<0.05 vs PBS (Student t-test on AUC). #: transient increase in MAP during waking up.

Conclusions: The sustained release of GSNO from ISI was demonstrated by the longer effects on MAP and PAP vs free GSNO. The extended effect on PAP vs MAP suggests a higher impact of GSNO on venous bed. This could be of particular interest, as PAP is an independent risk factor for cardiovascular disease. This work was financed by ANR NanoSNO.

8C.09 THE CARDIOPROTECTIVE ROLE OF THE POSTCONDITIONING EFFECTS OF EXENDIN-4 AND LIRAGLUTIDE IN BOTH WKY AND SHR-SP RATS WITH LEFT VENTRICULAR HYPERTROPHY

B. Faricelli[1], M. Salomonsson[2], A. Consoli[1], T. Engstrom[3], M. Treiman[2].
[1]G. D'Annunzio University, Department of Medicine and Aging Sciences, Chieti, ITALY, [2]University of Copenhagen, Faculty of Health Sciences, Department of Biomedical Sciences, Copenhagen, DENMARK, [3]Rigshospitalet-Copenhagen University Hospital, Heart Centre, Cardiac Catheterization Labortory, Copenhagen, DENMARK

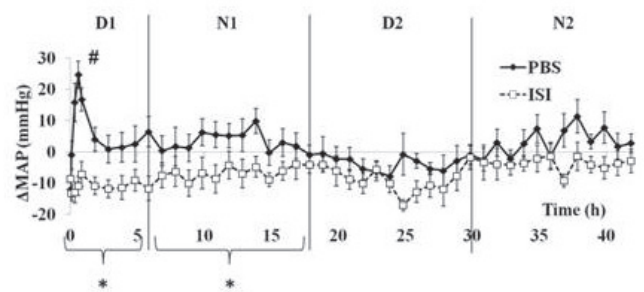
Introduction: Exendin-4 (exe4) postconditioning has been shown to limit reperfusion injury (RI) in experimental and clinical settings. Left ventricle hypertrophy (LVH) may be associated with increased RI. Our objective was to study exe4 and liraglutide postconditioning (PostC) in hearts with LVH, isolated from hypertensive SHR-SP (hypertensive LVH) rats.

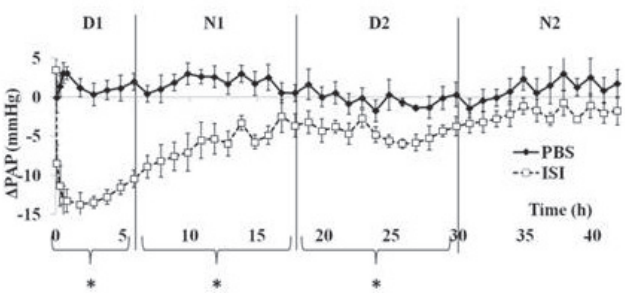
Methods: Hearts isolated from WKY (control) and SHR-SP rats (11-15 weeks old) were subjected to 35 min LAD occlusion-2 hrs reperfusion, with exe4 0.3 nM or liraglutide 0.3 nM present during the first 15 min in treated hearts. Evans blue/TTC method was used to determine area-at-risk (AAR) and infarct size (% of AAR). Akt phosphorylation (Akt-P) was measured on western blots after 3 min of reperfusion. Arterial blood pressure (BP) was measured in conscious animals by tail cuff method.

Results: BP and heart/body weight ratio were increased in SHR-SP compared to WKY rats ($p<0.0001$ for both parameters). Infarcts were larger in SHR-SP than in WKY after 35 min of ischemia (65.7 +/-3.2, N=7 vs 37.1 +/-3.4, N=12 respectively; $P<0.05$). Exe-4 and liraglutide PostC decreased infarct size (IS) after 35 min ischemia in WKY ($p<0.05$), but not after 45 min. Liraglutide and preconditioning, but not Exe-4, decreased IS after 35 min in SHR-SP ($p<0.05$). Exe4 PostC decreased IS after 15 min ischemia in SHR-SP ($p<0.05$). In WKY hearts, exe4 treatment significantly decreased diastolic contracture and increased left ventricle developed pressure. Liraglutide, but not exe4, decreased diastolic pressure in SHR hearts. In SHR-SP hearts Akt-P/Akt ratios were significantly reduced in both I/R and PostC subgroups ($n=5$ $p<0.05$).

Discussion: These data suggest that 0.3 nM liraglutide was more effective than 0.3 nM exe4 in limiting reperfusion injury in both WKY and SHR-SP. In both WKY and SHR-SP hearts there was a loss of response to PostC by exe4 with increasing ischemia time and infarct size. This loss of response to PostC occurs earlier in hypertrophy hearts.

Abstract 8C.08





ORAL SESSION

ORAL SESSION 8D
LARGE ARTERIES

8D.01 ADDITIVE VALUE OF LOWER EXTREMITY ARTERIAL STIFFNESS TO AORTIC STIFFNESS FOR PREDICTING TARGET ORGAN DAMAGE

P. Wohlfahrt[1], A. Krajcoviechova[1], J. Seidlerova[2], O. Mayer[2], J. Filipovsky[2], S. Laurent[3], R. Cifková[1]. *[1]Charles University Medical Faculty and Thomayer Hospital, Prague, CZECH REPUBLIC, [2]Charles University Medical Faculty and Teaching Hospital Pilsen, Pilsen, CZECH REPUBLIC, [3]Georges Pompidou European Hospital, INSERM U970 and Paris University Descartes, Paris, FRANCE*

Carotid-femoral pulse wave velocity (PWV), as a parameter of aortic stiffness, is an established marker of cardiovascular risk. There is a growing use of arterial stiffness parameters combining aortic and muscular arterial stiffness or parameter derived from PWV – the stiffness index beta (BETA= ln(systolic/diastolic blood pressure) × 2 blood viscosity/pulse pressure × PWV²). The purpose of this study was to compare different arterial stiffness parameters.

Methods: In 809 individuals from the Czech post-MONICA study (a randomly selected 1% representative population sample aged 54±13.5 years, 47% of men), we compared the association of carotid-femoral PWV (cfPWV), femoral-ankle PWV (faPWV), carotid-ankle PWV (caPWV), cfBETA and caBETA with cardiovascular risk factors, parameters of subclinical organ damage, and manifest cardiovascular disease presence.

Results: Both cfPWV and caPWV were similarly and significantly associated with blood pressure and glucose level, while cfPWV was more strongly associated with age, cholesterol and glomerular filtration rate while caPWV was more strongly associated with left ventricular hypertrophy detected by Sokolow-Lyon index. BETA derived from cfPWV and caPWV was less dependent on blood pressure, while it showed closer association with coronary heart disease presence, as compared to cfPWV and caPWV, respectively (cfBETA vs. cfPWV 0.731 ± 0.03 vs. 0.714 ± 0.04, p<0.05; caBETA vs. caPWV 0.740 ± 0.03 vs. 0.711 ± 0.04, p<0.05).

Conclusions: Addition of lower extremity to aortic stiffness has an effect on the association with cardiovascular risk factors, while having no effect on the association with manifest cardiovascular disease. Our data suggest that cfPWV and caPWV are not interchangeable, because muscular arterial stiffness confounds the former, with measurable effect on the association with certain cardiovascular risk factors and renal phenotypes. Beta transformation of PWV decreases its dependence on blood pressure and may increase its power in cardiovascular risk prediction.

8D.02 EFFECT OF SYSTEMIC HYPERTENSION ON AORTIC DIMENSIONS. CARDIOVASCULAR MAGNETIC RESONANCE STUDY

A. Maceira[1], J. Cosin-Sales[2], J. Ruvira[2], J. Diago[3], J. Aguilar[4], B. Igual[1], J. Monmeneu[1], M. Lopez[1], J. Estornell[1]. *[1]Cardiac Imaging Unit, ERESA Clinic, Valencia, SPAIN, [2]Department of Cardiology, Arnau de Vilanova Hospital, Valencia, SPAIN, [3]Department of Cardiology, Hospital General de Castellón, Castellón, SPAIN, [4]Department of Cardiology, Hospital de La Plana, Villarreal, SPAIN*

Objectives: Longstanding systemic hypertension (HT) may cause significant dilatation of the aorta, though little is known about this effect. Our objective was to characterize and quantify with cardiovascular magnetic resonance (CMR) the effect of HT on the thoracic aorta dimensions.

Methods: Consecutive patients who attended the CMR unit between Jan´08 and Jan´12, and did not have evidence of myocardial necrosis, cardiomyopathies other than hypertensive, significant aortic valve disease, congenital aortic disease and secondary hypertension were included. Patients were classified according to the presence (H) or absence (N) of HT. The CMR protocol included high resolution cine sequences in the necessary views in order to obtain specific planes perpendicular to the aortic long axis for each aortic segment. Aortic diameters were measured in end-systole at the level of the annulus, sinus portion, sinotubular junction, tubular portion at the level of the right pulmonary artery (RPA), middle arch and descending portion at the RPA level. All measures were indexed by body surface area. Left ventricular parameters were also recorded as well as complete clinical data.

Results: 1411 patients were included, 787 H (49% males, 65±10 yrs) and 624 N (63% males, 54±16 yrs). An ANOVA test was done (factors: group H/N, gender, age). In a per-group analysis, patients in group H showed a significantly increased aortic dimension of the tubular portion (H: 18,7±0,08cm2/m2 vs N: 18,1±0,09cm2/m2, p< 0,001), which correlated with left ventricular mass index. No differences were found between groups for other aortic segments. In a per-patient analysis, group H had a higher percentage of dilatation in all the studied aortic segments. Finally, lineal regression analysis showed that the presence of HT caused a mean increased of 0,6mm/m2 in the diameter of the tubular portion.

Conclusions: HT causes a mild but significant increase in the dimension of the ascending aorta at the level of the tubular portion, which is independent of the patients´ age and correlates with left ventricular mass.

8D.03 DOSE-DEPENDENT INWARD ARTERIAL REMODELLING AND DESTIFFENING AFTER OLMESARTAN IN HYPERTENSIVES WITH METABOLIC SYNDROME: THE VASCULAR MECHANISM STUDY

S. Laurent[1], P. Laeis[2], H. Rauer[2], P. Boutouyrie[1], Vm Study Collaboration. *[1]INSERM U970 and Assistance Publique Hopitaux de Paris, Paris, FRANCE, [2]Daiichi Sankyo Europe, Munich, GERMANY*

Background: Whether angiotensin receptor blockers can dose-dependently remodel the arterial wall during long-term treatment, has only been rarely studied. Olmesartan (OM) has previously shown a favourable pharmacodynamic profile for such an action.

Methods: In this phase 3, multi-centre, double-blind, randomized, parallel-group study, 133 subjects with hypertension and metabolic syndrome were assigned to three treatment groups and received either OM 20 mg (n=44), OM 40 mg (n=42), or OM 80 mg (n=47) once a day according to a force-titration design during a 1 year period. Office blood pressure (BP), 24hABPM, aortic stiffness (carotid-femoral pulse wave velocity-PWV) and carotid parameters (diameter, intima-media thickness, and stiffness) were measured at baseline, 24 weeks (W24) and 52 weeks (W52). A mixed-model was used for statistical analysis.

Results: PWV significantly decreased (P<0.001) with time in each group, with no significant time-dose interaction, despite a tendency for a smaller effect of 20 mg, compared to 40 and 80 mg at W52. When the 40 and 80 mg doses were combined (40/80 mg vs 20 mg), there was a tendency (p=0.0685) for a time-dose interaction in PWV reduction. After adjustment to changes in MBP, a significant BP-independent reduction in PWV was observed: PWV decreased by -0.61 m/s at W52 (p=0.0066) after 40/80 mg, whereas the non-adjusted reduction was -1.33 m/s (p<0.0001). Most carotid parameters were improved along with BP reduction, and at W52 significant reductions were observed for carotid PP (-7.15 mmHg) and internal diameter (-0.217 mm), indicating a chronic inward arterial remodeling. Patients receiving the highest dose of OM (40 and 80 mg) were shifted towards both a low elastic modulus and a low wall stress, indicating an improvement in the intrinsic elastic properties of the arterial wall material.

Conclusion: These data suggest that 40 and 80 mg Olmesartan are able to significantly remodel and destiffen the arterial wall during long-term treatment, partly independently of MBP, compared to 20 mg.

8D.04 ASSESSMENT OF AGE-ASSOCIATED CHANGES IN CAROTID PULSE WAVE VELOCITY BY MEANS OF AN ACCELEROMETRIC DEVICE

N. Di Lascio[1], E. Bianchini[1], V. Gemignani[1], R.M. Bruno[1], L. Ghiadoni[2], F. Faita[1]. *[1]Institute of Clinical Physiology, National Council of Research, Pisa, ITALY, [2]Department of Internal Medicine, University of Pisa, Pisa, ITALY*

In recent years, great attention has been placed on the role of carotid elasticity in cardiovascular risk evaluation. Carotid pulse wave velocity (cPWV) can be considered a surrogate marker for carotid stiffness assessment and it is expected to increase with ageing. Aim of this study was to determine noninvasively the age-associated changes in carotid stiffness using a new and easy-to-use accelerometric system for the cPWV assessment. Moreover accelerometric cPWV values (cPWVacc) were compared with ultrasound carotid stiffness (CS) measurements, relative distension (relD) and distensibility values (DC): results are presented.

Thirteen young healthy volunteers (34±6.9 years, 53.8% males, BMI 23.3±3.4 Kg/m2) and fourteen older healthy subjects (71.7±8.3 years, 42.8% males, BMI 26.3±4.7 Kg/m2) have been recruited. relD values were obtained by a contour tracking technique applied to ultrasound B-mode images sequences, while CS and DC ones were derived from relD measurements combined with tonometric local pulse pressure estimation and Moens-Korteweg equation. A small device, with two percutaneous accelerometers (distance: 2.4 cm) placed on a soft bracket and allowed to freely vibrate, was put on the neck of each subject. Beat-to-beat temporal shifts between the two accelerometric signals were assessed with an optimized correlation technique.

As we could expect cPWVacc values for young subjects (4.13±0.84 m/s) were lower than older participants' ones (8.19±0.86 m/s); these values were significantly different between the two groups (P<0.0001). cPWVacc values showed a good correlation with CS ones (R^2=0.60), relD (exponential fit, R^2=0.47) and DC ones (exponential fit, R^2=0.65). Comparison between cPWVacc evaluation and ultrasound CS values showed a mean difference of -0.14 m/s with a standard deviation of the difference of 1.43 m/s.

In conclusion, the proposed system could be useful for a non-invasive, reliable and simple cPWV assessment. Indeed, this study points out that cPWVacc values well discriminate between age groups and show a good correlation with carotid stiffness, relative distension and distensibility measurements in a full age range.

8D.05 EFFECT OF BARORECEPTOR FIELD STIMULATION ON RAT AORTIC STIFFNESS AND WAVEFORM PARAMETERS

M. Butlin[1], G. Lindesay[1], D. Georgakopoulos[2], P. Pilowsky[1], E. Goldys[1], G. Town[1], E. Dutkiewicz[1], A. Avolio[1]. *Macquarie University, Sydney, AUSTRALIA, [2]CVRx Inc., Minneapolis, MN, USA*

Objective: Long term baroreceptor field stimulation is used in humans as a treatment for resistant hypertension. This pilot study investigates the effect of field stimulation of the baroreceptors in rodents upon aortic parameters of stiffness and waveform shape.

Design and methods: Spontaneously hypertensive rats (13 weeks, n=3) were anaesthetised (urethane) and fitted instrumented with a field stimulator around the right carotid artery, and two pressure sensors in the thoracic and abdominal aorta. The blood pressure, pulse wave velocity (PWV), pulse pressure amplification (PPamp), and form factor (FF = (mean – diastolic) / pulse pressure, a parameter of waveform shape to continuous baroreceptor field stimulation, pulsed baroreceptor field stimulation (1 second on, 1 second off), and intravenous infusion of sodium nitroprusside (SNP, blood pressure control arm) were measured.

Results: Field stimulation of the baroreceptors caused the expected decrease in blood pressure, decrease in aortic PWV, PPamp, and FF. There were no significant differences in any of the parameters measured whether blood pressure was lowered through continuous field stimulation of the baroreceptors, pulsed field stimulation of the baroreceptors, or infusion of SNP (Table). This indicates that in terms of the aortic pressure waveform, and the peripheral vascular influence on aortic pressure through wave reflection, there is no difference between the use of baroreceptor field stimulation and the use of a peripheral vasodilator.

Conclusions: Acute use of field stimulation to invoke a baroreceptor response lowers blood pressure in a manner that has the same end effect on aortic stiffness and parameters of aortic waveform shape as when blood pressure is lowered with a peripheral vasodilator. Further investigations are required to quantify the effect of long term blood pressure lowering through field stimulation of the baroreceptors on aortic parameters.

8D.06 SERUM ALDOSTERONE LEVELS ARE INDEPENDENTLY ASSOCIATED WITH ARTERIAL STIFFNESS IN ESSENTIAL HYPERTENSION

P. Anyfanty, A. Triantafyllou, E. Gavriilaki, E. Gkaliagkousi, G. Triantafyllou, K. Petidis, P. Panagopoulos, N. Lazaridis, E. Christaki, A. Tsinaridis, A. Pyrpasopoulou, M. Doumas, C. Zamboulis, S. Douma. *2nd Propedeutic Department of Internal Medicine, Thessaloniki, GREECE*

Objective: While the detrimental effects of aldosterone on the cardiovascular system are well acknowledged, the relationship between aldosterone levels and arterial stiffness in essential hypertension remains understudied with often controversial results. We aimed at investigating the association between aldosterone levels and pulse wave velocity (PWV), the gold standard for the evaluation of arterial stiffness, in a group of naïve, never treated patients with essential hypertension confirmed by 24-hour ambulatory blood pressure monitoring (ABPM).

Design and method: We recruited consecutive patients who attended the Hypertension Unit of our department with newly diagnosed, never treated essential hypertension and no significant comorbidities. 24-hour ABPM was applied to all patients (Spacelabs 90207). Body mass index (BMI) and waist circumference were recorded. Serum blood samples were derived to determine glucose, total cholesterol, LDL-cholesterol, and triglycerides levels. Plasma renin activity (PRA) and serum aldosterone levels were estimated by radioimmunoassay. Applanation tonometry (Sphygmocor device) was used to assess central PWV according to a standard protocol.

Results: A total of 141 patients, 91 men and 50 women with a mean age of 43.9±11.5 years were included in the study. Mean PWV was 8.14±1.8 m/s, mean aldosterone levels were 11.09±6.0 ng/dl and mean PRA was 0.64±0.14 ng/ml/h. PWV was associated with age, office systolic blood pressure (SBP), 24-hour SBP, day-time SBP, night-time SBP, BMI, total cholesterol, LDL-cholesterol and aldosterone levels. In the multivariate analysis, age (=0.548, p<0.001), office SBP (=0.254, p=0.001) and aldosterone levels (=0.148, p=0.041) were identified as the only significant predictors of PWV.

Conclusions: Our findings suggest that aldosterone mediates arterial stiffness in newly diagnosed, never-treated patients with essential hypertension, even after adjustment for conventional cardiovascular risk factors. The effects of aldosterone on the mechanical properties of the arterial wall may be present even in the early stages of essential hypertension and with aldosterone levels within normal limits.

8D.07 LOCAL AND REGIONAL AORTIC STIFFNESS: DIFFERENT EFFECTS ON LEFT VENTRICULAR REMODELLING

T. Quinaglia Silva[1], M. Bensalah[1,2], A. Redheuil[1,2], L. Macron[1,3], E. Bollache[2], N. Kachenoura[2], P. Boutouyrie[1,3], S. Laurent[1,3], E. Mousseaux[1,2,3]. *[1]Hopital Européen Georges Pompidou, Paris, FRANCE, [2]Institut National de la Santé et de la Recherche Médicale, Unité 678, Paris, FRANCE, [3]Institut National de la Santé et de la Recherche Médicale, Unité 970/ Paris-Centre de recherche Cardiovasculaire, Paris, FRANCE*

Objective: Left ventricular (LV) remodelling predicts all cause and CV mortality in various subsets of patients. Large arteries stiffness, a major determinant of cardiac afterload, is also an independent predictor of CV events. Because elastic

Abstract 8D.05

	value at 30% decrease in MAP		
	ΔPWV (%)	ΔPPamp (%)	ΔFF (%)
continuous field stimulation	**-10.0±2.9**	**-58±44**	**-3.3±8.3**
pulse field stimulation	**-6.6±1.8**	**-79±58**	**-5.5±11.7**
SNP infusion	**-13.4±4.7**	**-183±159**	**-4.2±7.0**

properties of the arterial wall vary along the aortic pathway, we hypothesized that local and regional aortic stiffness could impact differently on LV remodelling.

Design and methods: Regional aortic stiffness was obtained from carotid-femoral pulse wave velocity (cfPWV, m/s) aplanation tonometry (Pulse Pen), and from aortic arch PWV phase contrast MRI. Local stiffness (m/s) was calculated in the ascending (aaPWV) and descending aorta (daPWV) using central pulse pressure measurement, cine MRI acquisition and surface change estimation after applying the Bramwell Hill equation. Left ventricular remodelling, MRI estimated, was expressed as LV mass over end diastolic volume ratio (M/V). Data are presented as means and standard deviation. Logarithm transformation was used when appropriate.

Results: We evaluated 146 patients (41+15 years old; 43.8% women) free of overt CV disease (hypertensives: 10.3%; smokers: 10.6%; diabetics: 7.9%; BMI: 23.8+3.5). Univariate analysis, demonstrated M/V was associated to age (R^2= 0.08, p<0.001), BMI (R^2= 0.10, p<0.001), sex (R^2= 0.14, p<0.001) and brachial diastolic blood pressure (R^2= 0.05, p=0.005). In a stepwise multivariate regression analysis cfPWV and aaPWV were strongly and independently correlated to M/V (partial R^2=0.0715, p=0.0013; and partial R^2=0.0745, p=0.0010, respectively) even after adjustment for age, sex, BMI and brachial DBP. When challenged together, both cfPWV and aaPWV were independently associated with M/V, with 5% of explained variance each. Although to a lower extent, daPWV (Partial R^2= 0.0313, p=0.0352) was also independently related to M/V. By contrast, arch PWV was not independently associated with M/V.

Conclusion: In this cross-sectional study of healthy individuals, all segments of local aortic stiffness were related to concentric LV remodelling, except arch PWV. Both the stiffness of ascending aorta and carotid-femoral pathway were the strongest explanatory variables for LV remodelling, after adjustment to classical CV risk factors. This finding shows that various parts of the aortic pathway, having different elastic properties, influence LV remodelling.

8D.08 LOCAL CAROTID WAVE SPEED IS SIGNIFICANTLY LOWER THAN CAROTID-FEMORAL PULSE WAVE VELOCITY, BUT SIMILARLY RELATED TO AGE, IN NORMAL SUBJECTS BELOW 65 YEARS

C. Palombo[1], C. Morizzo[1], N. Guraschi[4], S. Nava[2], F. Cesana[2], C. Giannattasio[2,3], M. Kozakova[1,4]. *[1]University of Pisa, Pisa, ITALY, [2]University Milano Bicocca, Monza, ITALY, [3]IV Cardiology Division, Niguarda Ca Granda Hospital, Milan, ITALY, [4]Esaote SpA, Genoa, ITALY*

Measurement of arterial stiffness is becoming widely used for assessing cardiovascular risk. Carotid-femoral pulse wave velocity (CF-PWV), a surrogate for aortic stiffness, represents so far the reference method. Recently, local carotid wave speed (C-WS) measured by radio-frequency (RF)-based wall tracking against time was proposed for carotid stiffness estimate. In the present study a direct comparison between CF-PWV and C–WS was performed in apparently healthy subjects.

Methods: Study population consisted of 111 volunteers (59 men) with a wide age range (14-61 years; mean 34±15), blood pressure within normal limits (117±10/70±8 mmHg), and fasting plasma glucose and LDL-cholesterol respectively <110 and <159 mg/dL. Fifty-five subjects were overweight-obese. Vascular examination was performed in subjects resting in supine position for at least 15 minutes. CF-PWV was measured by Complior (Alam, Paris) and C-WS by RF-based system (QAS) implemented in MyLab70 ultrasound scanner (Esaote, Genova, Italy). The two examinations were performed during the same session in random order.

Results: in the entire study population, CF-PWV values (mean 7.6±1.4 m/s, range 5.3-11.8 m/s) were higher (p<0.05) than C-WS (mean 5.3±1.3 m/s, range 2.6-8.5 m/s), but the two measures were highly correlated (r=0.64, p<0.0001). Both CF-PWV and C-WS correlated directly with age (r=0.74 and 0.76, respectively, p<0.0001), plasma glucose (r=0.40 and 0.39, respectively, p<0.001) and LDL-cholesterol (r=0.35 and 0.33, respectively, p<0.001). In multivariate analysis, after adjustment for gender and smoking habit, the only independent determinant of both CF-PWV and C-WS was age, that explained as much as 55 and 58% of stiffness variance. Overweight-obese subjects had higher CF-PWV and C-WS as compared to lean subjects (7.9±1.5 vs. 7.3±1.3 m/s and 5.6±1.2 vs. 5.0±1.2 m/s, respectively, p<0.05 for both).

Conclusions: in apparently healthy population, C-WS and CF-PWV are influenced by similar variables and seem to reflect above all vascular ageing and obesity-related changes in arterial stiffness. However, C-WS values are lower than those of CF-PWV, and large population-based studies are necessary for establishing the normalcy values.

8D.09 BIDIRECTIONAL FLOW DYNAMICS IN THE PROXIMAL DESCENDING AORTA: ASSOCIATIONS WITH AORTIC STIFFNESS AND CAROTID CIRCULATION

J. Hashimoto, S. Ito. *Tohoku University Graduate School of Medicine, Sendai, JAPAN*

Objective: Stiffening of the aorta often precedes sudden onset of cardiovascular diseases, including stroke. However, the underlying pathophysiological mechanism remains poorly understood. The objective of this study was to test whether the link between these abnormalities might be attributable to an altered central flow dynamics.

Design and method: The subject group consisted of 296 patients with uncomplicated hypertension (mean age, 54±13 years). Flow velocity pulse waveforms were recorded noninvasively with duplex ultrasound at the proximal descending thoracic aorta (using the suprasternal approach) and carotid artery to calculate the reverse/forward flow ratio and diastolic/systolic flow index, respectively. Tonometric signals were recorded to estimate the aortic pressure waveform from the radial pressure waveform and to measure the carotid-femoral (aortic) and carotid-radial (peripheral) pulse wave velocities (PWVs). Aortic characteristic impedance was computed from the aortic pulsatile pressure and flow.

Results: The descending aortic flow waveform was bidirectional in all subjects, consisting of systolic forward (downward) and early diastolic reverse (upward) components. The aortic reverse/forward flow ratio (35±10%) was positively associated with stiffness parameters including aortic characteristic impedance, aortic PWV, and aortic/peripheral PWV ratio (P<0.001); the associations were independent of age, body mass index, aortic diameter, and aortic pressure. The carotid flow waveform was unidirectional, with two maximal peaks in early systole and early diastole. There was a positive relation between the carotid diastolic/systolic flow index (28±9%) and aortic reverse/forward flow ratio (P<0.001). The relation remained significant even after adjustment for aortic stiffness and other related parameters (P=0.001). In addition, Bland-Altman plots showed a close time correspondence between the carotid diastolic and aortic reverse flow peaks.

Conclusions: Aortic stiffness was found to determine the magnitude of reverse blood flow from the descending aorta to the aortic arch, which contributes to the diastolic antegrade flow into the carotid artery. This hemodynamic relationship likely accounts for the pathophysiological link between precedent aortic stiffening and subsequent clinical stroke.

ORAL SESSION

ORAL SESSION 9A
BLOOD PRESSURE MEASUREMENT

9A.01 ISOLATED NOCTURNAL MASKED HYPERTENSION PHENOMENON: PREVALENCE AND FEATURES

E. Nasothimiou, M. Dafni, L. Roussias, G.S. Stergiou. *Hypertension Center, Third University Department of Medicine, Sotiria Hospital, Athens, GREECE*

Objective: In hypertension studies and several guidelines documents the masked hypertension phenomenon (MH) has been defined almost exclusively on the basis of daytime ambulatory blood pressure (ABP). Thus, nocturnal ABP has been largely ignored, with only few exceptions. This analysis investigated the proportion of subjects with MH due to isolated nocturnal hypertension, who have been miss-classified as normotensives due to low daytime ABP.

Method: Clinic BP (3 visits) and ABP were measured within 6 weeks. Diagnostic thresholds for hypertension were for clinic BP 140/90 mmHg, daytime ABP 135/85, nighttime 120/70 and 24-hour 130/80 mmHg.

Results: 613 hypertensives (mean age 53±12.4 years, men 57%, treated 41%) were analysed. The prevalence of MH defined using different aspects of the ABP profile is presented in table. Subjects with isolated nocturnal hypertension tended to have lower 24-hour ABP (123/76 mmHg) than those with MH with daytime ABP elevation only (126/79 mmHg), or those with day and nighttime elevation (134/83 mmHg). Average 24 hour ABP was normal in 24 of 27 subjects with isolated nocturnal MH.

Conclusions: In a population of subjects with stage I-II hypertension, if MH is defined taking into account nighttime ABP, there are few cases in whom the diagnosis is changed due to isolated nocturnal hypertension. However, most of these cases have normal average 24-hour ABP, which makes the diagnosis of ABP hypertension and the need of treatment in these cases questionable.

	Different definitions of MH			MH
BP measurements	Clinic BP	Day ABP	Night ABP	n (%)
Day MH (classic definition)	low	high	ignored	94 (15.3)
Day MH only	low	high	low	29 (4.7)
Day and night MH	low	high	high	65 (10.1)
Night MH only	low	low	high	27 (4.4)
Night MH only (clinically relevant)	low	low	high (>5 mmHg above night ABP threshold)	7 (1.1)

9A.02 PREVALENCE OF CIRCADIAN BLOOD PRESSURE PATTERNS AND ITS RELATIONS WITH CARDIOVASCULAR RISK IN A COHORT OF 7983 24-H AMBULATORY RECORDINGS

J. Polonia[1], J. Mesquita-Bastos[2], L. Barbosa[1], J. Silva[1], S. Ribeiro[1].
[1]Faculdade Medicina Porto e Unidade Hipertensao H. Pedro Hispano, Porto, PORTUGAL, [2]Universidade de Aveiro, Aveiro, PORTUGAL

Purpose: Ambulatory blood pressure monitoring (ABPM-24h) is an important tool for management of hypertensive conditions. We evaluate in a large cohort of referred patients to ABPM evaluation the circadian BP patterns and the prevalence of high cardiovascular (CV) risk levels (European Score Risk, ESR) in non-dippers subjects.

Methodology: Out from 20651 24-h ABPM recordings we selected 7983 recordings of subjects with information on therapy and clinical data (age, gender, cholesterol, smoking, BMI, diabetes, previous CV or renal events) enabling us to calculate ECR. High CV risk (HighRK) was if Score was >=5% 10 years fatal risk. A nondipping (ND) pattern was defined when nocturnal systolic BP (SBP) dip was <10% of daytime SBP, the remaining being classified as dipping.

Results: 1483 subjects were normotensives (NT) in ABPM (untreated and normal 24h ABPM i.e. 24-h BP < 130/80, daytime BP < 135/85, and nighttime BP < 120/70 mmHg), 24h BP 116/71±6/5 mmHg, 48±11 years, BMI 26±7 Kg/m2, 62% female, 43,6% of ND; 1316 were untreated hypertensives (HT-nT) (untreated and ABPM >normal), 24h BP 129/81±8/8 mmHg, 49±16 years, BMI 27±7 Kg/m2, 50% female, 58,1% of ND; 816 were controlled hypertensives (HT-controlled) (treated and normal ABPM) 24h BP 1176/70±7/5 mmHg, 56±17 years, BMI 27±8 Kg/m2, 60% female, 39,8% of ND and 4368 were treated and uncontrolled (HT- uncontrolled) 24h BP 141/84±13/11 mmHg, 60±15 years, 28±6 Kg/m2, 54% female, 58,2% of ND. In NT HighRK was in 29% in D and 32% in ND (n.s.). In HT-nT HighRK was in 38% in D and 61% in ND (p<0.05). In HT-controlled HighRK was in 43% in D and 59% in ND (p<0.04). In HT- uncontrolled HighRK was in 47% in D and 68% in ND (p<0.03).

Conclusion: Non-dipping pattern is very common in hypertensives but also in normotensives. Nondipping is associated with a higher score of CV risk in ambulatory hypertensives but not in ambulatory normotensives

9A.03 PREVALENCE OF POSTPRANDIAL HYPOTENSION IN ELDERLY HYPERTENSIVE PATIENTS DETECTED BY HOME BLOOD PRESSURE MONITORING

J. Alfie, J. Barochiner, L.S. Aparicio, M.A. Rada, P.E. Cuffaro, M.S. Morales, C.R. Galarza, G.D. Waisman. *Hypertension Section, Internal Medicine Department, Hospital Italiano de Buenos Aires, Buenos Aires, ARGENTINA*

Postprandial hypotension (PPH) is a frequently ignored phenomenon, associated with increased morbidity and mortality.

Objectives: Main objective: to assess the prevalence of PPH among elderly hypertensive patients in their usual environment; secondary objectives: to describe meal-induced blood pressure (BP) variation and its predictive factors and to evaluate the effect of meal-related BP readings on hypertension control rate.

Design and method: hypertensive patients >65 years derived to evaluate out-of-office hypertension control by means of home blood pressure monitoring (HBPM) were included. Medical records were collected and patients were instructed to measure BP at home (duplicate measurements) in the morning, 1 h before and 1 h after a usual lunch, and in the evening (OMRON 705 CP) for 4 days. PPH was defined as a meal-induced systolic BP decrease >20 mmHg 1 h after lunch. Relevant predictors of meal-induced BP variation (difference between pre and postprandial BP measurements) were entered into a multiple linear regression analysis model. Home BP was considered uncontrolled when BP average (discarding first day measurements) was >135/85 mmHg. Uncontrolled-hypertension rates were compared using the conventional HBPM protocol (only morning and evening measurements) and then including meal-related readings.

Results: 65 subjects were included (mean age 78 (±7) years, 64.6% women). Prevalence of PPH was 32.3%. BP showed a meal-related decrease of 6.62 (±9.56)/5.08 (±4.42) mmHg for systolic and diastolic BP, respectively. After adjustment for age, gender, office BP, diabetes and history of falls, dizziness or syncope, meal-induced BP variation was independently predicted by prepandial systolic and diastolic BP (beta-coefficient 0.23, 95%CI 0.05-0.41, p=0.01 and 0.15, 95%CI 0.02-0.28, p=0.02, respectively). Finally, mean home BP was 138.35±16.3/73±9.76 mmHg using the conventional protocol, and 134.06±14.47/70.49±9.06 mmHg when including meal-related readings (p<0.001 for systolic and diastolic BP). The prevalence of uncontrolled hypertension decreased from 53.8% to 40% when meal-related BP readings were included (p=0.001).

Conclusion: PPH is highly prevalent among elderly hypertensive subjects. HBPM could be a valuable tool to evaluate its presence.

9A.04 OUT OF OFFICE BLOOD PRESSURE AND TARGET ORGAN DAMAGE IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Kollias, M. Dafni, E. Poulidakis, G.S. Stergiou. *Hypertension Center, Third University Department of Medicine, Sotiria Hospital, Athens, GREECE*

Objective: In children and adolescents ambulatory blood pressure (ABP) monitoring is regarded as indispensable for the accurate diagnosis of hypertension. Preliminary evidence suggests that home blood pressure (HBP) monitoring is also useful in children. This work evaluated the available evidence on the association between out-of-office blood pressure (BP) measurements and target organ damage in children and adolescents.

Methods: A systematic search was performed at PubMed, Embase and Cochrane Library databases (1974-2012). From the initially 886 identified articles, 94 fulfilled the inclusion criteria.

Results: Ten studies (n=480, pooled age 14.4 years, 35% with hypertension, 27% nephropathy, 10% diabetes type-1) reported the association between systolic ABP and left ventricular mass index (LVMI) with pooled correlation coefficient r 0.40 (95% CI 0.30, 0.50). When the analysis included only studies conducted in otherwise healthy children/adolescents (4 studies, n=301) the respective pooled coefficient was 0.32 (95% CI 0.12, 0.52). A moderate association was also found between systolic ABP and carotid intima-media thickness (IMT) (3 studies, n=231, age 13.3 years) with pooled r 0.32 (95% CI 0.21, 0.44), as well as between diastolic ABP and urine albumin excretion (UAE) (6 studies, n=355, age 13.1 years, 42% diabetes type-1, 28% reflux nephropathy) with pooled r 0.32 (95% CI 0.05, 0.58). A single study investigated the association of pulse wave velocity (PWV) with ABP and HBP (n=76, r=0.52/0.30 and 0.50/0.28 respectively, systolic/diastolic). Two studies reported data on the association of HBP with LVMI, and one of them showed comparable correlation coefficients with ABP.

Conclusions: The available evidence suggests a moderate but significant association between ABP and LVMI, IMT and UAE, mainly from studies in children with nephropathy and/or diabetes. Scant evidence is available on the association of out-of-office BP measurements with PWV in children and adolescents, as well as on the association of HBP with target-organ damage. More research is needed in hypertensive populations, and particularly involving HBP monitoring.

9A.05 CLINICAL IMPLICATION OBTAINED FROM WITHIN-VISIT BLOOD PRESSURE VARIABILITY IS TO CAPTURE "TRUE" BLOOD PRESSURE

S. Hoshide, M. Shimizu, Y. Yano, K. Eguchi, J. Ishikawa, K. Kario. *Jichi Medical University School of Medicine, Shimotsuke, JAPAN*

Background: Recent studies have highlighted the utility of visit-to-visit blood pressure (BP) variability for identifying risk prediction. However, the clinical importance of within-visit BP variability has been debated.

Methods: In the baseline examination for the Japan Morning Surge-Target Organ Protection study, a multicenter randomized control trial, we evaluated 450 hypertensive outpatients (mean age 66 years) who had morning systolic BP (SBP) above 135 mmHg. The plasma brain natriuretic peptide (BNP) level and urinary albumin excretion (UAE) were measured as markers of target organ damage. Within-visit variability for each participant was defined using the standard deviation of three clinic SBP readings at one occasion.

Results: In multiple linear regression analysis, the average SBP obtained from three readings was positively associated with BNP (β=0.15, P<0.001) and UAE (β=0.17, P<0.001), while within-visit variability was negatively associated with UAE (β=-0.09, P=0.044) and marginally associated with BNP (β=-0.07, P=0.085). As shown in Figure, the group with high average BP levels and low within-visit BP variability had more advanced target organ damage compared with other groups.

Conclusion: This study showed that high-clinic-BP patients with lower within-visit BP variability had more advanced target organ damage. Clinic BP readings with higher within-visit BP variability do not reflect target organ damage.

9A.06 ACUTE EFFECTS OF THE EXPOSURE TO DIFFERENT TYPES OF MUSIC ON BLOOD PRESSURE MEASUREMENT

G. Crippa[1], C. Crippa[2], D. Zabzuni[1], E. Bravi[1], A. Cassi[1]. [1]*Hypertension Unit, G. da Saliceto Hospital, Piacenza, ITALY,* [2]*Environmental Sciences, University of Parma, Parma, ITALY*

Music listening may influences blood pressure and other variables by modulating the sympathovagal balance. In experimental models, exposure to certain music reduced blood (BP) pressure by increasing brain dopamine synthesis. Furthermore, in a study conducted in hypertensive patients, 4 weeks of 'music therapy' caused a small but significant reduction in BP.

The aim of our study was to evaluate how different types of music (classical or rock music) can acutely influence BP measurement. Forty-four hypertensive patients on pharmacological and non-pharmacological treatment underwent Automated Office Blood Pressure Monitoring in the doctor's office by using an oscillometric device. Respiratory rate (RR) was measured by impedance plethysmography. Patients were seated in a comfortable arm-chair, alone in the consulting room. The subjects were neither musicians nor trained in music. Six consecutive BP and heart rate (HR) readings were taken, at one minute intervals, during 3 consecutive periods, each of 8 minutes. During these periods patients were exposed, in random sequence, to silence (average room noise 30 dB), Mozart's Adagio from Divertimento No. 7 (K 205) and Queen's Bicycle Race (both at average sound level of 70 dB). The results are summarized in the table.

	Silence	Mozart	Queen
Systolic BP ± SD	144.6 ± 10.3	137.8 ± 8.1	148.3 ± 10.8
Diastolic BP ± SD	83.9 ± 9.8	80.1 ± 10.7	85.8 ± 11.9
Heart Rate ± SD	73.2 ± 10.9	71.4 ± 7.9	80.6 ± 12.1
Respiratory Rate ± SD	15.8 ± 2.9	14.7 ± 1.9	18.2 ± 3.2

Abstract 9A.05

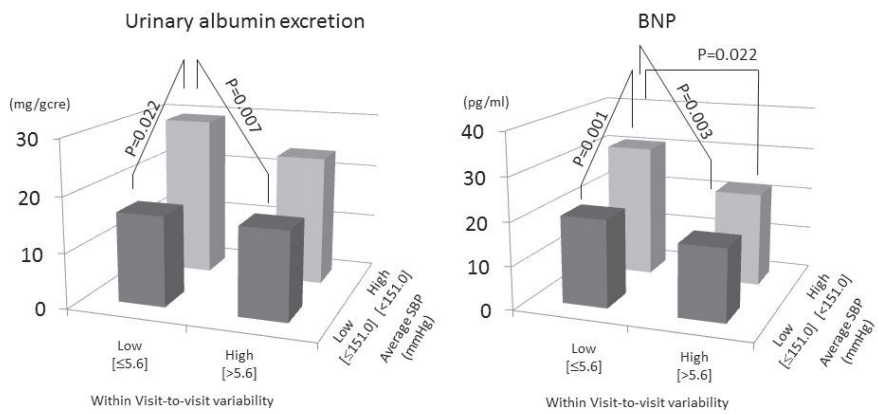


Fig. Association between biomarkers and within-visit blood pressure variability

P values were adjusted by age, sex, body mass index, hyperlipidemia, diabetes mellitus and the use of antihypertensive drug

Effects of classical (Mozart) or rock (Queen) music on systolic and diastolic blood pressure, heart and respiratory rate measurement. The comparison between BP taken during silence or music indicates that classical or rock music had opposite effects on BP. Queen's music caused a significant increase in systolic BP ($p < 0.05$) and in Heart Rate ($p < 0.025$). On the contrary, mean systolic and diastolic BP taken during Mozart's music significantly decreased ($p < 0.025$) as well as HR ($p < 0.005$). During exposure to Queen's music RR increased significantly with respect to both silence and Mozart's music.

These results suggest that listening to certain types of music can alter BP, HR and RR readings and therefore, it seems recommendable to avoid background music during BP measurements.

9A.07 FURTHER EVIDENCE FOR HYPERTENSION MISDIAGNOSIS DUE CUFF SIZE EFFECT IN JAPANESE FOLLOWED DURING 30 YEARS IN BRAZIL

E. Arcuri[1], A. Jordão[1], S. Silva[1], J. Santos[2]. *[1]University Guarulhos, Graduate Studies Center, Guarulhos, BRAZIL, [2]University of São Paulo, Medical School of Ribeirão Preto, Social Depatment, Ribeirão Preto, BRAZIL*

Background: In 1983 the American Heart Association guideline was used to study blood pressure (BP) in 999 subjects. Arm Circumference (AC)/Cuff Width ratio 0.40 was applied to select correct cuff (CC) size. Cuffs varied from 8 to14cm in width covering AC 19-36 cm. BP readings were compared to standard cuff ones (12 cm large). High BP values were only found in CC readings, particularly among 78 Japanese descendents, the most vulnerable to BP underestimation due to their lean arms.

Objective: To identify AC increase and to evaluate hypertension, cardiovascular and gestational complications rates in this ethnic group. Method- 70 subjects were studied in 2012, AC methodologically measured as in 1983. We defined as Risk Group (RG) 27 subjects whose BP values in 1983 were systolic higher than 129mmHg and diastolic 84mmHg. Lower values defined Control Group (CG=43). Information on hypertension diagnosis and cardiovascular and gestational complications were checked in health units where only standard cuff had been used.

Results: AC average increased from 23.8 cm in 1983 to 27.5cm in 2012. (ANOVA: Minimum AC value 22cm and Maximum 35cm). Body Mass Index resulted in 28.8% overweight and 3.8% obese. Fisher test showed significant higher rates in RG for hypertension ($p<0.001$), cardiovascular ($p=0.001$) and gestational complications ($p= 0.001$), particularly in women. Problems included stroke, coronary syndromes, pre-eclampsia, eclampsia, early placental displacement (drastic hemorrhage). Four subjects from RG died (14.8 %) against 01 from CG (2.3%).

Discussion: Our findings reinforce previous data regarding standard cuff inadequacy in AC lower than 29cm. Whereas attention to obesity overrules the discussed matter, BP underestimated readings, late hypertension diagnosis, cardiovascular and gestational complications and precocious deaths continue impacting cardiovascular morbimortality rates. We observed these problems in other ethnic groups, but Japanese biotype increases the risks.

Conclusions: This study suggests that if appropriated cuffs had been used in clinical practice such problems could have been better addressed. We suggest efforts toward knowledge advance in the matter.

9A.08 QUALITY OF LIFE MAY INFLUENCE THE SEVERITY OF SEASONAL VARIATIONS OF THE AMBULATORY BLOOD PRESSURE LEVEL IN PATIENTS WITH ARTERIAL HYPERTENSION

G. Andreeva, A. Deev, O. Isaikina, V. Gorbunov, O. Molchanova, O. Lerman, Y. Dmitrieva. *National Research Centre for Preventive Medicine, Moscow, Russia, Moscow, RUSSIA*

Objective: The aim of our study was to determine if the quality of life (QL) status can moderate seasonal ambulatory blood pressure variations of patients with arterial hypertension (AH).

Design and methods: We assessed 724 ambulatory blood pressure monitoring (ABPM) data (from 1996 until 2011) of AH patients without antihypertensive treatment. We determined the BP level for daytime period as 8.00-22.00 (BPd), nighttime - 0.00-6.00 (BPn), evening - 21.00-23.00 (BPn), morning - 6.00-8.00 (BPm), workplace period - 11.00-19.00 (BPw) and 24 hour period (BP24). We assessed the following QL scale scores (questionnaire by J.Siegrist): I - scale physical well-being, II - physical performance, III - positive psychological well-being, IV- negative psychological well-being, V - psychological performance, VI - social well-being, VII - social performance. We used the Procedure of General Linear Model for statistical analysis adjusted for age, sex and duration of AH.

Results: The lowest BP level was in summer for systolic and diastolic BP (SBP, DBP); the highest level was in autumn - for SBP, in winter - for DBP. We found the following factors which affected the seasonal BP levels (in addition to climatic factors): 1) VI scale scores (level of social support) were significant for SBP24 level (Fisher's test (F)=11,34, p<0,001), SBPd (F=11,91, p<0,001), SBPn (F=5,04, p<0,01), SBPw (F=9,98, p<0,002), SBPm (F=11,29, p<0,001 respectively), SBPe (F=5,73, p<0,02), DBPd (F=5,17, p<0,02); 2) IV scale scores (the negative emotional level) for SBPw (inverse relationship, F=4,33, p<0,03); 3) age for SBPm (F=5,01 p<0,03); 4) sex for SBPm (F=5,05, p<0,03).
Thus, we found that level of social support (family, friends and colleagues) was significant for seasonal SBP levels (for all time intervals during the day) and seasonal DBP values for day period, negative emotional level (inverse relationship) - for seasonal workplace SBP magnitudes, age and sex - for morning seasonal SBP levels.

Conclusion: Thus, the level of social support and negative emotions scores were significant for BP seasonal levels of patients and especially for SBP values than DBP, age and sex - for the morning seasonal SBP levels.

9A.09 DOES ETHNICITY AFFECT THE ACCEPTABILITY OF DIFFERENT METHODS OF BLOOD PRESSURE MONITORING?

S. Wood[1], M. Haque[1], P. Gill[1], S. Greenfield[1], J. Mant[2], U. Martin[3], M. Mohammed[1], R. McManus[4]. *[1]University of Birmingham, Primary Care Clinical Sciences, Birmingham, UNITED KINGDOM, [2]University of Cambridge, Primary Care, Cambridge, UNITED KINGDOM, [3]University of Birmingham, Clinical Pharmacology, Birmingham, UNITED KINGDOM, [4]University of Oxford, Primary Care Health Sciences, Oxford, UNITED KINGDOM*

Introduction: Recent UK guidelines recommend the use of out-of-office blood pressure (BP) measurement techniques, namely ambulatory (ABPM) and self-monitoring, to diagnose hypertension and prevent inappropriate treatment for normotensive individuals with white coat effect. However, little evidence is available regarding the acceptability of these methods to patients of different ethnic groups. This is important as cardiovascular outcomes are often worse in ethnic minorities and hypertension is a key risk factor.

Objective: To compare the acceptability of three modalities of BP monitoring in three different ethnic groups.

Design and methods: People of White British, South Asian and African Caribbean ethnic groups were recruited via primary care practices to take part in an acceptability study comparing BP measurement by different methods. Each participant underwent clinic, ambulatory (24 hours) and self-monitoring (1 week) before completing a validated acceptability questionnaire and ranking the methods. Analysis used a hierarchical model which took into account age, sex, ethnicity, deprivation, marital status, BMI, smoking status, diabetes or cardiovascular disease.

Results: 822 patients from 28 practices took part in the acceptability study of whom 63% had known hypertension. Mean "problem" scores for all participants ranged from (low most acceptable) 2.1 (self-monitoring) to 2.4 (clinic) and 2.9 (ABPM), all mean differences $p<0.01$. ABPM scored worse on domains concerning sleep, work and usual activities. South Asian and African Caribbean participants rated each type of monitoring less favourably than white British ($p<0.02$ for each comparison). Ranking data revealed similar preferences: self-monitoring was most favoured followed by clinic and ambulatory. This was consistent between different ethnicities.

Conclusions: In this large primary care sample, self-monitoring was significantly more favoured than either ambulatory or clinic monitoring. ABPM was reported as significantly affecting sleep, work and activities of daily living. People from minority ethnic groups found blood pressure monitoring less acceptable in general. When ordering out-of-office blood pressure monitoring, physicians should consider acceptability as well as efficacy.

ORAL SESSION

ORAL SESSION 9B
OBESITY AND METABOLIC ASPECTS

9B.01 RELATIONSHIP OF SERUM URIC ACID WITH BODY MASS INDEX AND WAIST CIRCUMFERENCE IN SUBJECTS WITH ABDOMINAL OBESITY. IMPACT ON NEW ONSET HYPERTENSION AND MORTALITY

M. Bombelli, D. Fodri, E. Toso, R. Dell'Oro, F. Ganz, M. Peronio, M. Cairo, F. Bianchi, R. Facchetti, G. Grassi, G. Mancia. *University of Milan-Bicocca, Department of Health Sciences, Internal Medicine, S. Gerardo Hospital, Monza, ITALY*

Background: There is a direct association between serum uric acid (SUA) and metabolic variables impacting cardiovascular (CV) risk, including that related to body fat depot. Our aim was to evaluate the relationship of SUA with body mass index (BMI) and waist circumference (WC) in subjects with abdominal obesity, and to determine the predictive value of SUA on new onset in and out-of-office hypertension and CV and all-cause mortality in these subjects.

Methods: In 840 subjects with abdominal adiposity (WC > or = 80 cm in females and 94 cm in males) belonging to a sample randomly selected from the general population of Monza (MB, Italy), aged 25 to 74 years, we measured: three office blood pressure (BP); 24 hour ambulatory BP; two home BP; anthropometric indices; metabolic variables, serum creatinine; SUA (urate oxidase); echocardiographic left ventricular mass (LVMI).
The same data were performed again after ten years. In a mean follow-up of 196 months, in subjects who died, was obtained copy of the death certificate and the causes of death coded (ICD-9).

Results: Mean age was 55±12 years; 48.3% were males. SUA was positively associated to BMI (r 0.17, p<0.0001) and more steeply to WC (r 0.37, p<0.0001). Such association persisted after adjustment for age and gender. New onset office, home and ambulatory hypertension found at the second examination were respectively 134, 96 and 131. After adjustment for relevant confounders, an increment of SUA (1mg/dL) was associated to an increase of risk of developing new onset home and ambulatory hypertension (OR 1.6, CI 1.03-2.46, p=0.04; OR 1.8, CI 1.23-2.56, p=0.002, respectively). During the follow-up there were 178 deaths, of which 62 of a CV nature. After adjustment for relevant confounders, SUA was an independent predictor of all-cause but not of CV death (HR 1.17, CI 1.01-1.36, p=0.04; HR 1.09, CI 0.85-1.4 p=NS, respectively).

Conclusions: SUA is an independent predictor of new onset out-of-office hypertension and of mortality in subjects with abdominal adiposity.

9B.02 MOLECULAR MECHANISMS OF HYPERTENSION-INDUCED HYPERTROPHY AND LEPTIN EXPRESSION IN VASCULAR SMOOTH MUSCLE

A. Zeidan, N. Soudani, Z. Farhat, L. Dib, C. Ghantous. *Dept. of Anatomy, Cell Biology and Physiological Sciences, American University of Beirut, Beirut, LEBANON*

Obesity is associated with hypertension and increased leptin production that contribute to cardiovascular pathology. Mechanical stretch (MS) has been shown to contribute to vascular remodeling through various mechanisms, including production of leptin and vascular smooth muscle (VSMC) hypertrophy.

In the present study, we used rat portal vein (RPV) organ culture to investigate the effect of mechanical stretch (mimicking hypertension) on leptin synthesis and the contributions of the RhoA/Rho kinase, actin dynamics, reactive oxygen species (ROS), and calcineurin activation. In addition, we studied the effect of exogenous leptin (3.1 nM) on blood vessels remodeling. Stretching the RPV for 15, 30 120 min or 24 h significantly increased leptin protein level in VSMC, which is associated with increased RhoA activity by 221 +/- 17%. Phosphorylation of RhoA downstream targets, including LIM kinase 1 and cofilin-2, was increased by 134 +/- 14 and 390 +/- 22%, respectively.

The effect of MS on reactive oxygen species (ROS) was investigated. MS and exogenous leptin significantly increased ROS production (5 and 3 fold increase respectively), effects that was significantly attenuated by the coadministration of an anti-leptin receptor antibody (166 ng/ml), the ROCK inhibitor Y-27632 (10 μM) as well the RhoA inhibitor C3, (30 ng/ml). Disruption of actin microfilaments with 50nM latrunculin B significantly attenuated MS-induced ROS production. The role of ROS in MS-induced leptin secretion and expression was further established when pretreatment of NADPH oxidase inhibitor apocynin (1 mM) potently attenuated leptin expression induced by MS. In addition, MS significantly increased polymerization of actin in unstretched blood vessels, as reflected by an increase in the F-/G-actin ratio, effects that were significantly attenuated by apocynin. The hypertrophic effect of MS was significantly attenuated by an anti-leptin receptor antibody and apocynin. Moreover, the hypertrophic effect of MS and exogenous leptin on VSMC was associated with an increase in calcineurin activation (4 folds).

Our results indicate that the activation RhoA pathway, ROS production and calcineurin activation plays a pivotal role in MS signaling, leading to leptin synthesis and secretion and the development of VSMC hypertrophy.

9B.03 DETERMINANTS OF WEIGHT SENSITIVITY IN HYPERTENSION

J. Kostis[1], J. Cabrera[2], W.J. Kostis[3], W.C. Hooper[4], P.K. Whelton[5], M.A. Espeland[6], N.M. Cosgrove[1], J.E. Sedjro[1], C. De Staerck[4], M. Pyle[4], C.A.M. Anderson[7]. *[1]UMDNJ-Robert Wood Johnson Medical School, Cardiovascular Institute, New Brunswick, NJ, USA, [2]Rutgers University, Biostatistics, Piscataway, NJ, USA, [3]Harvard Medical School, MGH, Cardiology, Boston, MA, USA, [4]Centers for Disease Control and Prevention, Atlanta, GA, USA, [5]Tune University School of Public Health and Tropical Medicine, New Orleans, LA, USA, [6]Wake Forest School of Medicine, Biostatistical Sciences, Winston-Salem, NC, USA, [7]Johns Hopkins Medical Institutions, Welch Center for Prevention, Epidemiology and Clinical Research, Baltimore, MD, USA*

Objective: Weight loss and sodium restriction are important lifestyle interventions for hypertension. Although there are many reports on salt sensitivity, there is scant information on weight sensitivity i.e. the heterogeneity of blood pressure response to changes in body weight. We examined factors associated with weight sensitivity among 975 participants in the Trial of Nonpharmacologic Interventions in the Elderly (TONE).

Design and method: TONE was a clinical trial of weight loss and/or sodium restriction among persons with hypertension aged 60 to 80. To examine weight sensitivity, we computed the relationship of body mass index change to the change in systolic and diastolic blood pressure while medications were kept constant. The association of demographic characteristics, medication use, lifestyle habits and 21 candidate gene polymorphisms (selected for their previously reported association with diabetes, obesity or hypertension) to weight sensitivity was analyzed using linear statistics, GLMNET lasso and recursive partitioning algorithms.

Results and conclusions: Higher level of habitual exercise, higher baseline body mass index, female gender, Black race and use of ACE inhibitors or beta blockers were associated with higher systolic blood pressure drop for a given weight loss i.e. more weight sensitivity. Among the 21 candidate gene polymorphisms, an ACE insertion/deletion polymorphism (rs4646994), a ryanodine receptor polymorphism (rs2820037) and a tissue necrosis factor-alpha (rs1800629) polymorphism were associated with higher weight sensitivity (more systolic blood pressure drop). The recursive partitioning algorithm identified persons with the combination of the following four polymorphisms: a polymorphism of tissue growth factor beta1 (rs1982073), a polymorphism of interleukin-10 (rs1800896), rs4646994 and rs1800629 as having the highest weight sensitivity for systolic blood pressure. Diastolic blood pressure was associated with rs4646994, rs2820037 and a polymorphism of interleukin-18 (rs5744292).
Selected polymorphisms previously associated with diabetes, obesity and hypertension are associated with weight sensitivity of elderly hypertensives. These data may be useful in counseling patients with hypertension and may possibly be considered by writers of clinical guidelines.

9B.04 CHANGES IN HYPERTENSION STATUS ASSOCIATED WITH PHENTERMINE AND TOPIRAMATE EXTENDED-RELEASE OVER 108 WEEKS

J. Jordan[1], K. Narkiewicz[2], W.W. Day[3]. *[1]Institute of Clinical Pharmacology, Hannover Medical School, Hannover, GERMANY, [2]Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, POLAND, [3]VIVUS, Inc., Mountain View, CA, USA*

Objective: Hypertension risk is increased in obese and overweight individuals; weight loss (WL) may improve blood pressure (BP) in these patients. In the 56-week CONQUER study and 52-week extension (SEQUEL), phentermine and topiramate extended-release (PHEN/TPM ER) demonstrated significant WL vs placebo in obese and overweight subjects with >=2 weight-related comorbidities including hypertension. The aim of this post-hoc analysis of SEQUEL was to evaluate changes in weight, BP, antihypertensive medication use, and hypertension status over 108 weeks based on their baseline hypertensive status.

Design and method: Subjects in SEQUEL maintained their original blinded 2:1:2 randomisation to placebo (n=227), PHEN 7.5mg/TPM ER 46mg (7.5/46; n=153), or PHEN 15mg/TPM ER 92mg (15/92; n=295) from CONQUER. Subjects were assessed at baseline for hypertension status: normotension (n=72; systolic BP/diastolic BP [SBP/DBP<120/80mmHg without antihypertensive medication use), prehypertension (n=113; SBP/DBP 120-139/80-89mmHg without antihypertensive medication use), and hypertension (n=490; SBP/DBP >=140/90mmHg, antihypertensive medication use, or documented history of hypertension).

Results: In all hypertension status categories, PHEN/TPM ER produced significantly greater WL vs placebo at week 108 (P<.005 vs placebo; Table). In the hypertension subgroup, SBP (mmHg) decreased by -5.1, -6.6, and -8.7, for placebo, 7.5/46 and 15/92, respectively (P<.01 for 15/92 vs placebo) from baseline to week 56. Decreases in SBP were maintained at week 108 (mmHg): -4.5, -6.3, and -6.4, respectively (not significant vs placebo). DBP decreased in hypertensive subjects across all treatment groups from baseline to week 108 (mean= -4.3 mmHg). In the hypertension subgroup, more subjects receiving placebo had a net increase in antihypertensive medication use at week 108, whereas subjects in PHEN/TPM ER groups decreased antihypertensive use (Table). More subjects with hypertension receiving PHEN/TPM ER achieved normotension than those receiving placebo (Table). Common adverse events included constipation, paraesthesia, and nasopharyngitis.

Conclusion: Taken together, improvements in hypertension status alongside reductions in antihypertensive medication use over 108 weeks suggest that WL due to PHEN/TPM ER may confer cardiovascular benefits in obese and overweight adults.

9B.05 ALISKIREN, BUT NOT LISINOPRIL, REDUCES RENAL VASCULAR RESISTIVITY IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME AND MICROALBUMINURIA

P. Aranda[1], L. Cermeño[2], E. Briceño[3], A. Jimenez[3], L. Perea[3], M. Martinez[3], D. Hernandez[3]. *[1]HRU Carlos Haya-Hypertension and Vascular Risk Unit, Málaga, SPAIN, [2]HRU Carlos Haya-Department Radiology, Málaga, SPAIN, [3]HRU Carlos Haya- Nephrology Service, Málaga, SPAIN*

Rationale: Hypertensive patients with Metabolic Syndrome (MS) are prone to develop nephroclerosis. Therefore, antihypertensive agents that reduce renal resistance and improve renal plasma flow could have long-term renoprotective effects in these patients.

Objective: To compare long-term effects on Renal Resistive Index (RRI) of a therapeutic regimen based on Aliskiren (A) 300 mg vs Lisinopril (L) 20 mg daily in hypertensives with MS (At least 3 components of NCEP III definition criteria) and Microalbuminuria (UAER) (30- 300 mg/24 h.).

Patients and methods: 78 patients were randomly (1:1) assigned either to A 300 mg (n-40) or L 20 mg (n-38) plus an average of 3 other antihypertensives, mainly diuretics (92%) and CCBs (83%) and followed during 12 months. At enrolment and end follow-up period BMI,WC,office BO (3 readings) and PP (mmHg) were measured as well as we determined fasting lrvrls of sCr, K+, Uric acid,glucose,lipidic profile and 24 -h. UAER.
At same periods a Doppler renal sonography was performed (All by the same eximiner) at interlobular renal artery level (upper,middle,lower third of both kidneys) to all patients, and then RRI was calculated according to usual formula.

Results: While mean BMI,WC, glucose and uric acid did not change over the study, both groups of treatment significantly reduced mean values of BP,PP and lipidic parameters..Rest of parameters changed as follows in patients with A and L respectively: RRI : 0,62 to 0,57 (p<0.001) and 0,61 to 0,81 (ns). sCr (mgdl): 1,09 to 1,07 ((ns) and 1,05 to 1,18 (p<0.001); eGFR (mil/min/1,73 m2): 71 to 72 (ns) and 75 to 73 (ns); UAER (mg/24 h): 141 to 27 (p<0,001) and 104 to 39 (p<0.02); and K+ (mml/L) 4,16 to 4,23 (ns) and 4,24 to 4,38 (p<0.001).

Conclusion: In hypertensive patients with MS and microalbuminuria log-term treatment with Aliskiren, but not with Lisinopril, was able to significantly reduce RRI. This effect could provide long-term protection against development of nephrosclerosis in these type of patients.

Abstract 9B.04

Table. Changes in Weight, Hypertension Status, and Antihypertensive Medication Use From Baseline at Week 108 (ITT-LOCF).

LS Mean Change	Subjects With Normotension at Baseline			Subjects With Prehypertension at Baseline			Subjects With Hypertension at Baseline		
	Placebo (n=24)	7.5/46 (n=12)	15/92 (n=36)	Placebo (n=33)	7.5/46 (n=32)	15/92 (n=48)	Placebo (n=170)	7.5/46 (n=109)	15/92 (n=211)
Weight, kg	-0.7	-9.4*	-9.3†	-3.1	-10.0*	-12.6†	-3.1	-10.8†	-11.9†
Weight, %	-1.2	-10.1*	-9.6*	-2.8	-9.7*	-12.2†	-2.8	-10.6†	-11.5†
Subjects progressing to hypertension, %	12.5	16.7	5.6	18.2	12.5	14.6	--	--	--
Subjects achieving normotension, %	--	--	--	30.3	43.8	27.1	3.5	4.6	4.7
Percentage of subjects with a net change‡ in antihypertensive medications use, %	12.5	16.7	5.6	12.1	6.3	6.3	0.6	-9.1	-16.1

*P<.005 vs placebo; †P<.0001 vs placebo; ‡Net change=% increasing minus % decreasing medications; ITT=intent-to-treat; LOCF=last observation carried forward; LS=least squares

9B.06 VISCERAL OBESITY IS A "NEW" MARKER OF ENDOTHELIAL DYSFUNCTION AMONG SUBJECTS AFFECTED BY CHRONIC KIDNEY DISEASE

C. Alfieri[1], S. Vettoretti[1], R. Floreani[1], A. Regalia[1], R. Meazza[2], P. Messa[1], F. Magrini[2]. *[1]Department of Nephrology and Dialysis, Fondazione Ca'Granda IRCCS Ospedale Policlinico Maggiore, Milan, ITALY, [2]Department of Cardiology, Fondazione Ca'Granda IRCCS Ospedale Policlinico Maggiore, Milan, ITALY*

Introduction: Patients affected by chronic kidney disease (CKD) have an increased cardiovascular morbidity and mortality rate. Endothelial dysfunction is a precocious index of worse cardiovascular prognosis. We evaluated the relationship between endothelial function and other possible cardiovascular risk factors in a population of subjects affected by CKD.

Methods: 191 patients affected by CKD (stage 1-4 NKF-KDOQI) and free for previous cardiovascular (CV) events.were undergone to: 1) collection of medical history and anthropometric parameters; 2) blood and urinary examinations; 3) ultrasionografic evaluation of flow mediated dilation of the brachial artery (FMD). Renal function was assessed by measured creatinine clearance (mCrCl), CKD-EPI (eGFR) and Crockroft-Gault (eCRCl) formulae. Albuminuria wad determined both as the mean value of three first morning samples of albumin/creatinine ratio (A/C) and as 24 hours urinary collection (protU).

Results: Characteristics of our cohort were: M/F 127/65; age 62±14 yrs; diabetes 48%; hypertension 84%; SBP 137±21 mmHg; DBP 79±12 mmHg; MAP 99±14 mmHg; PP 58±17 mmHg; BMI 28±4.9 Kg/m2; waist circumference 100.4±13.7 cm; total cholesterol 219±83 mg/dL; HDL 53±16 mg/dL; LDL 136±74 mg/dL; triglycerides 144±74 mg/dL; Patients were homogeneously distribuited between CKD stages (Stage 1 18%; Stage 2 24%; Stage 3 40%; Stage 4 18%); mCrCl 64±34 ml/min; eGFR 54±29 ml/min; eCrCl 53±31; logA/C 1.19±0.91; ProtU 1.27±2.24; FMD of brachial artery was 13±8.3%.
At univariate analysis, FMD correlated with: age (r=-0.153; p=0.04) and waist circumference (r=-0.20; p=0.00086) while it wasn't significantly correlated with any renal index or CV risk factors. Furthermore, when FMD was considered as the dependent variable of a multivariate regression analysis in witch main CV risk factors and indices of renal function were the independent variable, waist circumference was maintained as the only modifiablle and independent variable associated with FMD impairment.

Conclusion: Our results indicate that in a population of subjects affected by CKD, visceral obesity is an independent and modifiable risk factor associated with endothelial dysfunction and may be consequently associated with worse CV prognosis.

9B.07 METABOLIC SYNDROME AND RISK OF CANCER

H. Michalopoulou, P. Stamatis, J. Xenogiannis, G. Dimitriadis, C. Gekas, D. Stamatis. *Cardiology Department Metaxa Cancer Hospital, Athens, GREECE*

Objective: Metabolic syndrome (MS) is associated not only with cardiovascular morbidity and mortality but also with cancer risk.
We aimed to assess the prevalence of the MS in patients with breast cancer (BC) and the independent effect of MS on breast cancer risk.

Methods: We enrolled 384 health women and women with breast cancer (aged 35-78 years) in this nested case-control study.We adopted the National Cholesterol Education Program criteria to define MS.
Uni-and multivariate analyses were done ,generating odds ratios (Ors) as an expression of relative risks.

Results: Prevalence of MS was 47% in breast cancer patients and 23.6% in the control group (p,0.001).
A positive and independent association was observed between MS and BC risk (OR: 3.4 95% CI: 1.2-5,1).The OR s of breast cancer were 4.2 for waist circumference >88cm (95% CI: 2.5-6.7) , 2.6 for diabetes (95% CI: 1.9-3.8),1.4 for hypertension (95% CI;1.1-16) and 1.2 for hyperlipideamia (95% CI: 1.1-1.5).
Menopause when analyzed alone did not constitute a risk factor for MS. Patients with a later pathological stage of breast cancer were significantly more likely to be centrally obese (p=0.001),hyperinsulinemic (p=0.003) and hypertensives (p=0,04).

Conclusion: Our findings provide support for an association between MS and breast cancer incidence and could contribute to define high risk groups for targeted BC prevention.

ORAL SESSION

ORAL SESSION 9C
DIABETES

9C.01 DETERIORATION OF KIDNEY FUNCTION BY THE (PRO)RENIN RECEPTOR BLOCKER HANDLE REGION PEPTIDE IN ALISKIREN-TREATED DIABETIC TRANSGENIC (MREN2) 27 RATS

W. Batenburg[1], M. Van Den Heuvel[1], J. Van Esch[1], R. Van Veghel[1], P. Westenend[2], I. Garrelds[1], U. Bhaggoe[1], A. Bouhuizen[1], F. Leijten[1], A.H.J. Danser[1].
[1]Erasmus MC, Rotterdam, THE NETHERLANDS, [2]Laboratory for Pathology, Dordrecht, THE NETHERLANDS

Objective: Renal function in patients with diabetes mellitus (DM) might be influenced by the level of prorenin due to its binding to the (pro)renin receptor ((P)RR) and the subsequently occurring angiotensin production and/or the direct agonistic effects of prorenin mediated via this receptor. Indeed, in DM elevated prorenin levels are correlated with the development of microvascular complications such as nephropathy.

Design and methods: In this study we evaluated renal function in diabetic TGR(mREN2)27 rats (a high prorenin hypertensive model), treated with vehicle, the renin inhibitor aliskiren, or aliskiren plus the putative (P)RR antagonist HRP for 3 weeks. 24-hour urine was collected, and blood and kidney were evaluated for renin-angiotensin system components and pathology.

Results: Increased diuresis and proteinuria due to DM were prevented by aliskiren, but not aliskiren+HRP. Aliskiren+HRP additionally decreased creatinine clearance, and increased the plasma levels of the profibrotic marker plasminogen-activator inhibitor-1. The increased natriuresis and renal collagen-1 expression in this model were unaffected by aliskiren±HRP. Aliskiren increased rat renin expression in the renal cortex. This was associated with a decline in (P)RR and AT1 receptor mRNA expression, and these changes were unaffected by HRP. Glomerular volume and interlobar arterial lumen diameter modestly increased in the aliskiren+HRP group, and were unaffected by aliskiren alone.

Conclusions: HRP, when given on top of aliskiren in DM TGR(mREN2)27 rats worsens kidney damage and counteracts the beneficial effects of aliskiren. (P)RR blockade is therefore contraindicated in DM.

9C.02 ASSOCIATION OF VITAMIN D WITH METABOLIC TRAITS: META-ANALYSIS OF PROSPECTIVE EVIDENCE

H. Khan[1], S. Kunutsor[1], O. Franco[2], R. Chowdhury[1]. *[1]University of Cambridge, Cambridge, UNITED KINGDOM, [2]Erasmus MC, Rotterdam, THE NETHERLANDS*

Objective: Lower levels of Vitamin D have been associated with increased risk of metabolic disorders including diabetes and metabolic syndrome (MetS), however results remain inconsistent.

Design and method: We performed a systematic review and meta-analysis of prospective studies reporting on associations of circulating levels or dietary intake of vitamin D with risk of type 2 diabetes MetS and insulin resistance. Hazard ratios (HRs) were combined together using random-effects meta-analysis and heterogeneity was investigated by subgroup analysis.

Results: A total of 18 prospective studies comprising of 210,107 participants with 16,866 metabolic (incident diabetes and MetS) events, collected during a median follow up of 10 years (range 3-22 years), were included. Hazard ratios for individuals in top versus bottom thirds of baseline vitamin D status were 0.81 (95% CI: 0.71-0.92); 0.86 (95% CI: 0.80-0.92); and 0.84 (95% CI 0.64-1.12) for diabetes, MetS and insulin resistance, respectively. Moderate heterogeneity was found between 14 studies (I2 =67%, P<0.001) reporting on diabetes while findings were consistent for other metabolic parameters.

Conclusions: In summary, vitamin D status at baseline in apparently healthy adults is inversely associated with future risk of type 2 diabetes and metabolic syndrome. Interventions aimed to maintain adequate levels of vitamin D in addition to preventing deficiency may be a useful preventive measure for metabolic diseases. However, reliable evidence from carefully designed intervention studies, particularly based on healthy free-living individuals, is needed to confirm these observational findings.

9C.03 AT2 RECEPTOR STIMULATION REDUCES URINARY ALBUMIN EXCRETION IN ZUCKER DIABETIC RATS

G. Castoldi[1], C. Bombardi[1], C. Di Gioia[2], G. Zerbini[1], A. Ljunggren[3], P. Jansson[3], U. Steckelings[4], B. Dahlof[5], T. Unger[6], A. Stella[1]. *[1]Clinica Nefrologica, Az. Osp. San Gerardo, Dipartimento di Scienze della Salute, Università Milano-Bicocca, Monza, ITALY, [2]Istituto di Anatomia Patologica, Sapienza Università di Roma, Rome, ITALY, [3]Vicore Pharma, Gothenburg, SWEDEN, [4]IMM, Department of Cardiovascular and Renal Research, Odense, DENMARK, [5]Department of Medicine, Sahlgrensha University Hospital/Ostra, Gothenburg, SWEDEN, [6]CARIM, Maastricht University, Maastricht, THE NETHERLANDS*

Objective: Albuminuria plays a major role in the progression of diabetic nephropathy. Compound 21 (C21), a selective AT2 receptor agonist, shows anti-inflammatory effects and organ protection in the cardiovascular system and in the kidney in different experimental models of hypertension. Aim of the study was to evaluate the effect of compound 21 in the progression of nephropathy in obese Zucker diabetic (ZDF) rats.

Methods: Experiments were performed in 4 groups of ZDF rats. Starting from five weeks of age, before the onset of diabetes, seven ZDF rats were treated with C21 (0.3 mg/kg/day, intra-peritoneal injection), six ZDF rats were treated with losartan (10 mg/kg/day in drinking water), five ZDF rats were treated with C21 plus losartan, and eight ZDF rats were maintained without any treatment. Blood glucose, blood pressure (tail cuff), and urinary albumin excretion, were measured at 5, 11 and 20 weeks of age. At 5 weeks of age rats were normoglycemic. No differences were observed in blood pressure among the different groups at 5, 11 (6 week treatment) and 20 (15 week treatment) weeks of age. Table shows results on urinary albumin excretion (albumin/creatinine, A/C. *p<0.05 vs. ZDF rats).

Age	ZDF	ZDF+C21	ZDF+Los	ZDF+C21+Los
5 weeks *before treatment*	0.086 ± 0.008	0.093 ± 0.004	0.082 ± 0.010	0.065 ± 0.007
11 weeks *6 week treatment*	0.308 ± 0.035	0.226 ± 0.015*	0.102 ± 0.021*	0.077 ± 0.021 *
20 weeks *15 week treatment*	0.344 ± 0.026	0.329 ± 0.016	0.284 ± 0.026	0.215 ± 0.021*

Results and Conclusion: After 6 weeks of treatment C21 reduces urinary albumin excretion and losartan caused a marked reduction in A/C, while C21 plus losartan did not further decrease A/C with respect to losartan alone. In contrast, after 15 weeks of treatment, only the co-administration of C21 plus losartan significantly reduces A/C compared to ZDF rats without any treatment. These data suggest a beneficial effect of this drug combination to slow the progression of diabetic nephropathy.

9C.04 INSULIN-RESISTANCE AND LARGE ARTERY STRUCTURE AND FUNCTION IN NORMAL SUBJECTS

M. Kozakova[1,2], E. Muscelli[1], C. Morizzo[1], A. Casolaro[1], C. Palombo[3].
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, ITALY, [2]Esaote Spa, Genoa, ITALY, [3]University of Pisa, Department of Surgical, Medical, Molecular Pathology and Critical Care, Pisa, ITALY

A reduced insulin sensitivity (IS) is considered a primary pathophysiologic mechanism underlying a cluster of metabolic abnormalities (hyperinsulinemia, hyperglycemia, dyslipidemia, inflammation, changes in adipocytokines) that may result in accelerated atherosclerosis.

Aim of the study was to investigate whether some tissue markers of preclinical atherosclerosis, such as carotid intima-media thickness (IMT), maximal IMT thickness (IMTmax), local carotid stiffness (beta-index; BI) and carotid-femoral pulse wave velocity (PWV), are related to insulin resistance (IR) and associated metabolic abnormalities.

Methods: Study population consisted of 82 apparently healthy volunteers (45 men; mean age 46±9 years), free of comorbidities capable to influence arterial wall structure and/or function. Study subjects underwent in different days a 2-hour glucose tolerance test and an euglycemic hyperinsulinemic clamp to assess IS (expressed as M/I, i.e. M value normalized by free fat mass and mean plasma insulin). Metabolic parameters measured included fasting and 2-hour plasma glucose and insulin, LDL- and HDL-cholesterol, triglycerides, apolipoprotein B, free fatty acids, adiponectin and hs-CRP. Vascular examination was performed in subjects in supine position in a quite room since at least 15 minutes. CF-PWV was measured by Complior (Alam, Paris) and IMT and BI by a radiofrequency (RF)-based system (QAS®) implemented in a MyLab70 ultrasound scanner (Esaote, Genova, Italy). The two vascular investigations were performed in random order.

Results: In multiple regression models adjusted for sex and current smoking, IMT was independently related directly to age and carotid diameter, and inversely to adiponectin (cumulative R2=0.34), IMTmax to age, systolic BP and adiponectin (cumulative R2=0.35), BI to age and M/I (directly and inversely, respectively; cumulative R2=0.44) and carotid-femoral PWV to age and glucose (directly; cumulative R2=0.39).

Conclusions: Metabolic factors related to IR contribute to determine the structure and function of an elastic artery such as the common carotid, behind the main role of age. Adiponectin shows an independent effect on carotid structure and geometry, while IR and plasma glucose have a prevalent influence on local carotid and aortic stiffness. New high resolution ultrasound techniques expand the possibility of investigating preclinical vascular involvement in IR related states

9C.05 AORTIC STIFFNESS AND WAVE REFLECTIONS IN PREGNANCIES COMPLICATED BY GESTATIONAL DIABETES MELLITUS: A LONGITUDINAL STUDY

F. Battista[1,2], G. Pucci[1,2], C. Sorrentino[3], E. Torlone[4], S. Gerli[3], G. Schillaci[1,2].
[1]Dipartimento di Medicina, Università di Perugia, Perugia, ITALY, [2]Struttura Complessa di Medicina Interna, Ospedale 'S. Maria', Terni, ITALY, [3]Medicina Interna, Scienze Endocrine e Metaboliche, Azienda Ospedaliera di Perugia, Perugia, ITALY, [4]Clinica Ostetrica e Ginecologica, Università di Perugia, Perugia, ITALY

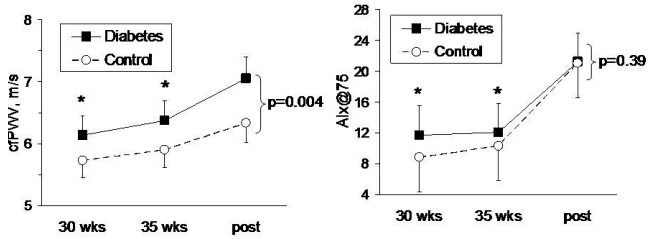
Pregnancy is associated with profound cardiovascular adaptation. A reduction in wave reflections has been reported early in the course of normal pregnancy, and cross-sectional studies show greater arterial stiffness in gestational diabetes than in normal pregnancy. However, the complex time-dependent behaviour of maternal cardiovascular hemodynamics in normal and diabetic pregnancy can only be appreciated in longitudinal studies.

Thirty-six women with gestational diabetes (34±4 years, BP 111/69±13/8 mmHg) and 32 with normal pregnancy (33±3 years, BP 113/69±9/8 mmHg) were examined 3 times, at a gestational age of 30 and 35 weeks, and 12 weeks after delivery. On each occasion, applanation tonometry (SphygmoCor) was used to obtain carotid-femoral pulse wave velocity (cfPWV) as a measure of aortic stiffness, and aortic augmentation index corrected for a heart rate of 75 bpm (AIx@75) as a measure of wave reflection. In order to account for missing data, the changes of hemodynamic parameters over time were assessed using mixed models with an unstructured covariance matrix, and time and status (normal vs diabetic pregnancy) as fixed effects.

The behaviour of cfPWV and AIx@75 is displayed in the Figure. Compared to women with normal pregnancies, women with gestational diabetes had a significantly higher cfPWV (p=0.004), both during pregnancy (6.1±0.9 vs 5.7±0.8 m/s at week 30, 6.4±0.9 vs 5.9±0.9 at week 35) and after delivery (p=7.0±1.0 vs 6.3±1.1 m/s). Adjustment for age and mean arterial pressure did not change the results. Heart-corrected AIx did not differ between the two groups (p=0.39). In both groups, cfPWV was significantly lower at 30 and 35 weeks than after delivery (Figure, both p<0.001). Also AIx@75 was markedly lower during pregnancy than after delivery (both p<0.001).

We conclude that (1) compared with normal pregnancy, gestational diabetes is associated with a higher aortic stiffness, which remains significantly elevated 3 months after delivery; (2) no significant differences in wave reflection are present in normal and diabetic pregnancies; and (3) compared with the post-partum period, aortic stiffness and aortic augmentation are significantly reduced during the third trimester of gestation, both in normal pregnancies and in gestational diabetes.

Abstract 9C.05



9C.06 FREQUENCY OF RESISTANT HYPERTENSION IN PATIENTS WITH TYPE-2-DIABETES - CURRENT EPIDEMIOLOGICAL DATA FROM THE T2DAY2.0-SCREENING

S. Jacob[1], E. Vondracek[1], W. Renn[1], B. Weger[2], F. Mahfoud[3]. *[1]University of Tübingen, Cardio Metabolic Institute, Villingen, GERMANY, [2]SERVIER Germany GmbH, Munich, GERMANY, [3]University of Homburg, Homburg, GERMANY*

Background: DM patients have an increased risk of vascular complications. Mostly, they have concomitant hypertension (RR) and further risk factors. Reduction of blood pressure is of the most important and efficacious aspects in the treatment of patients with DM (Ray et al 2008). Control of RR often requires several antihypertensive agents (AHT). However, RR is often uncontrolled even with a combination of different AHT. Resistant hypertension (RH) in DM is defined as blood pressure>139/85 mmHg in patients taking 2 antihypertensive agents and a diuretic; the prevalence of RH in DM in clinical practice, however, is not known.

Objective and methods: In 2011, GPs and internists participated in a nationwide survey of patients with DM. A standardized questionnaire was used to collect demographic data and to record the type and status of medical treatment. In the present analysis patients with DM were grouped according to the following criteria: no AHT, controlled with AHT (RR-C) and RH. Furthermore, concomitant diseases, medication and risk factors in the groups have been analyzed.

Results: All required data were available for 4391 of 4434 men and women with DM (average age 65.8 years) listed by the surveyed physicians. Mean DM duration was 8.7 years. Only 9 % of patients needed no AHT, 77% were in RR-C, but 14% had RH.

	Age	BMI	Waist	Duration DM	HbA1	Duration RR	Number of drugs for DM	Number of drugs for RR	CV complication
RR-C n=3408	66,2	30,3	104,4	8,7	7,0	11,0	1,4	1,9	0,7
RH n=623	68,4*	32,2*	108,6*	10,2*	7,2*	13,2*	1,5*	3,5*	1,3*

*P<0.05

Patients with RH had significantly more parameters with out-of-reference, a worse lipid profile* and more complications* were found. Therefore, patients with DM and RH are considerably sicker, but simultaneously– because of worse risk management –at a higher risk than patients with DM and RR-C.

Discussion: One of 7 patients with DM has also a RH. This group already has substantially more cardiovascular complications and more* and worse* controlled risk factors. Such patients therefore require better cardiometabolic risk management! Further evaluation is needed to explain why these patients have such an adverse cardiometabolic profile.

9C.07 RETINAL VASCULAR CHANGES IN A RODENT MODEL OF DIABETES AND EFFECT OF ANTIHYPERTENSIVE TREATMENT

M. Golzan[1], E. Salum[2], V. Gupta[1], P. Kampus[2], J. Kaals[2], A. Avolio[1], S. Graham[1], M. Butlin[1]. *[1]Macquarie University, Sydney, AUSTRALIA, [2]University of Tartu, Tartu, ESTONIA*

Objective: Diabetic retinopathy is a leading cause of acquired blindness in the young, mostly affected by type 2 diabetes. Retinal vascular changes are significant indicators in diabetes. Effects of diabetes on retinal microvasculature are poorly characterised. This study investigates retinal vasculature changes in a rat model of diabetes.

Design and methods: Diabetes was induced in 4 male Wistar rats by intraperitoneal injection of streptozotocin at age 6 weeks. A further 6 rats with induced diabetes were given a daily dose of the antihypertensive, telmisartan (10 mg/kg/day, gavage). Controls (n=8) and controls on the same antihypertensive treatment (n=8) were also conducted. At 12 weeks following streptozocin injection, tail cuff systolic blood pressure was measured before each rat was anesthetised (urethane) and blood glucose measured. Retinal vessels were scanned in either the left or right eye (pupil dilated using 1% tropicamide) using infrared optical coherence tomography (OCT, Spectralis) with a 30 degree field of view. Arterial and venous diameters and artery to vein ratio (AVR) were measured. Correlation between these parameters and blood glucose levels was also assessed.

Results: Induced diabetes caused significant increases in blood glucose levels, however there was no difference in systolic pressure between the diabetic and control rats (Table). Antihypertensive therapy successfully lowered blood pressure in both diabetic and control rats. Analysis of variance for venous and artery diameter and AVR across the four groups showed a significant difference between vein diameters ($p<0.001$) and AVR ($p<0.05$) but no significant difference between arterial diameters ($p=0.13$). There was a significant correlation between venous diameter and glucose ($r=0.75$, $p<0.0001$) but no significant correlation between AVR, arterial diameter and glucose. There were no significant difference in retinal vasculature between the diabetic group and diabetic treated with antihypertensive.

Conclusions: This study showed that retinal venous diameters are significantly dilated in diabetes and AVR is significantly smaller in diabetes. Venous and arterial diameters are less dilated in rats treated with anti hypertensive medication.

9C.08 PROTEIN DEACETYLASE SIRTUIN 2 REGULATES MITOCHONDRIAL FUNCTION IN HUMAN LIVER HEPG2 CELLS

V. Lesmos[1,2], R.M. Oliveira[3], V. Costa[4,5], T. Outeiro[3,6], P. Gomes[1,2]. *[1]Faculty of Medicine, University of Porto, Department of Biochemistry, Porto, PORTUGAL, [2]Faculty of Medicine, University of Porto, Department of Pharmacology, Porto, PORTUGAL, [3]Institute for Molecular Medicine, Cell and Molecular Neuroscience Unit, Lisbon, PORTUGAL, [4]Institute for Molecular and Cell Biology (IBMC), University of Porto, Porto, PORTUGAL, [5]Abel Salazar Institute for Biomedical Sciences (ICBAS), University of Porto, Porto, PORTUGAL, [6]University Medizin Göttingen, Department of Neurodegeneration and Restorative Research, Göttingen, GERMANY*

Objective: There is strong evidence that insulin resistance is associated with mitochondrial dysfunction. Caloric restriction (CR) delays the onset of metabolic disorders, such as insulin resistance, and increases mitochondrial respiration. Because sirtuin 2 (SIRT2), which is upregulated by CR, promotes the expression of PPARγ coactivator-1α (PGC-1α), that in turn activates mitochondrial respiration, we aimed at identifying a potential role for SIRT2 as a regulator of mitochondrial function.

Design and method: Insulin resistance, induced in human hepatocarcinoma cell line HepG2 by treatment with glucosamine (GlcN), was confirmed by insulin-stimulated glycogen synthesis assay. Basal oxygen consumption, oligomycin-independent respiration (proton leak) and FCCP-stimulated maximal respiration were assessed in intact HepG2 cells using an oxygen-sensitive electrode.

Results and conclusions: Insulin-resistant HepG2 cells displayed reduced SIRT2 protein expression. This was accompanied by increased oxidative stress levels, as determined by an elevation in H2O2 production, and failure to respond to FCCP-stimulated respiration, indicating mitochondrial dysfunction. Overexpression of wild-type SIRT2 in HepG2 cells caused an increase in both oligomycin-independent and FCCP-stimulated respiration in comparison with untransfected cells. Under insulin-resistant conditions, SIRT2-overexpressing cells also showed significantly higher oxygen consumption after oligomycin and FCCP stimulation compared to GlcN-treated untransfected cells. Cells expressing a catalytically inactive mutant of SIRT2 responded similarly to untransfected cells. These findings suggest that SIRT2 increases oxygen consumption, stimulating both mitochondrial electron transport and uncoupling capacity, thus improving mitochondrial function under insulin-resistant conditions.

9C.09 RENAL FUNCTION ALBUMIN CREATININE RATIO AND PULSE WAVE VELOCITY PREDICT CORONARY ARTERY DISEASE IN PRE-DIABETES AND DIABETES

R. Sanchez, A. Miranda, A. Ramirez. *Arterial Hypertension and Metabolic Unit, University Hospital, Favaloro Foundation, Buenos Aires, ARGENTINA*

Introduction: Type 2 diabetic patients (DBT) develop macro and micro-angiopathy during their evolution. Less is known regarding glucose intolerant subjects (GI, Pre-diabetics).

Aims: To evaluate in DBT or (GI) patients, with or without coronary arterial disease (CHD), the relationship of glomerular filtration rate (GFR) with 24h urinary albumin-creatinine ratio (ACR) and pulse wave velocity (PWV).

Methods: We studied 92 patients (Male: 44), from which 49 have DBT (60±7y) and 43 GI (43±4y). PWV, ACR, GFR (MDRD), and ischemic heart disease prevalence (Coronariography and coronary SPECT) were evaluated and the relationship between GFR and (CHD) or co-factors (ACR, PWV) was investigated.
DBT and GI patients received antihypertensive and hypoglycaemic treatment according ADA and ESH Guidelines.

Results: We found that 48.98% of DBT and 25.58% of GI had CHD. Compared to normal values (PWV: 8.0±1.0m/sec; ACR: <30mg/g and GFR: 100-120ml/min.), GI (PWV: 10.7±0.19m/sec; ACR: 134.5±6.99mg/g and GFR: 61.4±1.31ml/min) or DBT (PWV: 10.1±0.3m/sec; ACR: 89.9±15.0mg/g and GFR: 74.0±2.3ml/min) showed abnormal values.
In both, GI and DBT patients, GFR showed a negative correlation with ACR (GI: $r= -0.706$, $p< 0.001$; DBT: $r= -0.756$, $p<0.001$) and PWV (GI: $r= -801$, $p<0.001$; DBT: $r=0.803$, $p<0.001$). In GI with CHD, a negative and significant correlation between GFR and ACR ($r= -0.674$, $p<0.01$) or PWV ($r= -0.745$, $p<0.01$) was present. Similar data was observed in DBT with CHD (GFR with ACR: $r= -0.848$, $p<0.001$ or PWV: $r= -0.733$, $p<0.01$).
In subjects without CHD, a significant and negative correlation was observed between GFR and ACR or PWV in either GI (ACR $r= -0.731$, $p<0.01$; PWV: $r= -0.76$, $p<0.01$) or DBT (ACR: $r= -0.773$, $p< 0.01$; PWV: $r= -0.823$, $p< 0.001$).

Conclusions: Higher PWV, lower GFR and ACR predict the incidence of CHD in DBT. GI also represent a group of higher risk for CHD with the same predictors. On the other hand, either DBT or GI without macro vessel disease still developed renal micro-angiopathy where PWV seems to represent a reliable marker.

Abstract 9C.07

	diabetes	diabetes + telimisartan	control	control + telmisartan
weight (g)	404±15$^{***\#\#\#}$	414±32$^{***\#\#\#}$	579±46	543±40
blood glucose (mmol/L)	27±4$^{**\#\#}$	30±4$^{***\#\#\#}$	7±2	6±2
systolic blood pressure (mmHg)	139±19	127±9	146±17$^{\#\#}$	112±12
retinal vasculature parameters:				
vein diameter (mm)	0.22±0.01$^{***\#\#\#}$	0.21±0.02$^{**\#\#\#}$	0.17±0.01	0.16±0.01
artery diameter (mm)	0.13±0.02	0.12±0.01	0.13±0.01	0.11±0.01
artery to vein ratio	0.59±0.07	0.58±0.10	0.75±0.08	0.72±0.09

$^{**}p<0.01$, $^{***}p<0.001$ compared to control; $^{\#\#}p<0.01$, $^{\#\#\#}p<0.001$ compared to control+telmisartan

ORAL SESSION

ORAL SESSION 9D
THERAPEUTIC ASPECTS

9D.01 THE NEW RENIN INHIBITOR VTP-27999 ALTERS RENIN IMMUNOREACTIVITY AND DOES NOT BIND NATIVE PRORENIN

A.H.J. Danser[1], M. Krop[1], B. McKeever[2], R. Gregg[2]. *[1]Erasmus MC, Rotterdam, THE NETHERLANDS, [2]Vitae Pharmaceuticals, Fort Washington, MD, USA*

Background: Renin inhibitors like aliskiren not only block renin, but also bind prorenin, thereby inducing a conformational change in the molecule ('non-proteolytic activation', identical to the changed induced by low pH), allowing it to be detected in a renin-specific assay, although obviously it cannot display activity. Consequently, aliskiren can be used in vitro to measure prorenin on top of renin in a renin assay. VTP-27999 is a new renin inhibitor with an aliskiren-like IC50 and t½, and a much higher bioavailability.

Methods and results: This study addressed the changes in renin and prorenin during a 10-day treatment of salt-depleted volunteers with 150 mg VTP-27999 or 300 mg aliskiren. Both drugs increased renin immunoreactivity. Treatment of plasma samples from aliskiren-treated subjects with excess aliskiren yielded higher renin immunoreactivity levels, confirming the presence of prorenin. Unexpectedly, this approach did not work in VTP-27999-treated subjects, although an assay detecting the prosegment revealed that their blood still contained prorenin. Subsequent in vitro analysis showed that VTP-27999 increased renin immunoreactivity for a given amount of renin by 30% or more, but did not activate prorenin. Yet, it did bind to acid-activated, intact prorenin and then again increased immunoreactivity in a renin assay. However, no such increase in immunoreactivity was seen when measuring acid-activated prorenin bound to VTP-27999 with a prosegment-directed assay. The VTP-27999-induced rises in renin immunoreactivity could be competitively prevented by aliskiren, and antibody displacement studies revealed a higher affinity of the active site-directed antibodies in the presence of VTP-27999.

Conclusion: VTP-27999 increases renin immunoreactivity in renin imunoassays because it affects the affinity of the active site-directed antibody. Combined with its lack of effect on prorenin, these data show that VTP-27999 differs from aliskiren. The clinical relevance of this result needs to be established.

9D.02 LOW DOSE THIAZIDE DIURETICS AND RISK FOR NEW ONSET OF TYPE 2 DIABETES: RESULTS FROM DIURETICS IN THE MANAGEMENT OF ESSENTIAL HYPERTENSION (DIME) TRIAL

S. Ueda[1], T. Morimoto[2], S. Ando[3], K. Shimamoto[4], Y. Kawano[5], S. Takishita[6], T. Saruta[7], Dime Investigators[1]. *[1]University of the Ryukyus, Department of Clinical Pharmacology & Therapeutics, Okinawa, JAPAN, [2]Hyogo Medical Collage, Department of General Medicine, Hyogo, JAPAN, [3]Saiseikai Futukaichi Hospital, Department of Cardiology, Fukuoka, JAPAN, [4]Sapporo Medical University, Department of Medicine, Sapporo, JAPAN, [5]National Cardiovascular Research Center, Department of Hypertension and Renal Medicine, Osaka, JAPAN, [6]University of the Ryukyus, Department of Medicine, Okinawa, JAPAN, [7]Keio University, Department of Medicine, Tokyo, JAPAN*

Objectives: Antihypertensive treatment with thiazide diuretics effectively reduces cardiovascular risk in hypertensive patients but concern remains unsolved regarding adverse effects of diuretics on glucose metabolism and prognostic impact of such effects on cardiovascular events. We hypothesized that antihypertensive treatment with low dose thiazide diuretics may not be associated with higher risk of new onset of type 2 diabetes in Japanese patients with essential hypertension and designed an independent, investigator-initiated, multicenter, randomised, open, blinded-end point, parallel group study.

Methods: Non-diabetic patients with essential hypertension (n=1170) were randomly assigned to receive thiazide diuretics at low dose that was defined as 12.5mg/day of hydrochlorthiazide or equivalent adding any other antihypertensive drugs as required (Diuretics use group) or receive any antihypertensive drugs other than thiazide diuretics (No Diuretics group). The primary end point was new onset of type 2 diabetes.

Results: We collected complete endpoint information at the end of study for 1049 people after a median follow-up of 4.4 years. Diabetes developed in 26 participants (5%) in Diuretics Use group, as compared with 30 (5%) in No Diuretics group during the study (hazard ratio, 0.93; 95% confidence interval, 0.55 to 1.58; P = 0.8). Subgroup analysis did not identify any factors interacting with effects of use of diuretics on development of diabetes albeit statistically underpowered. Levels of either fasting glucose or hemoglobin A1c in Diuretics Use group throughout the study were not significantly higher than those in No Diuretics group. There were no apparent differences in measured secondary end points including gout. Serum potassium levels in Diuretics use group were significantly but only slightly lower by 0.1mmol/L than No Diuretics group. There was no difference in blood pressure at the end of the follow up between groups. Conclusion Our present randomised controlled trial suggest that current antihypertensive treatment with thiazide diuretics at low doses may not be associated with increased risk of new onset of type 2 diabetes and other clinically significant metabolic abnormalities.

9D.03 A RANDOMIZED CONTROLLED STUDY: EFFECTS OF BISOPROLOL AND ATENOLOL ON SYMPATHETIC NERVOUS ACTIVITY AND CENTRAL AORTIC PRESSURE IN PATIENTS WITH ESSENTIAL HYPERTENSION

W. Zhou, R. Wang, D. Chen, Y. Li, E. Chen, D. Zhu, P. Gao.
Department of Hypertension, Ruijin Hospital, Shanghai, CHINA

Background: Beta-blockers (BBs) with different pharmacological properties may have heterogeneous effects on sympathetic nervous activity (SNA) and central aortic pressure (CAP), which are independent cardiovascular factors for hypertension.Hence, we analyzed the effects of bisoprolol and atenolol on SNA and CAP in hypertensive patients.

Methods: This was a prospective, randomized controlled study with 109 never-treated hypertensive subjects randomized to bisoprolol (5 mg) or atenolol (50 mg) for 4~8 weeks. To evaluate SNA, baroreflex sensitivity (BRS) and heart rate variability (HRV) were measured by power spectral analysis using a Finometer. CAP and related parameters were determined with the SphygmoCor apparatus using pulse wave analysis.

Results: Both drugs were similarly effective in reducing brachial BP. However,central systolic BP (-14±10 mm Hg vs -6 ±9 mm Hg; P<0.001) and aortic pulse pressure (-3±10 mm Hg vs +3 ±8 mm Hg; P<0.001) decreased significantly with bisoprolol than with atenolol. The augmentation index at a heart rate (HR) of 75 bpm (AIxatHR75) was significantly decreased (29%±11% to 25%±12%; P=0.026) only in the bisoprolol group. Furthermore, the change in BRS in the bisoprolol group (3.99±4.19 ms/mmHg) was higher than that in the atenolol group (2.66±3.78 ms/mmHg), although not statistically significant (P>0.05). BRS was stable whenRHR was controlled (RHR <=65 bpm), and the two treatments had similar effects on low frequency (LF)/high frequency (HF) ratio and on HF.

Conclusion: BBs seem to have dissimilar effects on arterial distensibility and compliance in hypertensive subjects. Compared with atenolol, bisoprolol may a better effect on CAP.

9D.04 NUMBER NEEDED TO TREAT SUPPORTS REDUCTION OF CORONARY EVENTS AS THE BASIS OF MORTALITY REDUCTION WITH ACE INHIBITORS

J.J. Mourad[1], J.J. Brugts[2]. *[1]Avicenne University Hospital, AP-HP and Université Paris 13, Bobigny, FRANCE, [2]Department of Cardiology, Thoraxcenter, Rotterdam, THE NETHERLANDS*

Incorporating the results of randomized trials into clinical practice is of high priority for physicians. In this regard, number needed to treat (NNT) or harm (NNH) have given decision makers access to a more intuitive statistical tool to assess treatment efficacy than regular relative risk reduction (RRR).

Objective: Mortality and cardiovascular (CV) events were compared in hypertension trials involving angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) based on NNTs to illustrate differences in CV protection of these two classes.

Design and objectives: All-cause and CV mortality as well as coronary and cerebrovascular events were analyzed in a selection of 20 large randomized trials enrolling a total of 158 998 hypertensive patients as previously reported in a recently published meta-analysis (van Vark LC; European Heart Journal 2012). NNT was calculated over the 4.3 year-follow-up as the inverse of the absolute risk reduction between active treatment group and its comparator.

Results: ACE inhibitors efficiently prevented all-cause and CV mortality with on average 67 and 133 patients who would have to be treated to prevent one event. For ARBs, for the same objective, 432 and 254 patients would have had to be treated. Indeed, among renin-angiotensin-system antagonists, only ACE inhibitors significantly reduced all-cause mortality, a protective effect that appeared to rest on coronary event reduction with a NNT of 48. The non-significant trend for mortality reduction with ARBs was based on a decrease in cerebrovascular events rather than coronary events, with respective NNTs of 145 and 1181. Among the group of ACE inhibitors, perindopril-based regimens strongly supported all-cause mortality reduction with a 13% RRR (P-value <0.001). Perindopril/indapamide combination was particularly effective with respective NNT of 101 and 137 for coronary and cerebrovascular events.

Conclusion: NNT analysis of morbidity and mortality in hypertension trials provided a rapid way to compare the cardioprotective effect of treatments and confirmed that coronary event reduction is an important component of mortality reduction with ACE inhibitors.

9D.05 OLMESARTAN PLUS AZELNIDIPINE VERSUS DIURETIC IN HYPERTENSIVE PATIENTS WITH DIABETES AND ALBUMINURIA

S. Tanaka[1], M. Kojima[2], S. Yamashita[1], T. Sugiura[1], M. Ito[3], Y. Dohi[1], G. Kimura[1].
[1]Nagoya City University, Department of Cardio-Renal Medicine and Hypertension, Nagoya, JAPAN, [2]Komono Kosei Hospital, Department of Internal Medicine, Komono, JAPAN, [3]Mie University, Department of Cardiology and Nephrology, Tsu, JAPAN

Objective: A thiazide diuretic plus benazepril is superior to amlodipine plus benazepril in reducing albuminuria in patients with hypertension and diabetes. However, calcium channel blockers have diverse characteristics. The present study was designed to test the hypothesis that combining an angiotensin receptor blocker with either azelnidipine or a thiazide diuretic produced similar reductions in albuminuria in hypertensive diabetic patients for the same levels of blood pressure achieved.

Design and method: This study was a 24-week prospective randomized open blinded endpoint study assessing the effects of azelnidipine versus those of a diuretic in combination with olmesartan, an angiotensin receptor blocker, on urinary albumin excretion in hypertensive patients with diabetes and albuminuria. Hypertensive patients with type 2 diabetes and albuminuria (30–600 mg/g creatinine) under antihypertensive treatment (mean age, 67.0 ± 7.6 years; blood pressure, 134.2±12.4/74.8±9.3 mmHg) were instructed to stop all antihypertensive treatment and take a combination of olmesartan (20 mg, daily) and amlodipine (5 mg, daily) for 3 months (run-in period). Then, patients were randomly assigned to receive either olmesartan plus azelnidipine (16 mg/day; n=71) or olmesartan plus trichlormethiazide (1 mg/day; n=72) for an additional 6 months.

Results: Urinary albumin was 116.0 and 107.8 mg/g creatinine (geometric mean) in the azelnidipine and diuretic arms, respectively, at the time of randomization, and was reduced to a similar extent (79.8 [95% confidence interval 66.4–96.0] and 89.7 [74.6–107.7] mg/g creatinine, respectively, after adjustment for baseline values. In contrast, glomerular filtration rate was reduced in the diuretic, but not azelnidipine, group. Blood pressure was not different in the two groups throughout the study period.

Conclusion: Azelnidipine is equally effective as a thiazide diuretic in reducing urinary albumin when used in combination with olmesartan though the calcium blocker does not reduce glomerular filtration rate.

9D.06 ANTIHYPERTENSIVE DRUG THERAPY IN SOUTH ASIAN PATIENTS: A SYSTEMATIC REVIEW

R. Bindraban[1], P. Kewalbansingh[1], G. Oehlers[2], Y. Seedat[3], L.M. Brewster[1].
[1]Dept. of Vascular Medicine, AMC, Amsterdam, THE NETHERLANDS, [2]Dept. of Cardiology, AZP, Paramaribo, SURINAM, [3]Nelson Mandela School of Medicine, Faculty of Health Sciences, University of KwaZulu-Natal, Durban, SOUTH AFRICA

Background: South-Asian patients have a high risk of premature cardiovascular death. Hypertension treatment is a main risk reduction strategy in this ethnic group, however, the effects of different antihypertensive drugs are unclear.

Purpose: To critically assess the existing evidence on the efficacy of commonly used antihypertensive drugs in reducing blood pressure and morbidity and mortality outcomes in hypertensive patients of South-Asian descent.

Data Sources: The following databases were searched from their inception through May 2012: PubMed, EMBASE, LILACS, AIM and the Cochrane Library, without language restriction.

Study Selection: Randomized, controlled trials comparing single drug treatment with placebo treatment or single Drug Treatment With Other Single Drug Treatment.

Data Retrieval: A total of 696 reports or abstracts were retrieved in all databases, yielding a total of 16 trials with 7 classes of antihypertensive drugs in 1403 hypertensive patients of South-Asian descent, a minority of which were diabetics (n=192). Sample sizes ranged from 16 to 89 patients in each treatment group. No trials had morbidity or mortality outcomes.

Data Synthesis: Taking the small number of patients into account, the existing evidence showed no major differences in the efficacy of antihypertensive drugs in South-Asian patients. Diuretics showed a small benefit on systolic blood pressure reduction (SMD 0.33; 95% CI 0.01 to 0.61 mm Hg), and there was a trend for AT2 blockers to be more effective in reaching diastolic goal blood pressure than other drugs (RR 1.32, 95% CI, 0.94 to 1.85), and for beta-adrenergic blockers to have a lower efficacy in systolic and diastolic blood pressure lowering than other drugs, but these outcomes did not reach statistical significance. Studies did not provide information on side effects on glucose metabolism.

Conclusions: There are no major differences in blood pressure lowering efficacy of antihypertensive drugs in South-Asian hypertensives. The high cardiovascular mortality in South-Asians necessitates inclusion of this group in trials with morbidity and mortality outcomes.

9D.07 EARLY TREATMENT WITH AZILSARTAN COMPARED TO ACE-INHIBITORS IN ANTI-HYPERTENSIVE THERAPY – RATIONALE AND DESIGN OF THE EARLY HYPERTENSION REGISTRY

S. Potthoff[1], A.K. Gitt[2,3], P. Baumgart[4], P. Bramlage[5], F. Mahfoud[6], J. Senges[2], S. Schneider[2], H. Buhck[7], R.E. Schmider[8]. *[1]Medical Faculty, Department of Nephrology, University Düsseldorf, Düsseldorf, GERMANY, [2]Stiftung Institut für Herzinfarktforschung, Ludwigshafen, GERMANY, [3]Herzzentrum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, GERMANY, [4]Clemens-Hospital Münster, Klinik für Innere Medizin I, Münster, GERMANY, [5]Institut für Pharmakologie und Präventive Medizin, Mahlow, GERMANY, [6]Universitätsklinikum des Saarlandes, Klinik für Innere Medizin III, Homburg/Saar, GERMANY, [7]MedCommTools, Medical-Scientific Consultancy, Hannover, GERMANY, [8]Universitätsklinikum Erlangen, Medizinische Klinik 4, Erlangen, GERMANY*

Objective: Arterial hypertension is highly prevalent but poorly controlled. Blood pressure (BP) reduction substantially reduces cardiovascular morbidity and mortality. Recent randomized, double-blind clinical trials demonstrated that azilsartan medoxomil (AZM) is more effective in reducing BP than the ubiquitary ACE inhibitor ramipril. Therefore, we aim to test whether these can be verified under clinical practice conditions.

Design and methods: The "Treatment with Azilsartan Compared to ACE-Inhibitors in Anti-Hypertensive Therapy" (EARLY) registry is a prospective, observational, national, multicenter registry with a follow-up of up to 12 months. It will include up to 5000 patients on AZM or ACE-inhibitor monotherapy in a ratio of 7 to 3. A subgroup of patients will undergo 24-hour BP monitoring. EARLY has two co-primary objectives: 1) Description of the safety profile of azilsartan and 2) achievement of BP targets based on recent national and international guidelines for patients treated with azilsartan in comparison to those treated with ACE-inhibitors. The most important secondary endpoints are the determination of persistence with treatment and the documentation of cardiovascular and renal events. Recruitment commenced in January 2012 and will be completed by February 2013. Intermediary results and assessment from the enrollment visit and 6 month follow-up are expected by May 2013.

Results: As of the time of abstract submission (Jan 15th, 2013) a total of 3764 patients were enrolled. The contribution will illustrate the final patient characteristics, blood pressure readings, treatment assignment and results of the 6 months follow-up for the total cohort of patients enrolled.

Conclusions: The data obtained will supplement previous results from randomized controlled trials to document the potential value of utilizing azilsartan medoxomil in comparison to ACE-inhibitor treatment for target BP achievement in clinical practice.

9D.08 EARLY SYMPATHETIC INHIBITION AND IMPROVEMENTS IN LEFT VENTICULAR DIASTOLIC FUNCTION AFTER SURGICAL REMOVAL OF A PHEOCHROMOCYTOMA

D. Hering[1], K. Kunicka[1], E. Swierblewska[1], W. Kucharska[1], L. Obolonczyk[2], M. Siekierska-Hellmann[2], K. Sworczak[2], K. Narkiewicz[1]. *[1]Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, POLAND, [2]Department of Endocrinology and Internal Medicine, Medical University of Gdansk, Gdansk, POLAND*

Objective: While sympathetic activation is a pivotal mechanism linking hypertension and related disease, a pheochromocytoma has been shown to be associated with reduced central sympathetic outflow assessed by muscle sympathetic nerve activity (MSNA) and increased plasma catecholamines. This study examined whether cardiac amelioration are accompanied by concurrent sympathetic inhibition following a removal of a pheochromocytoma.

Design and methods: Sixteen patients with symptoms and/or scan imaging indicating a tumor secreting catecholamines underwent baseline office BP, heart rate (HR), MSNA, plasma and urine catecholamines, and transthoracic echocardiography (Vivid 7 ProTM GE assessing conventional 2D, Doppler mitral inflow parameters and tissue Doppler velocities) measurements. Histopathological diagnosis of a pheochromocytoma was confirmed in 12 out of 16 enrolled patients. Ten pheochromocytoma patients (5 males, age 43±4 years, BMI 25±1 kg/m^2, mean±SEM) underwent comparable measurements 1 month following surgical removal of a tumour.

Results: Changes in the parameters before and 1 month after removing a pheochromocytoma in 10 patients are shown in Table. Despite unchanged BP and HR, there were significant reductions in MSNA, catecholamines and cardiac function at 1 month follow-up (Table).

Conclusions: Both sympathoexcitation and left ventricular diastolic function evident in patients diagnosed with pheochromocytoma are rapidly and substantially reduced after tumour removal. Whether these beneficial effects associated with adrenalectomy are sustained over time warrant further exploration.

9D.09 CREATINE KINASE INHIBITION AS A NEW TARGET FOR HYPERTENSION TREATMENT

L. Oudman[1], F.A. Karamat[1,2], L.J.A. Spijkers[1], J.F. Clark[3], A.B.P. Van Kuilenburg[4], R. Leen[4], A.H.J. Danser[5], F.P.J. Leijten[5], G.A. Van Montfrans[1], L.M. Brewster[1,2,6]. *[1]Academic Medical Center, Department of Vascular Medicine, Amsterdam, THE NETHERLANDS, [2]Academic Medical Center, Department of Internal Medicine, Amsterdam, THE NETHERLANDS, [3]Cincinnati Children's Hospital, Department of Neurology, Cincinnati, OH, USA, [4]Academic Medical Center, Laboratory of Genetic and Metabolic Diseases, Amsterdam, THE NETHERLANDS, [5]Erasmus Medical Center, Department of Vascular Medicine and Pharmacology, Rotterdam, THE NETHERLANDS, [6]Academic Medical Center, Department of Social Medicine, Amsterdam, THE NETHERLANDS*

Background: Creatine kinase (CK) is reported to be the main predictor of blood pressure in the population. By catalyzing the reaction: ADP + PCreatine + H+ « ATP + Creatine, the enzyme is thought to provide ATP for vascular contractility and sodium retention. Beta-guanidinopropionic acid (beta-GPA) is a specific, competitive cellular creatine uptake inhibitor that reduces the flux through the CK reaction. Therefore, we hypothesized that beta-GPA will reduce blood pressure in the spontaneously hypertensive rat (SHR).

Methods: Male, 16-weeks-old SHR were randomly assigned to a diet with beta-GPA (3%) with standard chow as a control (N=8 per group). Conscious blood pressure measurements were performed weekly with the tail cuff method during 4 weeks.

Results: Treatment with beta-GPA significantly reduced blood pressure of compared to controls: Systolic –42.7 (SE 5.5) mm Hg ($p<0.001$); diastolic –35.3 (4.8) mm Hg ($p<0.001$, Figure). As a posthoc test we assessed reversibility in female, 30-weeks-old SHR treated during 3 weeks (N=6 per group), and followed blood pressure thereafter. In these rats systolic and diastolic blood pressure decreased with 24.1(4.4) and 21.5(4.4) mm Hg respectively ($p<0.01$), and returned to hypertensive control values after withdrawal of beta-GPA within 2 weeks.

Conclusion: To our knowledge, these are the first data indicating that CK inhibition reduces blood pressure in an animal model of hypertension. The data are in line with previous findings that CK predicts blood pressure on a population level and that microvascular contractility is highly CK dependent. The results suggest that inhibition of the CK-system may be a promising new target for hypertension treatment.

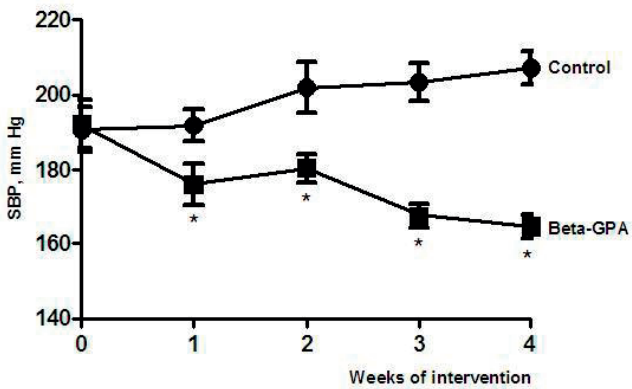


Figure: Effect of treatment with beta-GPA on systolic blood pressure in spontaneously hypertensive rats.

Legend: Systolic blood pressure (SBP) reduction with CK inhibition with beta-GPA in spontaneously hypertensive rats from 16 to 20 weeks of age (N=8 per group). Data are presented as means with standard error bars. *$p<0.001$ for the difference between groups.

Abstract 9D.08

	At Baseline	At 1 month follow-up	P
Office SBP	125±7	124±7	P=0.88
Office DBP	79±5	79±5	P=0.95
Office HR	85±5	79±4	P=0.22
MSNA (bursts/min)	53±3	41±3	P=0.0018
MSNA (bursts/100heartbeats)	74±5	59±5	P=0.039
Plasma Adrenaline (pg/ml)	259±100	138±42	P=0.26
Plasma Noradrenaline (pg/ml)	9183±8465	817±186	P=0.34
Urine metanephrine (µg/24h)	1599±621	55±10	P=0.03
Urine normetanephrine (µg/24h)	2870±507	251±59	P=0.0005
IVSd (mm)	1.05±0.05	0.95±0.04	P=0.007
PWd (mm)	1.06±0.04	0.95±0.03	P=0.0025
LA volume (ml/m^2)	62.8±5.7	54.6±4.7	P=0.0035
LVMI (g/m^2)	90.6±3.9	82.1±3.0	P=0.013
E/E' ratio	7.3±0.7	5.9±0.5	P=0.0075

SBP-systolic BP, DBP-diastolic BP, IVSd-intraventricular septal diameter, PWd-posterior wall diameter, LA–left atrium, LVMI-left ventricular mass index, E-early diastolic mitral flow, E'-early diastolic mitral annulus velocity

LATE-BREAKER SESSION

LATE-BREAKER SESSION 3

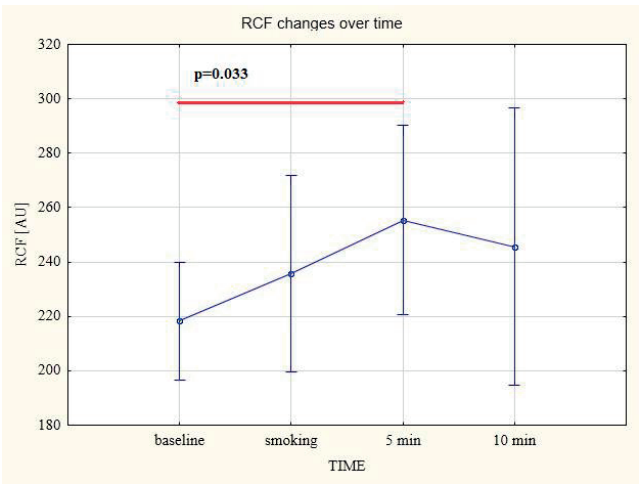
LB03.01 THE ACUTE EFFECT OF SMOKING ON RETINAL CAPILLARY FLOW IN NORMOTENSIVE INDIVIDUALS

K. Polonis[1], E. Miszkowska-Nagórna[1], J. Harazny[2], R.E. Schmieder[2], K. Narkiewicz[1]. *[1]Hypertension Unit, Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, POLAND, [2]Department of Nephrology and Hypertension, University of Erlangen-Nuremberg, Erlangen, GERMANY*

Objective: It is generally accepted that acute cigarette smoking increases sympathetic nerve traffic to blood vessels, to skin and, to the heart. However, the effect of smoking on retinal circulation remains unclear. The investigation of retinal arterioles offers the unique opportunity to analyze non-invasively the structure of microvasculature in vivo. Therefore, we aimed to investigate the effect of acute smoking on retinal blood flow in healthy subjects.

Design and methods: Twelve healthy non-chronic smoking young individuals (mean age 23.58±1.31) were examined. Retinal capillary flow (RCF) was determined in arbitrary units [AU] using Scanning Laser Doppler Flowmetry (Heidelberg retinal flowmeter) on four occasions: before (baseline), immediately after smoking 2 cigarettes, 5 minutes, and 10 minutes after smoking. At the same time blood pressure and heart rate were measured. The average values of three consecutive pulse and blood pressure measurements were taken to analysis. ANOVA of repeated measurements and Dunnett's test were done to see the effect of smoking on all above mentioned parameters before and after smoking.

Results: The mean retinal capillary flow tended to increase immediately after smoking (235.62 vs. 218.22 [AU], p=0.29) reaching significant difference 5 minutes after smoking (255.35 vs. 218.22 [AU], p=0.033) in comparison to baseline measurements. The growth in RCF just after and 5 minutes after smoking represented the linear trend (p=0.0042). Systolic and diastolic blood pressure did not reveal significant changes during the experimental period. However, we found the statistically significant difference between mean heart rate at baseline and, immediately after and 5 minutes after smoking (74.86 vs. 85.53 [bpm], p= 0.0001 and 74.86 vs. 81.19 [bpm], p= 0.01, respectively).



Conclusions: Acute smoking in healthy subjects significantly increased retinal capillary blood flow 5 minutes after exposure. This finding is not consistent with previously described vasoconstrictive effect of nicotine. The exact reason behind the increased retinal capillary flow from cigarette provocative stimuli needs further investigations. It could shed light on mechanisms by which cigarette smoking influences vascular function.

LB03.02 TARGETS AND SELF-MANAGEMENT FOR THE CONTROL OF BLOOD PRESSURE IN STROKE AND AT RISK GROUPS (TASMIN-SR): A RANDOMISED CONTROLLED TRIAL - MAIN RESULTS

R. McManus[1], J. Mant[2], M. Haque[3], E. Bray[3], S. Greenfield[3], M. Jones[3], S. Jowett[3], P. Little[4], C. O'Brien[3], M. Penaloza-Ramos[3], C. Schwartz[3], H. Shackleford[3], J. Varghese[3], B. Williams[5], F. Hobbs[1]. *[1]University of Oxford, Oxford, UNITED KINGDOM, [2]University of Cambridge, Cambridge, UNITED KINGDOM, [3]University of Birmingham, Birmingham, UNITED KINGDOM, [4]University of Southampton, Southampton, UNITED KINGDOM, [5]University College, London, UNITED KINGDOM*

Introduction: Self-monitoring of blood pressure with self-titration of antihypertensives (self-management) results in lower blood pressure in hypertension but there are no data in high risk groups. This trial assessed the added value of self-management in stroke and other high cardiovascular risk groups compared to usual care.

Design and setting: Pragmatic primary care, unblinded, randomised controlled trial of self-management of blood pressure (BP) versus usual care. Eligible patients had a history of stroke, coronary heart disease, diabetes or chronic kidney disease and were individually randomised to usual care or self-management. Self-management comprised self-monitoring of blood pressure combined with an individualised self-titration algorithm agreed at baseline. A target of 130/80mmHg adjusted for home measurement was used in all groups. The primary outcome was the difference in office SBP between intervention and control at 12 months. Secondary outcomes included self-efficacy, lifestyle behaviours, health-related quality of life and adverse events.

Results: 552 patients were randomised from 58 UK General Practices. After 12 months, primary outcome data were available from 450 patients (82%). Baseline blood pressure was 143.1/80.5mmHg (intervention) and 143.6/79.5mmHg (control). After 12 months this had dropped to 128.2/73.1mmHg (intervention) and 137.8/76.3mmHg (control), a difference of 9.7mmHg (95%CI 8.6 to 10.8) in systolic and 2.5mmHg (1.4 to 3.5) in diastolic following correction for baseline blood pressure and covariates. These are late breaking results; subgroups and side effects will be presented.

Conclusions: Self-monitoring with self-titration of antihypertensive medication is feasible and effective for those at high risk of cardiovascular disease through co-morbidities. The effect size observed was greater than that seen in lower risk hypertensives which may reflect the lower blood pressure targets used in this trial. Patients with stroke and other high risk conditions whose blood pressure is above target should be offered self-management to control their blood pressure.

LB03.03 DIETARY SODIUM AND POTASSIUM INTAKE IN THE ADULT HYPERTENSIVE POPULATION IN ITALY: RESULTS OF THE MINISAL-SIIA STUDY

F. Galletti[1], A. Barbato[1], E. Agabiti Rosei[2], G. Bernini[3], R. Boero[4], G. Desideri[5], F. Fallo[6], F. Mallamaci[7], A. Morganti[8], M. Castellano[2], P. Nazzaro[9], B. Trimarco[1], P. Strazzullo[1]. *[1]Università di Napoli Federico II, Naples, ITALY, [2]Università degli Studi di Brescia, Brescia, ITALY, [3]Università di Pisa, Pisa, ITALY, [4]Ospedale Martini, Turin, ITALY, [5]Università degli Studi dell'Aquila, L'Aquila, ITALY, [6]Azienda Ospedaliera di Padova, Padua, ITALY, [7]Azienda Ospedaliera Melacrino Bianchi Morelli, Reggio Calabria, ITALY, [8]Università degli Studi di Milano, Milan, ITALY, [9]Università degli Studi di Bari, Bari, ITALY*

Introduction: The aim of the MINISAL-SIIA study was the assessment of the age-, sex- and region-specific average sodium and potassium intake and of its relationship to anthropometric features in a large national sample of the adult hypertensive population. In addition the prevalence of resistant hypertension (RH) was evaluated by a questionnaire on drug consumption.

Methods: 1232 hypertensive patients were recruited. Data on antihypertensive drug therapy were available for 1177 (96%) subjects. The population was divided into three groups (North, Central and South), according to center geographical location.

Results: The average 24hUNa was 172 mmol and 138 mmol respectively in men and women. The average 24hUK was 63 and 56 mmol/die, respectively in

men and women. No significant geographic differences were observed. There was a statistically significant trend (p<0.05) to a gradual decrease in sodium intake with age, in both genders. There was also a graded direct association between BMI and sodium intake in both genders, regardless of age (p<0.001). An association between BMI and potassium intake was detected only in women (p=0.008). One-hundred-fiftyfour patients (13.1%) were found to have RH. The prevalence of RH in the southern, central and northern regions was respectively: 6.7%, 13.8% and 17.4% (p<0.001). The prevalence of RH was higher in obese subjects (17.5%) compared to those overweight (12.7%) or normal weight (9.5%). Individuals with RH were older than those with non-RH (63 vs 59 years; p<0.001). There was no difference in the urinary excretion of sodium, potassium and creatinine in this subgroup. Finally, the risk of having RH was increased by 1.51 fold (95%CI:1.25-1.83) for one unit increase in the standard deviation score of age, and by 1.41 fold (95%CI:1.19-1.67) for one unit increase in the standard deviation score of BMI.

Conclusions: In this national sample of the Italian hypertensive population, in all geographical areas dietary sodium intake was largely higher and potassium intake much lower than the recommended intakes. The prevalence of RH was similar compared to other studies. Age and BMI were found to be directly associated with the increased risk of RH in hypertensive subjects.

LB03.04 SALT INTAKE AND PREVALENCE, AWARENESS, TREATMENT AND CONTROL OF HYPERTENSION IN PORTUGAL; CHANGES OVER A TEN-YEAR PERIOD

J. Polonia, L. Martins, F. Pinto, J. Nazare.
Portuguese Society of Hypertension, Lisbon, PORTUGAL

Objective: To determine 24-h urinary sodium (UNa+) and potassium (UK+) excretion and the prevalence, awareness, treatment and control of hypertension (HT) in the Portuguese adult population thereby examining how it changed from a similar study done in 2003.

Methods: A population-based cross-sectional survey was conducted in 2001-2012. A multistage stratified (by age and gender) sampling method was used to select a representative sample of 18-90 years old population yielding 3720 subjects (52.6% women, 97,1% caucasians). After 15 min rest 3 blood pressure (BP) were obtained by trained observers with an OMRON M6 and complete clinical information was collected with standard questionnaire (V1-visit1). This procedure was repeated 10-15 days after (V2-visit2) and 24-h urinary sample was collected for UNa+, UK+ and creatinine excretion. HT was defined as a mean systolic BP >=140 or diastolic BP >=90 mm Hg and/or use of antihypertensive medication.

Results: The overall prevalence oh HT (V1) was 42.2% (44.4% in men, 40.2% in women), (42.1% in 2003). The age-specific prevalence of HT was 6.8%, 46.9% and 74.9% in people <35yrs, 35-64yrs and >64yrs. Co-morbidities were 2.2-6.3 times more common in hypertensives vs normotensives. Overall of hypertensive patients, 76.8% were aware of HT condition, 74.9% were treated and 42.6% were under control (<140/90 mmHg) i.e respectively 1.7, 1.9 and 3.8 times higher vs. data in 2003, with lower values in men vs women and younger vs older people. Global mean BP was 124.4/74.6 ± 0.2/0.2 vs 134.7/80.4 ± 0.3/0.2 mmHg in 2003. In average control of HT increased by 14.8% from V1 to V2. UNa+ (84.4% of validated urinary samples) was 182±1 mmol/day (10.7 g salt/day vs 11.9 g/day in 2005 and UK+ was 76.2±0.4 mmol/day. UNa+ correlated with systolic BP (r=0.06) and BMI (r=0.1) p<0.01 and was greater in patients with HT than in normotensives (186±1 vs 177±1 mmol/day, p<0.02).

Conclusions: HT prevalence among Portuguese population remains stable in the last decade, but proportions of awareness, treatment and control of HT improved significantly. Salt intake is still high being almost double than the WHO recommendations.

LB03.05 META-ANALYSIS OF HYPERTENSION TRIALS TARGETING ON DIFFERENCE IN ACHIEVED BLOOD PRESSURE

C. Thomopoulos[1], G. Parati[1,2], A. Zanchetti[3]. *[1]Dept. of Cardiology, San Luca Hospital, IRCCS Istituto Auxologico, Milan, ITALY, [2]Chair of Cardiology and Dept. of Health Sciences, University Milano-Bicocca, Milan, ITALY, [3]Istituto Auxologico Italiano, Milan, ITALY*

Objective: Different trials were designed to create blood pressure (BP) difference between groups undergoing either active treatment vs placebo or active treatments of different intensity. We investigated the effect of intentionally imbalanced BP lowering between groups on hard clinical endpoints.

Design and methods: From randomized controlled trials of antihypertensive agents published until mid-April 2013, we excluded those in heart failure, acute myocardial infarction and acute stroke. Additionally, trials with hypertension prevalence below 40% at baseline were also excluded. This resulted in selection of 35 trials with more than less intensive treatment or placebo-controlled design. The meta-analysis was conducted according to PRISMA statement. Random-effects of Risk Ratio (RR) estimates were reported when significant heterogeneity was detected among studies. Outcomes were: (1) fatal and non-fatal myocardial infarction, (2) fatal and non-fatal stroke, (3) heart failure, (4) major cardiovascular events [(1)+(2)] or (5) [(1)+(2)+(3)], (6) cardiovascular mortality, and (7) all-cause mortality.

Results: Lower compared to higher achieved BP was accompanied by 15% RR reduction of myocardial infarctions (outcome 1) (95%CI: 0.80-0.90, difference between groups in achieved systolic/diastolic BP: 13.4/7.1 mmHg); by 32% RR reduction of strokes (outcome 2) (0.63-0.75, 13.7/7 mmHg); by 37% RR reduction of heart failure (outcome 3) (0.51-0.78, 16.3/8.1 mmHg); by 20% RR reduction of major cardiovascular events (outcome 4) (0.75-0.84, 13.7/7.2 mmHg); by 24% RR reduction of major cardiovascular events including heart failure (outcome 5) (0.69-0.83, 15.9/8.1 mmHg); by 17% RR reduction of cardiovascular mortality (outcome 6) (0.76-0.90, 13.7/7.4 mmHg); and by 10% RR reduction of all-cause mortality (outcome 7) (0.84-0.95, 13.7/7.3 mmHg). In meta-regression analyses the outcomes 2, 3, 4 and 5 were significantly associated with the achieved between-group systolic and diastolic BP difference.

Conclusions: In trials with at least moderate prevalence of hypertension at baseline, lower compared to higher achieved BP was associated with significant reduction of all hard clinical endpoints. The RR was dependent on the extent of the BP difference for strokes, heart failure and major cardiovascular events, but not for myocardial infarction and mortality.

LB03.06 PREVENTION OF LEFT VENTRICULAR REMODELING IN TYPE 2 DIABETES WITH OLMESARTAN IN THE ROADMAP STUDY: ECG-LVH RESULTS

R.E. Schmieder[1], L.M. Ruilope[2], H. Haller[3], C. Ott[1], U. Raff[1].
[1]Nephrology and Hypertension, University Hospital, Erlangen, GERMANY, [2]Hypertension Unit, Complutense University, Madrid, SPAIN, [3]Abteilung Nephrologie, Universität Hannover, Hannover, GERMANY

Background: Cardiac structural adaptation develops early in hypertension and diabetes and is aggravated if both conditions coexist. Blockade of the angiotensin receptors may attenuate these cardiac processes and we tested the ability of olmesartan to prevent or delay left ventricular (LV) remodeling and hypertrophy.

Methods: In the ROADMAP study, a double blind, placebo controlled, multicenter, phase IIIb study, comparing olmesartan 40mg vs. placebo (additional anti-hypertensive medication allowed, except ACEI & ARBs), on prevention of microalbuminuria in diabetic patients, also 12-lead ECGs have been conducted at baseline and in yearly intervals during follow-up of 3.2 years. All ECGs were centrally and independently evaluated. The primary ECG parameter of LV remodeling and hypertrophy was Cornell voltage QRS duration product.

Results: Of the 14.074 ECG recorded in the ROADMAP study, 9.418 have been found evaluable and 1.513 patients were identified in whom interpretable ECGs were available at baseline and one after at least 2 years (N=736 in the placebo and N=777 in the olmesartan group). Dividing the study population into 4 quartiles defined by the Cornell voltage QRS duration product at baseline, the prevalence of patients in the highest quartile (ie. >=200 mV*msec) increased from 24% to 26,5% in the placebo but decreased from 25% to 22.3% in the olmesartan group (odds ratio 0.598 [95 % CI: 0.440-0.813], p=0.001). When adjusted for potential differences in clinical baseline parameters (incl. blood pressure), the odds ratio did not change. In accordance with the findings above, at study end 38.7% of patients in the placebo group and 34.7% in the olmesartan group shifted from a lower to a higher quartile or remained in the highest quartile of the Cornell voltage QRS duration product (odds ratio 0.797 [95% CI 0.64-0.99], p=0.0465), reflecting an attenuated progression of ECG-LV remodeling with olmesartan.

Conclusion: Olmesartan significantly decreased the process of ECG left ventricular remodeling in patients with type 2 diabetes independent of differences in blood pressure. Thus, olmesartan delayed not only the onset of microalbuminuria (NEJM 2011), but also ECG signs of cardiac structural adaptation in type 2 diabetes.

LB03.07 LOW SODIUM INTAKE INDUCES FUNCTIONAL CAPILLARY RECRUITMENT AND INFLUENCES ENDOTHELIAL SURFACE LAYER DIMENSIONS IN HEALTHY MALE SUBJECTS

T. Van Hirtum[1], I. Khoyske[2], I. Oudman[2], R.H.G. Olde Engberink[1], D.W. Eeftinck Schattenkerk[2], B.J.H. Van Den Born[2], L.M. Brewster[2], L. Vogt[1].
[1]Academic Medical Center, Department of Nephrology, University of Amsterdam, Amsterdam, THE NETHERLANDS, [2]Academic Medical Center, Department of Vascular Medicine, University of Amsterdam, Amsterdam, THE NETHERLANDS

Objective: Reduction of capillary density increases total peripheral resistance, thereby increasing blood pressure (BP), as demonstrated in several animal models and in hypertensive patients. Currently, the sublingual microcirculatory network can be investigated non-invasively by a new technique called Sidestream Darkfield Imaging (SDF). Additionally, SDF can estimate the endothelial surface layer (ESL), a complex sugar layer composed of negative-charged glycosaminoglycans (GAGs) lining the endothelium. In this pilot study, our aim was to determine the effects of dietary sodium reduction on the microcirculation and ESL dimensions in healthy male subjects.

Design and method: Twenty-one healthy male subjects (mean (SD) age 38±9 yrs) adhered to a 7-d low sodium diet (50 mmol/d) followed by a 3-d high sodium diet (200 mmol/d). After each diet period, BP, body weight (BW), blood and 24-h urine were assessed. Capillary recruitment and ESL dimensions were assessed by SDF. An impaired ESL results in an increased Perfused Boundary Region (PBR), reflecting the erythrocyte-permeable part of the ESL. Red blood cell (RBC)-filling determines the erythrocyte-density in the capillary. Functional density determines the percentage of perfused vessels. Furthermore, P50 reflects red-blood-cell-column-width and thus vessel diameter.

Results: As shown in the table, the 7-d low sodium diet decreased BW, systolic BP, P50 and PBR, while functional density and RBC-filling were increased. PBR was increased when switching to a high sodium diet. Twenty-four-hour urinary sodium excretion indicated adequate compliance to the diets.

Conclusions: Along BP reduction, dietary sodium restriction induces functional capillary recruitment in healthy male subjects as shown by an increased RBC-filling and functional density indicating increased perfusion. A high sodium intake increases PBR, suggesting perturbation of the ESL. These findings indicate that low sodium diet improves microcirculatory flow and oxygenation as well as endothelial barrier function, possibly contributing to prevention of BP-associated end-organ damage.

LB03.08 PREVALENCE OF ARTERIAL HYPERTENSION IN SERBIA - PAHIS STUDY

D. Lovic[1], V. Stojanov[2], B. Jakovljevic[3], K. Paunovic[3], B. Lovic[1], M. Zdravkovic[4], M. Krotin[4], D. Djordjevic[5], D. Simonovic[5], D. Bastac[6], Z. Brankovic[1], R. Zivkovic[7]. *[1]Clinic for Internal Disease InterMedica, Nis, SERBIA, [2]Clinic for Cardiology, Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, SERBIA, [3]Institute of Hygiene and Medical Ecology, Faculty of Medicine, University of Belgrade, Belgrade, SERBIA, [4]University Hospital Medical Center KBC Bezanijska Kosa, Belgrade, SERBIA, [5]Institute Niska Banja, Nis, SERBIA, [6]Outpatient Clinic, Dr. Bastac, Zajecar, SERBIA, [7]Primary Healtcare Unit Stari Grad, Belgrade, SERBIA*

Arterial hypertension (AH) is the most common cardiovascular disease, affecting between 30% and 50% of the adult population in developed countries. A steady increase of the prevalence of arterial hypertension by about 60% is expected by year 2025.

Methods: Serbian Society of Hypertension conducted a prevalence study from February to May 2012 on a sample of 3878 adult respondents. The study included 2066 women (53.3%) and 1812 men (46.7%). Average age was 48.89±17.48 years. Most participants resided in urban areas (2956 people, 76.2%), whereas 922 resided in rural areas (23.8%).

Results: The prevalence of arterial hypertension in Serbia is 42.7%. Hypertension is more frequently diagnosed among women (53.3%), than in men (46.7%). 1412 respondents were previously diagnosed and treated for hypertension. Out of all diagnosed cases of hypertension, 390 persons (27.7%) have well-regulated blood pressure values, whereas 1022 persons (72.3%) do not have their blood pressure under control.

Conclusion: Serbia belongs to countries with high prevalence of arterial hypertension. A poor control of AH may be explained in view of socio-economic problems. High prevalence of AH may indicate a very high cardiovascular disease mortality in Serbia.

LB03.09 LONG-TERM TELEMETRY RECORDINGS DEMONSTRATE INCREASED RENAL SYMPATHETIC NERVE ACTIVITY AND BLOOD PRESSURE IN RATS WITH CHRONIC KIDNEY DISEASE

J. Phillips[1], I. Salman[1], J. Harrison[2], C. Hildreth[1]. *[1]Australian School of Advanced Medicine, Macquarie University, Sydney, AUSTRALIA, [2]School of Veterinary and Life Sciences, Murdoch University, Perth, AUSTRALIA*

Objective: To establish long-term dual mean arterial pressure (MAP) and renal sympathetic nerve activity (RSNA) recordings in healthy and chronic kidney disease (CKD) animals, examining the hypothesis that elevated RSNA is a key pathological feature of CKD.

Design and methods: 10 week old Lewis polycystic kidney (LPK) and Lewis control rats (total n=11) were instrumented with dual renal sympathetic nerve and arterial blood pressure radiotelemetry probes (TRM56SP–Telemetry Research/Millar Instruments). After a 1-week recovery period to re-establish circadian rhythms, 5 min recordings of MAP and RSNA (μV) were taken every 15 minutes for 48 hours each week. Quality of RSNA was evaluated using pulse modulation. We recorded responses to acute stress (open field) in conscious animals. In anaesthetised animals prior to euthanasia, we tested baroreceptor responses to phenylephrine (50 μg/kg i.v.) and used ganglionic blockade (hexamethonium (20 mg/kg i.v.) to assess background activity.

Results and conclusions: High quality nerve recordings were obtained in 70% and 35% of animals at 12 and 18 weeks of age respectively. Baseline RSNA was significantly greater in the LPK vs. Lewis at 12 weeks of age (2.8±1.1 vs. 0.5±0.4 μV, P<0.05). In two LPK where we were able to obtain viable recordings out to 18 weeks of age, RSNA increased by at least 36% and MAP by 25%, while no significant increase was seen in the Lewis (n = 2) for these variables. Acute stress induced reproducible increases in RSNA in both groups. In anaesthetised animals, PE caused an increase in MAP alongside a significant reflex suppression in RSNA and pulse modulation of RSNA was abolished by ganglionic blockade. This data indicate the capability of this technique to determine long-term progressive alterations in RSNA and hypertension in CKD.

Abstract LB03.07

Mean ±SD	Baseline (BL) (n= 21)	Low Sodium Diet (LSD) (n=21)	High Sodium Diet (HSD) (n=21)	Repeated Measurement test/paired t-test *p-value*
BW (kg)	78.6 ±9.8	77.3 ±9.4$^{\$,\ddagger}$	79.0 ±10.0	0.000
SBP (mmHg)	125 ±13	121 ±13*,‡	126 ±12	0.006
DBP (mmHg)	77 ±10	76 ±9	77 ±8	0.195
24-h urinary Na$^+$ (mmol/d)	NA	33 ± 25 ‡	329 ± 188	0.000
Functional density (%)	55.6 ±14.1	68.2 ±11.1$^{\$,\ddagger}$	63.2 ±11.6	0.001
RBC-filling (%)	71.3 ±6.2	75.5 ±6.2*	73.1 ±5.1	0.063
P50 median (micron)	12.4 ±1.4	11.5 ±1.4*	12.6 ±2.0	0.047
PBR 10-19 (micron)	2.20 ±0.26	1.98 ± 0.39*,†	2.17 ±0.28	0.040

Posthoc analysis was performed by using a Tukey LSD test.

- *BL vs LSD* $^{*}p < 0.05$, $^{\$}p < 0.01$
- *LSD vs HSD* $^{\dagger}p < 0.05$, $^{\ddagger}p < 0.01$
- *BL vs HSD* $^{\ddagger}p < 0.05$, $^{\P}p < 0.01$

POSTER SESSION

POSTER SESSION P01
EPIDEMIOLOGY AND HEALTHCARE ORGANISATION

PP.01.01 ROLE OF COMMUNITY PHARMACIES IN THE CONTROL OF HYPERTENSION. POINT OF VIEW OF PRIMARY CARE CENTRES' PROFESSIONALS. FARMAPRES-CV PROJECT

V. Giner Galvañ[1], V. Pallarés Carratalá[2], I. Bonig Trigueros[3], J.J. Tamarit García[4], B. Reig Espert[5], F. Valls Roca[6], M.M. Reig Botella[1], M. Adell Alegre[7], J. Cantero Llorca[8], L. Calduch Herrera[9], J. Casanova Izquierdo[10]. *[1]Hypertension Unit, Internal Medicine Department, Verge dels Lliris Hospital, Alcoy (Alicante), SPAIN, [2]Union de Mutuas, Castellón, SPAIN, [3]Internal Medicine Department, Vinaroz Hospital, Vinaroz (Castellón), SPAIN, [4]Internal Medicine Department, Dr. Peset Aleixandre Hospital, Valencia, SPAIN, [5]Internal Medicine Department, Manises Hospital, Manises (Valencia), SPAIN, [6]Beniganim Primary Care Centre, Beniganim (Valencia), SPAIN, [7]Castellón Provintial Official College of Pharmacists, Castellón, SPAIN, [8]Primary Care Director, Health Department Dr Peset, Valencia, SPAIN, [9]Grao Primary Care Centre, Castellón, SPAIN, [10]Primary Care Director, Health Department of Manises, Manises (Valencia), SPAIN*

Objective: To know what is the potential function of community pharmacies (CPh) in the control of HT in opinion of physicians and nurses working in Primary Care centres (PCc).

Method: As a part of the FARMAPRES-CV Project, a specifically designed survey with 12 questions about the role of CPh in the control of HT, was sent during 2012 to the physicians and nurses working in the PCc of 4 Health Departments of the Comunitat Valenciana, in the southeast of Spain.

Results: 210 professionals have answered (Valencia 130, Alicante 50, Castellón 30), 144 physicians and 66 nurses with 19±11 yrs of experience. The three commonest answers for the question "Which is in your opinion the role of CPh in the control of HT?" were: 26.2% "Coordinated help with PCc", 22.8% "Detection of uncontrolled HT and new HT" 17.1% "None". Potential advantages of BP measurement in the CPh are (%): 22.4 "time flexibility", 18.1 "accessibility", 16.7% "less white coat effect". 5.9% of the participants opine that the CPh "don't have any advantage". 2% of the respondents say that CPh BP measurement is cheaper, and 0.5% say the opposite. One third think that CPh are not fulfilling their role in HT management, mainly due to an incorrect measurement method (21.2%) or lack of knowledge about HT (18.3%). Other argued reasons were "the CPh alarm the patients" (9.9%) and "absence of coordination with PCc" (7.0%). There were not significant differences comparing the opinion of physicians and nurses. However, for the physicians the main reason for the CPh not to accomplish their role is due to a "incorrect measurement method" (25.0%), meanwhile for nursery the main reason is the "alarmism induced to the patients (26.7%).

Conclusion: Although PCc professionals think that CPh have some advantages compared with PCc for the measurement of BP, they also have a generalized negative perception of CPh mainly because of incorrect methodology and lack of knowledge.

PP.01.02 CHANGE IN APPROACH CONTROL OF HYPERTENSION AND IN CONSECUTIVE CHECKS OF BLOOD PRESSURE IN CONSULTATION

M. Vida Pérez, J. Martínez De La Iglesia, J. Redondo Sánchez, M. Cano García, S. Ruiz Rejano, M. Agudo De La Paz, B. Muñoz Díaz, J. Prados Castillejo. *Primary Care Center Lucano Sas, Córdoba, SPAIN*

Objectives: Rate how to modify the degree of control in hypertensive patients considering the 1st, 2nd or 3rd taking blood pressure (BP) in consecutive measurements in medical consultation.

Design and method: Descriptive observational study made in a primary care clinic in which were selected 140 hypertensive patients by opportunistic sampling who were performed three consecutive shots of blodd pressure (BP) with the same semiautomatic apparatus (Omron M-6). Patients were classified in different degrees of hypertension (HT). In 33 patients, these results were compared with the results obtained from the self-measurement of blood pressure (SBPM). Statistical analysis was performed assessing frequency distribution for qualitative variables and means with standard deviation (SD) for quantitative. We made an analysis of variance to compare quantitative variables and chi-square for qualitative variables considering a significance level of p <0.05.

%	1ª	2ª	3ª	SBPM
BP systolic				
Normal	7,9	12,9	21,4	30,3
Grado 1	42,1	45,0	45,0	60,6
Grado 2	37,1	30,7	27,1	9,1
Grado 3	12,9	11,4	6,4	0,0
BP diastolic				
Normal	68,6	76,4	82,1	78,8
Grado 1	21,4	15,7	13,6	21,2
Grado 2	9,3	7,9	4,3	0
Grado 3	0,7	0	0	0

Results: The 57.9% of the sample were women with a mean age of 70.25 years (SD = 11.0). The blood pressure obtained in the 1st, 2nd and 3rd respectively were taken: systolic BP 161.2 (SD = 17.4,), 157.5 (SD = 17) 152 5 (SD = 18.5), diastolic BP: 83.5 (SD = 12.3) 81.5 (SD = 11.4) , 79.6 (SD = 11) and heart rate 78.4 (SD = 13), 78.7 (SD = 15) and 77 4 (SD = 12.7). In table reflect measurements. Significant differences were found when comparing all groups, both when considering the average size of each as BP to consider by diagnostic group (P<0,05).

Conclusions: Taking consecutive BP measures in consultation provides us that measures go down gradually. The 3rd shot shows normal control level three times higher than the 1 st in the systolic and 4 times in the diastolic. To sum up, the 3rd blood pressure is more similar to those obtained by SBPM.

PP.01.03 HYPERTENSION PREVALENCE INCLUDING MASKED HYPERTENSION AND COMPARE PULSE WAVE VELOCITY IN A COMMUNITY IN KOREA

S. Kim[1], J. Bae[2], T. Hwang[3], K. Lee[3]. *[1]Dongguk University, College of Medicine, Department of Preventive Medicine, Gyeongju-si, SOUTH KOREA, [2]Dongguk University, College of Medicine, Department of Internal Medicine, Gyeongju-si, SOUTH KOREA, [3]Yeungnam University, College of Medicine, Department of Preventive Medicine and Public Health, Daegu, SOUTH KOREA*

Object: Masked hypertension(isolated ambulatory hypertension) is normotensive by clinic measurement but proves to be hypertensive by 24 hour Ambulatory Mornitoring of Blood Pressure(24 hour-AMBP) is important because of high cardiovascular risk. This study was conducted to evaluate the prevalence of masked hypertension and relevance to target organ damage in a community.

Design and methods: The study was conducted among 278 subjects among Community Health Survey participants in Gyeongju, Korea, from March 2011 to July 2012. Masked hypertension was defined mean BP less than 140/90 mmHg and daytime mean BP over 135/85 mmHg. We also evaluated target organ damage by brachial-ankle pulse wave velocity (baPWV). Subjects with the history of any cardiovascular disease were excluded from the study.

Results: In all subjects, 77 subjects (27.7%) were in the hypertension treatment. The frequency of hypertension was 52.2% (145 subjects) including being treated

subjects by clinical BP and 68.3% (190 subjects) by ambulatory BP. Rates of hypertension control was 62.3% by clinical BP and 40.3% by ambulatory BP. In non-treatment group, masked hypertension were 54 subjects (26.9%) and their mean baPWV (13.8±1.8 m/sec) was significantly more fast than normotension group (13.1±2.1 m/sec) (p<0.05). In treatment group, masked hypertension were 25 subjects (32.5%) and mean baPWV between masked hypertension group (14.8±2.1 m/sec) and normotension group (14.9±3.0 m/sec) were not significantly different.

Conclusion: The prevalence rate of hypertension including masked hypertension was very high in community. Detection and management of masked hypertension are required in order to reduce adverse cardiovascular outcome.

PP.01.04 WHAT IS THE CLINICAL PICTURE OF THE HYPERTENSIVE CRISES BROUGHT TO THE EMERGENCY DEPARTMENT? A CROSS-SECTIONAL OBSERVATIONAL STUDY FROM A SINGLE ESH EXCELLENCE CENTRE

M. Fedecostante, F. Spannella, L. Landi, P. Dessì Fulgheri, R. Sarzani. *University Politecnica delle Marche, Ancona, ITALY*

Objective: Hypertensive crises (HC) are a major cause of access to the emergency department (ED). Aim: full clinical evaluation of the patients referred to us for HC in relation to age, BP control, drug therapy, secondary hypertension (SH).

Design and method: An observational cross-sectional study of 197 consecutive from January 2011 to August 2012, sent from the ED for HC. Inclusion criteria were age >= 18 years and acute increases in BP >= 180 mmHg for systolic and / or >= 110 mm Hg for diastolic BP.

Results and conclusions: Mean age was 61.1 ± 15.0 years and 54.3% were males. Hypertensives already under drug treatment were 70.1%. Mean BP during crisis (BPc) was 198.7 ± 20.3/108.3 ± 13.7 mmHg without difference between genders. Systolic BPc increased linearly with increasing age: $\beta = 0.278$, $p < 0.001$. In contrast, diastolic BPc decreased with increasing age: $\beta = -0,463$, $p < 0.001$. ABPM performed during the first week after the crisis showed that 85.4% of patients without drug therapy (before the crisis) were indeed hypertensives and 79% of treated patients were not controlled. These patients had a greater number of peaks (>= 180 mmHg for systolic and / or >= 110 mm Hg for diastolic) compared with normotensives/controlled patients ABPM (5.7 vs. 0.2, P <0.001). At the end of the investigation, 84.3% of patients were essential hypertensives (EH), 9.6% had SH, 6.1% was found to be normotensive (N). Patients with SH had higher systolic BP at crisis (212.2 mmHg vs 197.9 mmHg in EH and 188.3 mmHg in N, $p = 0.002$). SH showed also a greater number of pressure peaks at ABPM: 17.5 vs 4.2 in EH and 0.2 in N, $p = 0.005$. Not controlled or off-therapy EH are most commonly affected by HC, the majority of patients being grade 2 or 3 EH. Greater awareness and optimal treatment of hypertension may drastically reduce access to the ED for HC.

PP.01.05 HYPERTENSION MANAGEMENT IN PRIMARY CARE IN TURKEY: FOCUS ON CALCIUM CHANNEL BLOCKERS (HIT-CCB) - BASELINE DATA ON COEXISTING CARDIOVASCULAR DISEASE

N. Koylan[1], F. Fici[2], N. Caglar[3], Y. Erdem[4], I. Nalbantgil[5]. *[1]Anadolu Health Center, Cardiology Department, Istanbul, TURKEY, [2]University of Milan, Milan, ITALY, [3]Ankara University, Cardiology Department, Ankara, TURKEY, [4]Hacettepe University, Nephrology Department, Ankara, TURKEY, [5]Ege University, Cardiology Department- Retired, Izmir, TURKEY*

The aim of HIT- CCB study was to assess the rate of control of hypertension (HT) in patients treated with dihydropyridine (DHP) calcium channel blockers (CCB) as monotherapy or in combination with other drugs among the primary care centers in Turkey.

The secondary objectives of the study were to determine the rate of blood pressure control, the prevalence of DHP CCB (CCB) related adverse events, treatment adherence rates, and the quality of life parameters among hypertensive patients participated in the study. The aim of this presentation is to discuss the coexisting cardiovascular (CV) disease data of the study. The data of a total of 7310 patients (pts) (4651men and 2945 women, mean age 61.2 years) who were already being followed by primary care centers for hypertension, whom blood pressures (BP) were <210/115 mmHg and who were receiving DHP CCB drugs as either monotherapy or in combination were analyzed. Among these pts, 1658(23%) had diabetes, 175(2,4%) had renal disease, 1403(19%) had coronary heart disease, 277(4%) had previous stroke, and 625(9%) had peripheral artery disease. Any kind of cardiovascular disease was present at 1756 pts (24%) and Isolated systolic hypertension (ISH) was present at 1741 pts (24%). BP control was established in 2317 pts (32%) while 3538 pts (48%) were receiving monotherapy while 3772 (52%) were receiving combinations.

The BP control rates were significantly lower in those with diabetes (8%), with previous stroke (25%), peripheral artery disease (29%), and cardiovascular disease (31%, p=0,02) while none of the ISH pts were under control. More men were using monotherapy (4651/2945) while more women used combinations (2185/1353) (p<0,001). Combination use was significantly more at those with diabetes (597/1061, p<0,001), coronary heart disease (422/981, p<0,001), history of stroke (105/172, p<0,001), peripheral artery disease (240/385, p<0,001), and cardiovascular disease (582/1174, p<0,001). No significant difference was observed in between the use of various DHP CCB drugs either alone or in combination.

These results suggest that the presence of coexisting cardiovascular disease and/or diabetes is a threat on BP control and these patients need more combinations.

PP.01.06 EFFICIENCY OF DIAGNOSTIC AND TREATMENT OF ESSENTIAL HYPERTENSIVE'S IN POLYCLINICS OF RUSSIA (THE DATA FROM THE REGISTRY FOR ESSENTIAL HYPERTENSION)

S. Evstifeeva, E. Oschepkova. *Russian Cardiology Research and Production Center, Moscow, RUSSIA*

The Russian Registry for essential hypertension (EH Registry) include automatic information-analytical system and real time Internet-technologies. The EH Registry was work from 2005 to 2013 years in 54 polyclinics from different cities in Russia.

Objective: The aim of our study was to evaluate diagnostic, treatment and total cardiovascular (CV) risk in the EH pts from 2005 to 2011 years.

Design and method: EH patients (n=77559) were observed (42,3 % M., av. age 55,2±10,8 y and 57,7 % F., av. age 60,1±11,2y.) during 2005 to 2011 y. Blood pressure level 150/80 mmHg had 50% EH pts, [Me(25%;75%)] 25% Eh pts had 140/80 mm Hg. and 75 % pts had 160/95 mm Hg. CV risk (SCORE model) in the EH patients 4,8 had 50% EH pts, [Me(25%;75%)] 25% Eh pts had 2,0 and 75 % pts had 10,4. All pts were treated according National Recommendations by management of arterial hypertension.

Results: 7-year follow-up: modified risk factors (MRF) was 60,1% (2005y.), 68,7% (2006 y.), 69,0% (2007 y.), 81,6% (2008 y.), 85,3% (2009 y.), 74,0% (2010 y.) and 70,0% (2011 y.); Subclinical organ damage (OD) and/or established cardiovascular or renal disease was 65,0 (2005y.), 84,0% (2006 y.), 86,0% (2007 y.), 78,0% (2008 y.), 90,0% (2009 y.), 89,9% (2010 y.) and 90,0% (2011 y.); Goal BP at the treatment (low BP 140/90 mm Hg) was 50,0% (2005y.), 59,0% (2006 y.), 56,0% (2007 y.), 38,0% (2008 y.), 55,0% (2009 y.), 59,1% (2010 y.) and 39,0% (2011 y.); Save goal BP at the treatment was 9,0% (2005y.), 21,0% (2006 y.), 26,0% (2007 y.), 22,0% (2008 y.), 20,0% (2009 y.), 20,0% (2010 y.) and 20,0% (2011 y.).

Conclusion: from 2005 to 2011 y-s in Russia about 90% EH patients had high and very high additional CV risk because they are in the allotted time apply to see a physician. The most part of EH patients didn't save goal BP during from 2005 to 2011 y. and non-compliant to treatment.

PP.01.07 POPULATION MORBIDITY IN REPUBLIC OF MOLDOVA FROM ARTERIAL HYPERTENSION AND CEREBROVASCULAR DISEASE

N. Catanoi, O. Gherman, G. Chiobanu. *State University of Medicine and Pharmacy, National Scientific Practical Center of Emergency Medicine, Chisinau, MOLDOVA*

Introduction: The arterial hypertension represents an actual medical, economic and social problem, due to its high incidence amongst the population and major risks that it implies. According to the data of the World Health Organization, 600 million people in the whole world have an exceeded arterial hypertension. Through its high prevalence amongst the population, its invaliding character of complications and its extensions towards more and more young groups of population, the arterial hypertension obtains also a social and economic connotation, besides the medical one.

Materials and methods: The data presented here are collected from records of emergency care, through National Scientific and Practical Emergency Centre, Chisinau, between years 2008-2012. The analysis provides information on the prevalence and incidence of cerebral vascular diseases associated with hypertension.

Results: In 01.01.2013 in Republic of Moldova were 57 699 patients who have suffered a stroke. Of the total stroke morbidity(57 699) 35 387 (61,3%) are associated with hypertension and 22 312 (38,67%) are cases without hypertension.

Stroke morbidity with hypertension increased from 19 052 cases in 2008 to 35 387 cases showed an increase in morbidity 2012. If the stroke population without hypertension from 15 796 cases in 2008 to 22 312 cases in 2012. Of 11 060 new cases of stroke in 2012, 5 894(53,29%) were on a background of hypertension and 5 166(46,7%) cases without hypertension.

Conclusion: Cerebrovascular diseases increases every year, both in incidence and prevalence, the WHO is appreciated that it will become by 2030 the leading cause of mortality in the world. Given the seriousness of stroke, high mortality rate, high degree of disability and incapacity to work of survivors, social reintegration difficulties and high cost of necessary expenses for care of these patients, primary prevention of stroke is central, along with organizing services emergency medical assistance, emergency treatment and rehabilitation time cerebrovascular patients.

PP.01.08 COMPLEX EVALUATING OF THE EFFECTIVENESS OF CARDIOVASCULAR RISK SELF-ASSESSMENT AMONG PHYSICIANS AND THEIR AWARENESS OF CLINICAL PRACTICE GUIDELINES

L. Drozdova, S. Martsevich, V. Voronina. *National Research Center for Preventive Medicine, Moscow, RUSSIA*

Aim: To evaluate cardiovascular risk factors self-assesment among physicians of and to estimate of physicians awareness about up-to-date clinical guidelines.

Material and methods: The program included 607 doctors. Special selection of doctors by specialty, place of workwas not performed. Further analysis showed that 168 doctors who participated in the program were non-therapeutic profile (surgeons, gynecologists, ophthalmologists, etc.). Only data obtained from the nternists, cardiologists, neurologists, endocrinologists (n = 439) was analysed. Thus, in the final analysis included data from 280 physicians who participated in both in interactive inquiry and screening of the program.We made an assessment of main cardiovascular risk factors, and conducted interactive inquiry, which included questions about preventive and treatment measures for cardiovascular diseases.

Results: During interactive inquiry doctors had difficulties in selection of treatment in specific clinical situations, despite the relatively good knowledge of the basic concepts of risk adjustment. The average age of the physicians was 46 years (min - 21, max - 75), among them men - 28, women - 252. Study included both hospital doctors (n = 107) and physicians working in outpatient clinics (city clinics , departmental clinics, clinical and diagnostic centers) (n = 173). During SCORE asessment, 251 patients had had SCORE less than 5% Doctors experienced great difficulties in assessing their own cardiovascular risk. Totally 29 were at high risk of cardiovascular diseases.44% of those with high risk estimated it as low.Normal body weight had only 12 (41%)of high-risk physicians, one-third of doctors (35%) were obese. Totaly 22 physicians in the group of doctors with high and very high risk had hypertension (75.9%), 19 (86%) of physicians with high-risk hypertension were aware of it , but control was poor, only 8 (36.4 %) patients in this group effectively controlled blood pressure. Lack of awareness and low efficiency of the control of cardiovascular risk factors was revealed.

Conclusion: Knowledge of cardiovascular risk problems and necessity of their correction was adequate in the whole; however physicians failed to apply their knowledge to practice, even thei own health.

PP.01.09 THE PREVALENCE OF PREHYPERTENSION AND METABOLIC DISORDERS IN YOUNG PEOPLE OF THE ALTAI REGION

A. Osipov[1], E. Popova[2], L. Borisova[1], I. Osipova[1], R. Neupokoeva[1].
[1]*Altai State Medical University, Barnaul, RUSSIA,*
[2]*Center for Health, Hospital 6, Barnaul, RUSSIA*

Aim: To estimate the prevalence of prehypertension and metabolic disorders in young people.
The study included 522 residents of the Altai Region at the age of 16 to 29 years (21,9±3,8) passed examination at the Center for Health: men 79% (21,9±3,7), women 21% (21,9±4,1).
The main risk factors were estimated: blood pressure (BP), body mass index, cholesterol, glucose. During BP examination, 65% of the patients revealed an optimal BP, 35% prehypertension (120-139/85-89 mm Hg). In women optimal BP was identified 1,8 times more frequently than men (72 and 39%, p>0,001). Prehypertension were more frequent male than female (48 and 27%, p<0,001). Prehypertension is more in men 24-29 years (36%). 67% of the patients had normal body weight, 18% - overweight and obesity. Normal weight dominated by 20% in women (72% and 52%, p>0,005); overweight (23% and 10%, p<0,005) and obesity (10% and 3%, p>0,005) in men. Obesity is prevalent in men aged 25-29 years (29%), women in the same age category (7%, p<0,005). Physical inactivity presented in 90% cases, cholesterol 84% of patients had no abnormalities, 16% had hypercholesterolemia (for men and women 25-29 years 36 and 36%). Smoking diagnosed significantly more often in men 20-24 years (63%), in women 16-19 years (26%, p<0,005). Hyperglycemia was detected in 6%.

Conclusions: Among the patients of the health center a high level of risk factors (Prehypertension, cholesterol, overweight, smoking) was detected in young people, mostly in men. These findings point to the need for early prevention.

PP.01.10 CARDIOVASCULAR MORBIDITY AND MORTALITY IN HYPERTENSIVE PATIENTS AND THE ASSOCIATED CARDIOVASCULAR RISK FACTORS

M.V. Papavasileiou, A. Karamanou, I. Tsiantis, S. Vrakas, M. Stangou, S. Karas. *Sismanoglion General Hospital, Athens, GREECE*

Objective: The aim of this study was to investigate the conventional cardiovascular risk factors and their impact on the cardiovascular events.

Design and method: The studied population consisted of 475 hypertensive patients, treated or untreated without history or overt cardiovascular disease. All patients were under regular follow-up for 10 years. The patients were divided into two groups: Group A(N=214)who suffered at least one major cardiovascular event in 10 years (MI, stroke, aortic aneurysm or sudden death) and group B(N=261) who did not. All major cardiovascular risk factors were recorded at baseline. All patients underwent a treadmill test and the SBP / DBP, HR levels were recorded at the baseline as al so at the peak exercise. Furthermore we estimated the creatinine clearance in all patients. ANOVA was performed to assess the differences of the above mentioned parameters between the two groups.

Results: Table 1. ANOVA of the measured parameters between the two groups.

Abstract PP.01.10

	Group A N=214	Group B N=261	p-Value
MA(years)	61.7	52.9	0.000
DBP(mmHg)	94	96.4	0.032
WC(cm)	99.5	95.9	0.05
DH(years)	7.8	4.6	0.000
MaxSBP/DBP (mmHg)	199.3/99.7	189.7/94.2	0.044/0.033
maxHR (bpm)	152.7	160.9	0.032
Cr.Clearance	51.9	61.8	0.000
Glu0	113.8	96.3	0.000
HBA1C(%)	6.2	5.6	0.008
HDL	47.7	52.7	0.001
TGL	141.2	118.2	0.001
UA	5.58	4.9	0.000

	Number of observations	Outcome
Female	238(50.1%)	86(40.2%)
Male	237(49.9%)	128(59.8%)

Conclusions: The conventional cardiovascular risk factors as also the subclinical renal impairment, the duration of hypertension, the blood pressure and heart rate at the peak of the exercise as also the male gender, are significantly correlated with the cardiovascular outcome of hypertensives.

PP.01.11 THE ESTIMATION OF BLOOD PRESSURE VALUES, ANTHROPOMETRICAL PARAMETERS AND PHYSICAL ACTIVITY AMONG PRIMARY CARE PATIENTS IN THE DISTRICT OF PLESZEW

K. Hoffmann[1], P. Matyjaszczyk[1,2], W. Bryl[1]. *[1]Poznan University of Medical Sciences, Department of Internal Medicine, Metabolic Disorders and Arterial Hypertension, Poznan, POLAND, [2]Primary Care Physician Practice Matyjaszczyk, Pleszew, POLAND*

Objective: Hypertension, excessive body mass and low physical activity are more often detected cardiovascular risk factors. The aim of this study was to estimate blood pressure, anthropometrical parameters and physical activity among primary care patients in the district of Pleszew, a town with 18 thousands of inhabitants, located in western part of Poland.

Design and method: 681 patients at age 35-55 y., including 299 males (43,9%) and 382 females (56,1%), were recruited to this study. There were 295 subjects aged 35-45 y., including 113 males (38,3%) and 182 females (61,7%), and 386 subjects aged 46-55 y.: 186 males (47,6%) and 200 females (52,4%). We took the anthropometric and blood pressure measurements. Patients answered questions concerning lifestyle in the study questionnaire.

Results: We showed that in comparison to younger subjects both male and female older patients had statistically significant higher mean systolic (men:143,9±21,1 v. 134,6±15,1mmHg, p<0,05; women: 135,4±18,8 v. 128,0±15,7mmHg,p<0,05) and diastolic blood pressure values (men:89,4±12,0 v. 82,8±10,7mmHg,p<0,05). They had a larger body mass (men:88,8±15,0 v. 87,7±15,6kg, p<0,05; women:73,7±15,6 v. 70,6±13,4kg, p<0,05), BMI (men:28,7±4,5 v. 27,7±4,5kg/m^2, p<0,05; women:27,8±4,5 v. 25,8±4,7kg/m^2, p<0,05) and hip circumference (men:98,5±11,5 v. 95,0±9,2cm, p<0,05; women: 88,8±9,2 v. 82,7±11,6, p<0,05). The active lifestyle (physical activity lasting >30 minutes, at least 5 times a week) was declared by 180 patients (26,4%), including 111 females and 69 males (29,1% v. 23,1%, p<0,05). In younger group 69 persons had active lifestyle, whereas in older group 111 patients (23,6% v. 28,8%, p<0,05). We found statistically significant difference in declared active lifestyle between female and male subjects aged 35-45 y. (28,0% v. 23,6%, p<0,05) and between younger and older male patients (15,9% v. 27,4%, p<0,05).

Conclusions: 1. In comparison to younger patients, subjects aged 46-55 y. had statistically significant higher mean systolic and diastolic blood pressure, body mass, BMI and hip circumference. 2. Among older (46-55 y.) patients and all women significantly more often declared active lifestyle was the health beneficial behaviour.

PARAMETER	FEMALES AGED 35-45 YEARS x ± SD	FEMALES AGED 46-55 YEARS x ± SD	P	MALES AGED 35-45 YEARS x ± SD	MALES AGED 46-55 YEARS x ± SD	P
Body weight [kg]	70,6 ± 13,4	73,7 ± 15,6	p<0,05	87,7 ± 15,6	88,8 ± 15,0	p<0,05
BMI [kg/m2] $BMI = \frac{body\ mass\ [kg]}{body\ height\ [m]^2}$	25,8 ± 4,7	27,8 ± 4,5	<0,001	27,7 ± 4,5	28,7 ± 4,5	p<0,05
WC [cm]	82,7 ± 11,6	88,8 ± 9,2	<0,001	95,0 ± 9,2	98,5 ± 11,5	<0,001
SBP [mmHg]	128,0 ± 15,7	135,4 ± 18,8	p<0,05	134,6± 15,1	143,9 ± 21,1	p<0,05
DBP [mmHg]	80,4 ± 10,0	83,8 ± 10,6	p<0,05	82,8 ± 10,7	89,4 ± 12,0	p<0,05
DECLARED PHYSICAL ACTIVITY MINIMUM 5 TIMES A WEEK ≥30 MIN	51 persons (28%)	60 persons (30%)	p>0,05	18 persons (15,9%)	51 persons (27,4%)	p<0,05

PP.01.12 EPIDEMIOLOGY OF STROKE IN UKRAINE

I. Revenko. *NSC Institution of Cardiology, Department of Essential Hypertension, Kiev, UKRAINE*

Introduction: Currently, stroke is one of the main medicosocial problems in Ukraine as it ranks second among causes of mortality and first among causes of disability.

Sources and methods: The analysis of indices dynamics of morbidity and mortality from stroke in the country was carried out based on the sources of official statistics published by the Centre of Medical Statistics of the Ministry of Public Health of Ukraine on morbidity and mortality for 2002 -2011 and by the method of continuous epidemiological study.

Results: Morbidity from stroke rose by 19.2% over the decade of 2002 – 2011 and totalled 294.6 per 100000 people in 2011. This increase was brought about by population aging, advance in identification and diagnosis of the nosology and by the growth of the risk factors. Hypertension is a leading risk factor for stroke in Ukraine as well as worldwide. In 2011, 12292642 patients were registered with the diagnosis of hypertension, its prevalence totalled 32 697.6 per 100000 people and its morbidity amounted to 2485. Stroke morbidity among hypertensive patients totalled 163.3 per 100000 people, i.e. 55.4% in the stroke morbidity structure.
Stroke mortality increased by 20.1% and totalled 86.9 per 100000 people. In 2011, 51.6% in its structure corresponded to mortality from ischemic stroke (51.6 per 100000 people); 32.0% was represented by mortality from intracerebral bleeding (32.0 per 100000 people); 3.2% corresponded to mortality from subarachnoid hemorrhage (2.9% per 100000 people); and 13.1% corresponded to mortality from the stroke unspecified as ischemic stroke or hemorrhagic one (11.4 per 100000 people). Over the decade mortality form ischemic stroke rose by 13.2%, mortality from intracerebral bleeding, subarachnoid hemorrhage and unspecified stroke decreased by 4.8%, 13.7% and 53.3% correspondingly.

Conclusions: Morbidity and mortality from stroke grew over 2002 – 2011 in Ukraine. The leading risk factor for stroke is arterial hypertension, identification and diagnosis of which is one of the key approaches to stroke prevention.

PP.01.13 DIAGNOSTIC INERTIA FOR DIABETES IN WHOLE POPULATION. ESCARVAL STUDY

V. Pallares Carratala[1], A. Palazon[2], A. Sepehri[2], D. Orozco[2], C. Sanchis[3], F. Valls[4], J. Navarro[5], A. Fernandez[2], J. Redon[6], J. Martin Moreno[6], V. Gil-Guillen[2]. *[1]Union de Mutuas, Castellón, SPAIN, [2]Universidad Miguel Hernandez, Alicante, SPAIN, [3]CS Algemesi, Valencia, SPAIN, [4]CS Beniganim, Valencia, SPAIN, [5]CS Salvador Pau, Valencia, SPAIN, [6]Universidad de Valencia, Valencia, SPAIN*

Objective: Analyze the magnitude of diagnostic inertia in nondiabetic population in Valencian Region, identify associated factors and determine the influence of a course in cardiovascular prevention.

Design and method: Through computerized medical record that covers 100% of the population of Valencian Region (5,120,343), people are selected without prior diagnosis of type 2 diabetes (T2DM) over 45 years (n = 870,405). We studied the possible factors influencing in diagnostic inertia and if the primary care provider (PCP) performed or not the previous training course. The definition of diagnostic inertia by clinical history (fasting glucose> 126 mg / dl and no diagnosis of T2DM) is based on the definition of Philips. We define three types of diagnostic inertia: limit (glucose between 126-139 mg / dl), moderate (body glucose 140-159 mg / dl) and strong (glucose> 160mg/dl). Logistic regression was performed.

Results: The 2.4% of the population over 45 years with screening had diagnostic inertia (n = 21 208). Associated factors were: Does the PCP has taken the course? (OR 0.753), male (1.742), age (1.038), atrial fibrillation (0.981), hypertension (1.119), dyslipidemia (0.744), previous cardiovascular events (0.940), and number of visits (0.982). Of the total, 65.1% are in extreme situation, 21.4% moderate and 13.5% strong.

Conclusions: Diagnostic Inertia demonstrates a new problem that is easily solved through alarm systems in the computerized record of the patient's history.

PP.01.14 POPULATION SCREENING ANALYSIS OF DIABETES IN THE VALENCIAN REGION. ESCARVAL STUDY

V. Pallares Carratala[1], A. Palazon[2], A. Sepehri[2], D. Orozco[2], F. Valls[3], C. Sanchis[4], J. Navarro[5], A. Fernandez[2], J. Redon[6], J. Martin Moreno[6], V. Gil-Guillen[2]. *[1]Union de Mutuas, Castellón, SPAIN, [2]Universidad Miguel Hernandez, Alicante, SPAIN, [3]Centro de Salud Beniganim, Valencia, SPAIN, [4]Centro de Salud Algemesi, Valencia, SPAIN, [5]Centro de Salud Salvador Pau, Valencia, SPAIN, [6]Universidad de Valencia, Valencia, SPAIN*

Objective: Analyze the screening of type 2 diabetes (T2DM) in Valencian Region, and determine how it affects the performance of a training course on cardiovascular prevention.

Design and method: Of a total of 5,120,343 are selected those without a previous diagnosis of T2DM and more than 45 years (n = 2,730,450). Associated factors that influence the detection of T2DM are analyzed according to whether the prima-

ry care provider (PCP) performed the course or not. The screening was performed with a determination of fasting glucose. Logistic regression was performed.

Results: Screening was performed in 31.9% of the population older than 45 years (n = 870,405). Associated factors include: training course by the PCP (OR 2.13), being male (OR 0.75), age (OR 0.75), atrial fibrillation (OR 1.25), hypertension (1.91), dyslipidemia (4.39), cardiovascular event (1.08), and the number of visits (2.13).

Conclusions: The screening rate was 31.9% of the population. Associated factors for this were that the PCP had done the training course, being a woman, patients with cardiovascular risk factors (atrial fibrillation, hypertension, dyslipidemia, cardiovascular event) and people with more visits.

PP.01.15 CARDIOVASCULAR RISK FACTORS MANAGEMENT IN TYPE 2 DIABETES MELLITUS PATIENTS IN PRIMARY CARE IN SPAIN

V. Giner[1], E.M. Gil[2], J. Martinez[2], A. Palacios Del Cerro[3], D.F. Stancu[2], C. Andres[3], V. Blanes[2], M.C. Nicolau[1], M.J. Esteban[1], M.M. Reig[1]. *[1]Hypertension Unit, General Internal Medicine Department, Verge dels Lliris Hospital, Alcoy, SPAIN, [2]Primary Care Centers, Alcoy Health Department, Alcoy, SPAIN, [3]Primary Care Centers, Elda Health Department, Elda, SPAIN*

Objective: To describe the prevalence of cardiovascular risk factors (CVRF) and its management in patients with type 2 diabetes mellitus (T2DM) in Spanish Primary Care usual clinical practice.

Design and method: Multicentric, observational, cross-sectional study including 211 T2DM patients (54.5% men aged 68.46±9.77 yrs. with 10.1±7.6 yrs. of evolution) from 9 Primary Care Centres in the province of Alicante, Spain.

Results and conclusions: CVRF prevalence was (%): hypertension 71.1, dyslipidemia 67.3, global obesity (Ob) 48.3, abdominal Ob 47.9, metabolic syndrome 73.9, and smoking 18.0. 27.5% of the patients were on secondary prevention. Prevalence of patients on high CV risk was 53.1% and 49.3% according to 2002 ATP III Framingham and 2007 ESH criteria, respectively.
LDL <100 mg/dL was present in 53.6% of the patients, with 14.2% < 70 mg/dL. HbA1c <7.5% was achieved in 65.4% of the cases, with 50.7% <7%. BP< 140/90 mmHg was present in 59.2%, and <135/85 mmHg in 43.1%. Only 17.1% patients had three risk factors controlled, and compared with the rest of patients there were not significant differences in terms of age, gender, time of T2DM evolution, used drugs (number of daily drugs and daily antidiabetics, antihypertensives, antiagregants/anticoagulants, or statins), prevalence of secondary prevention, prevalence of high CV risk, and prevalence of Ob and abdominal Ob. ATP III Metabolic syndrome prevalence was higher amongst patients with uncontrolled risk factors (p=0.031).
T2DM patients had high cardiovascular risk in primary care in Spain. Although control of individual CVRF is high, it is not the case for the global control.

PP.01.16 MANAGENEMT OF HYPERGLYCEMIA IN TYPE 2 DIABETES MELLITUS IN THE USUAL CLINICAL PRACTICE IN SPANISH PRIMARY CARE CENTERS

V. Giner[1], E.M. Gil[2], C. Olivares[3], E. Pappalardo[2], J.V. Vaquer[3], C. Sanchez[2], F. Pellin[3], V. Alemany[2], M.J. Esteban[1], M.M. Reig[1]. *[1]Hypertension Unit, General Internal Medicine Department, Verge dels Lliris Hospital, Alcoy, SPAIN, [2]Primary Care Centers, Alcoy Health Department, Alcoy, SPAIN, [3]Primary Care Centers, Elda Health Department, Elda, SPAIN*

Objective: To assess how hyperglycemia is managed in patients with type 2 diabetes mellitus (T2DM) in Spanish Primary Care Centers (PCc).

Design and method: Multicentric, observational, cross-sectional, descriptive study of usual PCc clinical practice with T2DM patients recluted in 9 PCc in the province of Alicante (Spain).

Results and conclusions: 211 T2DM patients (54.5% men) aged 68.46±9.77 years; with T2DM diagnosed 10.1±7.6 before, were included. An average of 5.7±2.7 drugs/patient/day were taken, with 89.6% of the patients having oral antidiabetics, 70.6% antihypertensives, 63.0% hypolipidemiants, 26.1% insulins, 19.0% anticoagulants/antiplatelets. In 89.1% of the cases non-pharmacological instructions were specifically present in medical history. A mean of 1.5±0.7 oral antidiabetic drugs/patient/day were taken (77.7% metformin, 37.4% dipeptidyl peptidase IV inhibitors, 13.3% meglitinides, 10.9% sulfonylureas, 1.9% thiazolidinediones), 22.3% on combination. Metformin was used independently of microalbuminuria (p=0.384), and sulfonylureas irrespectively of the presence of obesity (p=0.521). During the year before inclusion 2.3±1.8 laboratory tests/patient were performed, 94.3, 93.9 and 96.2% included HbA1c, lipid profile and renal function. 2.6±2.9 programmed digital blood glucose (pDBG)/patient/month were made at the PCc. Mean HbA1c was 7.2±1.2%. Well-controlled patients (HbA1c < 7.5%) had shorter T2DM duration, took fewer anti-diabetics and insulin as well as other drugs not related to DM.
It is noteworthy the high level of well-controlled T2DM glycemia, high specific indications of non-pharmacological treatments and very high use of pDBG. Use of antidiabetics drugs seem to be independent of patient characteristics, meanwhile bad control can be related with therapeutical inertia as well as long-term evolution.

PP.01.17 MANAGEMENT OF TARGET ORGAN DAMAGE IN TYPE 2 DIABETES MELLITUS IN SPANISH PRIMARY CARE CENTERS

V. Giner[1], A. Genoves[2], A. Cuco[3], M.L. Campoy[2], R. Pastor[2], I. Boix[2], T. Quilis[3], M.J. Esteban[1], M.M. Reig[1], S. Martinez[1]. *[1]Hypertension Unit, General Internal Medicine Department, Verge dels Lliris Hospital, Alcoy, SPAIN, [2]Primary Care Centers, Elda Health Department, Elda, SPAIN, [3]Primary Care Centers, Alcoy Health Department, Alcoy, SPAIN*

Objective: To describe how target organ damage (TOD) in type 2 diabetes mellitus (T2DM) is managed in the Primary Care (PC) setting in Spain.

Design and method: Multicentric, observational, cross-sectional, descriptive study of usual clinical practice with T2DM patients consecutively recluted in 9 PC Centres in the province of Alicante (Spain). Clinical assessment and review of patients' health records were made.

Results and conclusions: 211 T2DM patients with 10.1±7.6 yrs. of evolution were included. At least one ophthalmological and neurological revision had been carried out in 66.4% and 17.1% patients during the previous year, with 91.46% of the patients with at least one microalbuminuria determination (2.2±2.9 (range 1-19)/patient). Ankle-brachial index was present in 7.6% of patients' previous registries. 23.7% patients had nephropathy, retinopathy or neuropathy, with 1, 2 and 3 of them in 18.5%, 6.2% and 1.4% of patients. Comparing with those without any TOD, patients with at least one TOD showed higher number of daily medications (p=0.021). Table shows comparation of TOD prevalences before (Known) and after (Actual) evaluation at the inclusion:

	Retinopathy	Nephropathy	Neuropathy	Per. Vasc.	Erect.Dysf.
Known	16.6	9.5	6.2	5.7	6.6
Actual	-	13.3	-	8.5	22.7

Renal function was evaluated in 60.7% of patients at inclusion; 51.2% had normal renal function, while microalbuminuria and proteinuria was found in 13.3% and 0.9% of the patients. Albumin/creatinine ratio and urine albumin mean values were 29.6±52.5 mg/g and 19.0±47.2 mg/L.
There is a huge variability in the way how Spanish PC physicians look for the presence of TOD in T2DM. There is a valuable under diagnose, especially when macrovascular TOD.

PP.01.18 COMPARATIVE ASSESSMENT THE INFLUENCE OF MULTIMORBIDITY IN HYPERTENSIVE PATIENTS OF DIFFERENT AGE ON MEDICAL INTERVENTION QUALITY

S. Tykhonova, P.S. Vimalanathan.
Odessa National Medical University, Odessa, UKRAINE

Background: Comorbidity may be used as a prognostic indicator for length of hospital stay and outcome. It is required to elaborate individual forms of medical care to the patients with multimorbidity, improve the methods of management of these populations. To determine whether a comorbidity index is needed to predict efficacy and quality of pharmacotherapy, we compared the Charlson comorbidity index (CMI) and feature of prescribed treatment in the patient with hypertension (AH) of different age.

Design and methods: We used data of observation of 175 hypertensive patients (64,6% females) in Internal Medicine Clinic of Center of Reconstructive and Recovery Medicine (University Clinic), Ukraine, which divided into 4 groups: 1 gr. (n=15) – patients aged less 45 years; 2 gr. (n=53) – 46–54, 3 gr. (n=53) – 55–64, and 4 gr. (n=54) – more 65 years. We extracted all the diagnoses for every patient from cards to score the Charlson CMI and Charlson probability (10 year mortality). Data for age, sex, medical treatment and conformity of it to current guidelines of AH management were also collected. We calculated the Pearson correlation coefficients (r) of the Charlson CMI and probability with number of prescribed medication and other confounders.

Results: Multimorbidity was revealed in 100% of patients in every group. With each decade of life and an increase in disease number significantly reduced the proportion of males (60% in 1gr. vs. 29,6% in 4 gr., p=0.019). The Charlson CMI and probability significantly increase since the age 46 years old, and were associated with polypharmacy and non-conformity to current guidelines of AH management. In young (1 gr.) and elderly (4 gr.) patients total number of prescribed medication is associated with increase Charlson probability (1 gr. – r=0.307, p=0.030; 4 gr. – r=0.324, p=0.012).

Conclusion: Comorbidity in patients with AH in therapeutic hospital is high, both in young and elderly, and has negative impact on quality of pharmacotherapy, creates the risk of polypharmacy and uncertainty posthospital forecast.

PP.01.19 ASSESSMENT AND THERAPEUTIC MONITORING OF HYPERTENSIVE PATIENTS IN A MEDICAL CONSULTATION IN UNIVERSITY HOSPITAL IN BLIDA, ALGERIA

A. Bachir Cherif[1], A. Taleb[1], A. Bouamra[2], A. Benetos[3], S. Benkhedda[4], A. Chibane[5], M. Temmar[6], M. Bouafia[1]. *[1]Cardiology Department University Hospital, Blida, ALGERIA, [2]Department Epidemiology University, Blida, ALGERIA, [3]Geriatric Department of University Hospital, Nancy, FRANCE, [4]Cardiology Department University Hospital, Alger, ALGERIA, [5]Internal Department University Hospital, Ain Taya, ALGERIA, [6]Cardiology Center, Ghardaia, ALGERIA*

Objectives: To determine the cardiovascular risk factors associated with hypertension, identify different therapeutic classes, assess compliance blood pressure in hypertensive patients at high cardiovascular risk.

Design and method: The study was conducted at the University Hospital of Blida in cardiology department,on 1023 subjects, aged between 25-85 years, between December 2010 and March 2012. Were considered hypertensive subjects when SBP> 140mmHg and / or DBP> 90 mmHg or anti-hypertensive treatment. Hypertension was considered controlled if the SBP <140mmHg and DBP <90mmHg, and uncontrolled if the SBP> 140mmHg and / or diastolic> 90mmHg. The information is collected during the examination of patients and from the clinical and biological parameters anthropometric, hemodynamic and therapeutic.

Results: The average age of our population was 60 ± 12 years. Risk factors associated with hypertension are: 20% dyslipidemia, 21% diabetes mellitus, 31% tobacco, 56% of the metabolic syndrome, 70% overweight and 82% are sedentary. 48% of our populations are at high cardiovascular risk versus only 15% of low-risk and 2% risk free. 34% among hypertensive patients on calcium antagonists (IC), 25% achieved the target blood pressure (TBP), 34.1% for ACE inhibitors in conversion reached 26% TBP, 40% among beta-blockers in hypertension, 23% have reached the TBP. For ARA2 42%, only 21% reached the TBP. Of the 34% on diuretics, 23% have reached the TBP. Among patients who were started on combination therapy, 56% in ARA2 + diuretic reached the target BP versus 44% by the same association (p <0.001), followed by IC + diuretic in 52% of cases (p <0.001). For patients at high cardiovascular risk, triple therapy is prescribed in 63% of cases, followed by 38% for double therapy and 20% for monotherapy (p <0.0001).

Conclusions: In Algeria, the control of blood pressure in hypertensive patients remains difficult especially in patients at high cardiovascular risk. In most cases the normalization of blood pressure can not be achieved by combining different class of drugs.

PP.01.20 HUNGARIAN HYPERTENSION REGISTRY 2002 - 2011

E. Kékes, R. Dechatel, C. Farsang, I. Kiss.
Hungarian Society of Hypertension, Budapest, HUNGARY

It was initiated in 2002 so that it reduces the mortality and morbidity of cardiovascular diseases. Among our aims were to get detailed information about risk factors of hypertension patients and also having better understandings of co-morbidities and clinical practice. In consecutive years distribution and mean age of individuals were the followings: in 2002 (n=25 211, 64,1 y / women and 62,1 y/men), in 2005 (n=38 849, 61,8 y/women and 60,09 y/men), in 2007 (n=18 113, 62,2/women and 58,71/men), in 2011 (n=28 890, 62,7 y/ women and 59,3 y/men).

In hypertension patients metabolic disorders are highly frequent. The waistline is above the normal limit in 36,1 % at men and in 64,7 % at women. We found elevated serum levels of total cholesterol (61 %), triglyceride (54,7 %), while there was decreased level of serum HDL in 15,9%. Among patients with hypertension the blood sugar concentrations were between 5,6 and 6,1 mmol/l in 16,4 %, while this value above 6,1 mmol/l were in 33 %. Prevalence of metabolic syndrome was 53,7 % in men and 63,7 % in women. The frequency of type 2 diabetes mellitus was 33,5 %.

Prevalence of co-morbidities were the followings 31,92 % ischemic heart disease, 18,01 % stroke, 33,6 % diabetes mellitus, 18,38 % peripheral arterial disease, 7,33 % kidney disease. In 39 % there was only one, following two in 21,9 %, three in 19,2 % and four or more co-morbidities in 5,21 %. In case of diabetes mellitus frequency of the co-morbidities was significantly higher. Proportion of drugs in hypertension treatment significantly changed during observation. Basic of the treatment was RAAS inhibition and in the past years the AT1R blocker usage increased significantly.

Prescription of diuretics is increased and calcium channel antagonists are in the fourth position in prescription frequency. Usage of beta blockers is unchanged, however, proportion of 3rd generation drugs increased from 2007. Achievement of target blood pressure increased above 40 %, but with special care it reached 60 %. In type 2 diabetes mellitus achievement did not reach 20 %.

PP.01.21 HYPERTENSION CONSULTATION: 18 MONTHS OF EXPERIENCE

A. Serafim, C. Carmo, C. Maltez.
Internal Medicine, Barreiro Hospital, Barreiro, PORTUGAL

Cardiovascular diseases are the leading cause of death worldwide and represents an important factor of disability and costs to health systems. Hypertension is referred to by WHO as one of the major risk factor of cardiovascular diseases. However, at a significant percentage of cases it does not appear in isolation, but rather associated with other risk factors such as dyslipidemia, obesity, and diabetes mellitus. The presence of multiple risk factors potentiates its deleterious effect contributing to global cardiovascular risk.

Objective: Retrospective study with review of all patients followed in hypertension and cardiovascular risk consult in a district hospital.

Results: The process of 181 patients was reviewed, with respect to its origin, demographics characteristics (73 female and 108 male; mean age 56.7), cardio-

Abstract PP.01.20

Percent of using of antihypertensive drugs (%)	2002	2005	2007	2009	2011
ACEi	64,7	56,5	59,3	51	42
AT1R blocker	2,6	13	18,4	31	57,1

Target blood pressure (mmHg)	2002	2005	2007	2011
<140/90	30,5%	38,8%	43,9%	40,2%

vascular risk factors (namely diabetes 23.8% and dyslipidemia 71.8%, among other factors); severity of hypertension at baseline, target organ damage and antihypertensive therapy.

Conclusion: We performed a discussion of hypertensive patients referred for consultation, as well as its evolution after 18 months of follow up. Management of patients with hypertension is a challenge that requires a global view of the patient and often a multidisciplinary approach.

PP.01.22 MANAGEMENT OF ARTERIAL HYPERTENSION IN ADULTS: 2013 GUIDELINES OF THE FRENCH SOCIETY OF ARTERIAL HYPERTENSION

J. Blacher, J. Halimi, O. Hanon, J.J. Mourad, A. Pathak, B. Schnebert, X. Girerd. *Societe Francaise d'Hypertension Arterielle, Paris, FRANCE*

Objective, design and method: To improve the management of hypertension, the French Society of Hypertension has decided to update the national guidelines with the following characteristics: usefulness for practice, synthetic form, good readability, comprehensive writing for non-doctors, emphasizing the role of patient education in the management of hypertension, wide dissemination to health professionals and the population of hypertensive subjects, impact assessment among health professionals and the public health goals. These guidelines include the following 15 recommendations, divided in 3 chapters, according to the timing of the medical management.

Results: The key schedules for the management of the hypertensive patient:
Before starting treatment
1. Confirm the diagnosis, with blood pressure measurements outside the doctor's office
2. Implement lifestyle measures.
3. Conduct an initial assessment.
4. Arrange a dedicated information and hypertension announcement consultation.

Initial treatment plan (first six months)
1. Main objective: control of blood pressure in the first six months (SBP: 130-139 and DBP<90 mmHg).
2. Favour the five classes of antihypertensive agents that have demonstrated prevention of cardiovascular complications in hypertensive patients.
3. Individualized choice of the first antihypertensive treatment, taking into account persistence.
4. Promote the use of (fixed) combination therapy in case of failure of monotherapy.
5. Monitor safety.

Long term care plan
1. Uncontrolled hypertension at 6 months despite appropriate triple-drug treatment should require specialist's opinion after assessment of compliance and confirmation of ambulatory hypertension.
2. In case of controlled hypertension, visits every 3 to 6 months.
3. Track poor adherence to antihypertensive therapy.
4. Promote and teach how to practice of home blood pressure measurement.
5. After 80 years, change goal BP (SBP<150 mmHg) without exceeding 3 antihypertensive drugs.
6. After cardiovascular complication, treatment adjustment with maintenance of same blood pressure goal.

Conclusions: We hope that a vast dissemination of these simple guidelines will help to improve hypertension control in the French population from 50% to 70%, an objective expected to be achieved in 2015 in France.

PP.01.23 MULTIPROFESSIONAL APPROACH OF HYPERTENSIVE DIABETIC PATIENTS – IS THIS THE SOLUTION?

J. Thiago, P. Jardim, A. Severino, D. Nunes, D. Faria, T. Motta, F. Magalhães, T. Rolim, I. Motta. *Liga de Hipertensão Arterial, UFG, Goiania, BRAZIL*

Objective: Diabettes mellitus (DM) is a disease that is frequently associated with high blood pressure (HBP), and this combination is related to an elevated incidence of cardiovascular events. The approach of this kind of patient is extremely complex due to the multifactorial aspects of both conditions. A number of studies have shown that a multiprofessional intervention may be the most effective way to deal wih them. Our objective was to analise the results of a multiprofessional approach in the treatment of diabetic hypertensive patients from an antihypertensive specialized treatment centre.

Design and methods: We conducted a retrospective study with data from a representative sample of diabetic hypertensive patients with regular visits to an antihypertensive specialized treatment centre. Data from their first visit (V1) and last visit (V2) were compared (systolic blood pressure – SBP, diastolic blood pressure – DBP, glycemia, Hb1C, lipids profile and body mass index – BMI). Patients with only one visit were excluded. Statiscal analises were conducted with the softwre SPSS® version 17 and values of p<0,05 were considered significant.

Results: A group of 162 patients was included with a mean age of 62 years old (±14,2) and 80,25% of them were females. The mean time of follow up was 78 months and there was a significant improve of most variables compared between the two visits (table 1).

Table1 – Comparison of BP, Glycemia, Hb1C, Lipids profile and BMI between V1 and V2

Variable	V1	V2	p
SBP*(mmHg)	140,1±19,8	133,5±19,2	0,002**
DBP* (mmHg)	87,7±12,9	79,6±11,5	0,000**
Glycemia*(mg/dL)	150,9 ± 67,6	147,7±56,6	0,834
Hb1C*(%)	7,9±1,7	7,3±1,6	0,001**
Total Cholesterol*(mg/dL)	206,9±52,1	175,7±45,7	0,000**
LDL Cholesterol*(mg/dL)	121,0±45,3	100,4±38,0	0,000**
HDL Chleterol*(mg/dL)	42,2±10,4	43,2±10,4	0,185
TRIGLYCERIDES*(mg/dL)	220,6±168,1	176,4±133,4	0,001**
BMI*(kg/m²)	30,8±5,4	30,5±5,8	0,409

***Teste de Wilcoxon. **p<0,05**

Conclusion: Multiprofessional intervention was effective in improving most cardiovascular risk factors in our group of hypertensive diabetic patients.

PP.01.24 TEMPORAL TRENDS IN MANAGEMENT AND CONTROL OF HYPERTENSION AMONG ISRAELI ADULTS PRESENTING WITH ACUTE CORONARY SYNDROME 2002-2010

G. Shlomai[1], E. Kopel[2], I. Goldenberg[2], E. Grossman[1]. *[1]Internal Medicine D and Hypertension Unit, The Chaim Sheba Medical Center, Tel-Hashomer, ISRAEL, [2]Heart Institute and the Neufeld Cardiac Research Institute Leviev Heart Center, the Chaim Sheba Medical Center, Tel-Hashomer, ISRAEL*

Objectives: The aim of the present study was to evaluate trends in blood pressure (BP) control and pharmacological management of hypertension over the past decade and their effect on BP control among patients admitted with acute coronary syndromes (ACS).

Methods: The study population comprised 7658 ACS patients enrolled in the Acute Coronary Syndromes Israeli Survey (ACSIS) between 2002 and 2010. We compared patients' characteristics, admission systolic BP levels and antihypertensive therapy between those hospitalized during the early (years: 2002-2004) and late (years: 2008-2010) periods.

Results: Among 7658 study participants, 4421 (58%) were hypertensive. Hypertensive patients presenting on 2008-2010 tended to exhibit improved BP control (p<0.001). The use of angiotensin converting enzyme inhibitors (ACEi)/ angiotensin receptor blockers (ARB) and beta-blockers has increased over the years among all hypertensive patients (p<0.001 for both), whereas the use of diuretics and calcium antagonists has remained stable (p=0.77 for both). The use of diuretics tended to increase in hypertensive subjects without prior cardiovascular disease (p=0.05,). In addition, the late period was characterized by a significant increase in the usage of combination therapy compared with the early period (50% vs. 57%; p<0.001). Multivariate analysis showed that admission during the late period was independently associated with a significant lower likelihood for increased admission BP (odds ratio=0.82; Confidence interval 0.75-0.90, p<0.001).

Conclusions: BP control has improved among Israeli hypertensive patients presenting with ACS between 2002 and 2010. This trend was mainly associated with increased usage of ACEi /ARB, and combination therapies.

PP.01.25 BLOOD PRESSURE CONTROL AND CARDIOVASCULAR RISK PROFILE IN 9544 HYPERTENSIVE PATIENTS IN BULGARIA: RESULTS OF THE BP-CONTROL-BG STUDY

D. Raev. *University Hospital St. Anna, Clinic of Internal Medicine, Sofia, BULGARIA*

Objective: Limited information is available on office blood pressure (BP) control and cardiovascular (CV) risk profile in treated hypertensive patients in Bulgaria. The aim of this survey was to assess the rate of BP control.

Design and methods: In 2012, a survey on 9544 treated hypertensive patients (male 42%, age 66.8±10.6 years) followed by 200 general practitioners was carried out in Bulgaria using BP-CARE design. CV risk assessment was based according the last ESH guidelines. The rate of BP control was accepted as optimal at BP<140/90 mmHg in the presence of a low-to-moderate CV risk profile, and at BP<130/80 mmHg in the presence of a high/very high CV risk profile.

Results: Average office BP was 138.3±13.6/84.7+8.5 mm Hg, heart rate – 73.1±12 bpm, BMI – 28.7±4.6 kg/m2. 73.4% of patients displayed a high/very high-risk profile. Half of patients (50.1%) had BP<140/90 mmHg, but only 33.7% of them had optimal controlled BP concerning CV risk profile. BP control was worse for systolic than for diastolic BP, unrelated to patients' sex and age, and more unsatisfactory in high/very high-risk hypertensives. Central obesity was found in 75.9% of patients, metabolic syndrome - in 67.8%, and smoking – in 19.8%. ECG was performed in 99% of patients, echocardiography in 56%, carotid ultrasound in 13%, fundoscopy in 58%, and search for microalbuminuria in 20%. 50% of hypertensives had LV hypertrophy, 11% - retinopathy, 31.8% - microalbuminuria, and 36% - pathological intima media thickness. There is a wide use of combination treatment – in 90% of patients.

Conclusions: This is the first large population-based study in Bulgaria on BP control in treated hypertensive patients. It revealed the BP control is unsatisfactory, particularly in patients at high/very high CV risk, and not differ from that seen in other developed countries. It also show that assessment of subclinical organ damage is quite common, except for microalbuminuria, and that combination drug treatment is frequently used.

PP.01.26 PHYSICIAN ATTITUDES TOWARD HEALTHY LIFESTYLE CHANGES IN HYPERTENSION: DIFFERENCES AMONG SPECIALTIES

B. Aliler, H. Yikilkan, Z. Uysal, C. Aypak, S. Gorpelioglu. *Diskapi Yildirim Beyazit Training and Research Hospital Family Medicine Department, Ankara, TURKEY*

Objective: Current guidelines recommend healthy lifestyle changes as an important first step for lowering blood pressure. The aim of our study is to investigate the differences in attitudes toward healthy lifestyle changes in hypertension (HT) among different medical specialties.

Design and method: A random sample of 206 general practitioners (GPs) (n=39), family physicians (FPs)(n=47), general internists (n=40), nephrologists (n=40) and cardiologists (n=40) working in Ankara were included in the study. Data were collected by face-to-face interviews using a structured questionnaire. Physicians were asked to score importance of life style factors by a Likert scale from 1to 5.

Results: Among physicians, 37,8% were smoking, only 38,8% exercising regularly and 58,3% with body mass index >25. Nephrologists and FPs gave higher scores of importance for quitting smoking in HT (4,70 and 4,36 respectively), but cardiologists gave lowest (4,02) . The importance of sodium reduction was highest scored by nephrologists (4,87) and lowest scored by GPs (4,40). Education for stress management and healthy diet were cared especially by nephrologists (4,45 and 4,50 respectively). There were not statistically significant differences between specialties in scores of imporance for exercising and weight loss.

Conclusion: Physicians' lifestyles seem to affect their suggestions. Overweight physicians are found to care to suggest weight loss more than others. Cardiologists are found to care drug therapy more than lifestyle change recommendations. Additionally, GPs should be investigated about not caring enough sodium reduction in management of HT.

PP.01.27 BLOOD PRESSURE CONTROL IN NIGERIAN HYPERTENSIVE PATIENTS: A REVISIT

O. Ogunleye, S. Ogundele. *Lagos State University College of Medicine and Teaching Hospital, Ikeja, Lagos, NIGERIA*

Objective: Hypertension remains the leading non communicable disease in Nigeria and the commonest cardiovascular disease in Africans. Despite its high prevalence, public and professional education regarding its risks and the benefits of treatment, hypertension remains inadequately treated in the majority of patients worldwide. This study examined the proportion of patients achieving blood pressure control in a population of Nigerian hypertensive patients after three months of initiation of treatment.

Design and method: This was a cross sectional study of patients managed at the hypertension clinic of the Lagos State University Teaching Hospital, Nigeria over a year period between January and December 2008. The blood pressure category at presentation using the JNC7 classification was evaluated and the mean blood pressure at presentation was compared with the mean blood pressure at three months of follow up using the student Paired 't' test. The proportion of patients achieving a blood pressure below 140 mmHg systolic and 90 mmHg diastolic at the end of three months of follow up was also obtained.

Results and conclusions: A total of 397 patients were seen over this period with mean age of 57.0(13.7) years. There were 160 males (40.3%) and 237(59.7%) females. The mean blood pressure at presentation were 166.5(73.1) mm Hg systolic and 99.2(17.2) mmHg diastolic. They were mostly in stage 2 hypertension, 279 patients (70.3%). Despite the significant reduction of blood pressure at three months of follow up in the total population ($p < 0.001$), blood pressure was only controlled in 37% of patients studied. The leading identifiable cause of uncontrolled blood pressure was poor drug compliance due to inability to sustain the cost of prescribed medications.
The majority of our patients presented with advanced disease and the level of blood pressure control in the population remained poor during the period studied. The need for more pro-active measures to identify patients with high blood pressure and ensure better control in our population became more obvious.

PP.01.28 OBJECTIVE FOR 2015: 70% OF TREATED AND CONTROLLED HYPERTENSIVE PATIENTS. 7 KEY POINTS TO REACH THIS GOAL IN PRACTICE. THE FRENCH CALL FOR ACTION

J.J. Mourad[1], X. Girerd[1,2]. [1]*French League against Hypertension, Paris, FRANCE,* [2]*French Society of Hypertension, Paris, FRANCE*

For the past 50 years, the implementation of therapeutic advances to the largest number of people has made it possible to have an exemplary reduction in cardiovascular mortality, contributing to extension of life expectancy observed in France. Nevertheless, such gains are fragile, and largely dependent on the quality of blood pressure control. The relative stagnation of blood pressure control in France for the last 5 years is potentially one of its early markers.

The French League against Hypertension and the French Society of Hypertension, with the support of the French Ministry of Health, have decided to combine their efforts to provide a new impetus to management of this disease and to make blood pressure control a priority. An ambitious improvement of the percentage of controlled hypertensive patients from 50% to 70% in 2015 is targeted.

To achieve this goal, a simplified decisional algorithm is proposed:
seven key points dedicated to general practice are emphasized:
1. Confirmation of high BP level outside the office
2. Active screening for poor adherence
3. Switching from monotherapy to fixed dose combination therapy in case of lack of control after initial treatment
4. Proposing prescription of three-drug therapy in patients not controlled by a two-drug therapy
5. Screening for signs in support of a cause of non control of arterial hypertension
6. Organising a healthcare course for hypertensive subjects and access to specialists
7. Evaluating the performance of management

The rationale of these 7 key-points as well as the way this joint call for action had been disseminated will be developed

PP.01.29 POINT-OF-CARE TESTING IN DECENTRALISED SCREENING FOR DYSLIPIDAEMIA

E. Matteucci[1], L. Rossi[2], L. Della Bartola[2], O. Giampietro[1]. [1]*Department of Clinical and Experimental Medicine, Pisa, ITALY,* [2]*Clinical Pathology Laboratory, Azienda Ospedaliero Universitaria Pisana, Pisa, ITALY*

Objective: Hypertension and dyslipidaemia often co-exist and contribute to the global cardiovascular risk. Point-of-care testing (PoCT) for the analysis of lipid panels may improve risk stratification in primary prevention. Quality control is required to ensure that PoCT laboratory testing is high quality and cost effective, in order to contribute to optimal patient care. The aim of this study is to evaluate the accuracy and precision of PoCT devises for lipid screening compared with laboratory lipid test results in healthy subjects and patients with dyslipidaemia.

Design and methods: 2 CardioChek PA Analysers (CCA) (PTS, Indianapolis, USA), which employ light reflectance to measure enzymatic chemical reactions using PTS PANELS Lipid Panel test strips to measure total cholesterol, HDL cholesterol and triglycerides in whole blood, were evaluated on 20 consecutive days by designed quality control kit (ChekMate) and PTS Panel Quality Control materials. Fasting venous samples from 50 subjects were analysed on both

CCA whose results were compared with the routine clinical laboratory assay of plasma lipids (COBAS 6000, Roche Diagnostics, Milano, Italy). Fasting finger-stick samples of 25 subjects were analysed on one CCA device and compared with laboratory venous results.

Results: There was no difference between portable measurements of total cholesterol, HDL cholesterol, and triglycerides vs. clinical laboratory results using paired Student t test. Capillary values of total cholesterol, HDL cholesterol, and triglycerides well correlated with laboratory results on venous blood (r from 0.96 to 1.0, p<0.001). Within-run variation coefficient was 1.8 and 0.8% (total cholesterol 146±3 and 275±2 mg/dl, respectively), 8.3 and 3.8% (HDL cholesterol 29±2 and 78±3 mg/dl), 2.3 and 1.1% (triglycerides 153±3 and 126±1 mg/dl).

Conclusions: Preliminary results suggest that CCA provides sufficiently high-quality results. At its completion, the quality evaluation protocol intends to recruit 200 subjects (venous blood) and 80 subjects (capillary blood) in addition to determining within-run precision (repeatability), within-device precision (reproducibility), within-lot and between-lot variability of portable measurements at multiple plasma lipid levels.

PP.01.30 HYPERTENSIVE URGENCIES: SEASONAL AND MONTHLY VARIATION

V. Gessi[1], A.M. Maresca[1], C. Marchesi[1], F. Dentali[1], C. Mongiardi[1], L. Robustelli Test[1], L. Guasti[1], R. Manfredini[2], A.M. Grandi[1]. *[1]Department of Clinical and Experimental Medicine, University of Insubria, Varese, ITALY, [2]Department of Internal Medicine, University of Ferrara, Ferrara, ITALY*

Objective: Blood pressure (BP) shows a circadian and seasonal variability with highest BP values during daytime and winter. It is also known that there is an increase in cardiovascular mortality in winter. Patients with poor BP control may experience abrupt increase in BP known as 'hypertensive urgency'. The aim of the study is to investigate whether monthly or seasonal variation are present also in hypertensive urgencies (defined as systolic BP > 180 and/or diastolic BP > 120 mmHg, in absence of acute target organ damage).

Design and method: The analysis included all cases of hypertensive urgency admitted to the Emergency Department (ED) of Varese Hospital between December 2010 and 2011. BP was measured at admission to the ED, at least 3 times within one hour. For the purpose of the study the mean of the last two values was used. For data analysis, day of hypertensive urgency onset was categorized both into 12 one-month intervals and 4 three-month intervals. Chronobiological analysis was performed using the Chronolab software.

Results: We enrolled 360 subjects (mean age 67.1 ± 14.3 years, 243 females). The peak number of hypertensive urgency occurred in December (n=45, 12.5%) and the nadir in May (n=15, 4%), the difference being statistically significant (X2=23.5, P=0.015). Similar results were obtained for the subgroups by gender (243 females, X2=25, P<0.01; 117 males, X2=31, P<0.001). Inferential chronobiological analysis identified a significant annual pattern in hypertensive urgency, with a peak in December for total sample (P=0.006). Hypertensive urgency was most frequent in winter (n=106, 29.4%) and least in spring (n=66, 18.3%) the difference being statistically significant (X2=12.3, P=0.007). Similar results, although not statistically significant for males, were obtained for subgroups by gender (males P =0.14 and females P=0.012).

Conclusions: In analogy with major CV events, a peak of winter preference is demonstrated also in the occurrence of hypertensive urgency. Future studies should evaluate if knowledge of this variability may improve the management of hypertensive patients.

PP.01.31 THE VERITABLE PREVALENCE OF ARTERIAL HYPERTENSION IN RUSSIAN POPULATION: EPOCHA STUDY

I. Fomin, E.V. Shcherbinina, Y.V. Badin, D.S. Polyakov.
Nizhny Novgorod Medical State Academia, Nizhny Novgorod, RUSSIA

Purpose: Epidemiological trial (EPOCHA-AH) studied the veritable prevalence of Arterial Hypertension (AH) in Russian population.

Methods: The representative sample included eight subjects of the Russian Federation: the Nizhniy Novgorod, Kirov, Voronezh, Orenburg and Ryazan regions, Stavropol Territory, republic of Tatarstan and Chuvash republic. 19503 respondents from 10 to 100 years old were included in 2002. The patients with the diagnosis of AH have been allocated. Criterions of AH were: blood pressure over 140/90 mm Hg or taking antihypertensive drugs at the time of examination. The respondents were re-examined in representative sample in 2007. Losses respondents amounted to 12.3% of the representative sample.

Results: The veritable prevalence of AH in the European part of Russia amounted to 33.9% of cases in 2002. Five years later this data increased to 39,7% cases. 67% patients with AH have three or more risk factors in 2002. After five years these data increased by 5%. Hypertension is present in almost all patients with coronary artery disease (91%), diabetes mellitus (64%) and chronic heart failure (88%). 30,3% of hypertensive patients not treated. 58,4% patients treated but not control blood pressure. And only 11,3% of patients effectively treated and controlled their blood pressure. Use at least one prolonged drug reduces the effectiveness of treatment to 4,5 percent in population of patients with AH. The effectiveness of the treatment of hypertensive patients does not change even in the presence of cardiovascular complications. We asked about the possible complications of hypertension: stroke, acute myocardial infarct, chronic heart failure and kidney failure. 46,2% patients does not inform about any complication. 22,1% patients know only about one complication and 28,9% - about two complications. About the stroke or myocardial infarct know 42,4% respondents.

Conclusions: The study found very high prevalence arterial hypertension and risk factors in Russian Federation, and very low level of awareness about complications.

PP.01.32 DETERMINANTS OF BLOOD PRESSURE CONTROL AND TOTAL CARDIOVASCULAR RISK REDUCTION IN THE BELGIAN EUFORIA STUDY

P. Van Der Niepen[1], A. Aerts[2], E. Daci[3], S. Vancayzeele[3], I. Abraham[4], A. Fieuw[3]. *[1]Department of Nephrology and Hypertension, University Hospital Brussels, Brussels, BELGIUM, [2]Novartis Pharma, Basel, SWITZERLAND, [3]Novartis Pharma, Vilvoorde, BELGIUM, [4]Center for Health Outcomes and Pharmacoeconomic Research and College of Pharmacy, University of Arizona, Tucson, AZ, USA*

Objective: To identify determinants of blood pressure (BP) control and total cardiovascular (TCVR) reduction in patients treated with aliskiren +/- hydrochlorothiazide for 90 and 180 days (D).

Design and methods: Prospective, observational, open-label, multicenter pharmaco-epidemiologic study of daily clinical practice in Belgium from November 2009 till January 2011. According to study protocol, general practitioners could recruit patients aged 18 years or older for whom they had already decided to start aliskiren +/- hydrochlorothiazide (HCTZ) as per their clinical judgment and according to the label and local reimbursement guidelines. Patients were seen at baseline, 90D and 180D. BP control was defined as systolic BP (SBP) and diastolic BP (DBP)< 140/90 mmHg (ESH 2009). TCVR was calculated according to the ESH/ESC 2007 guidelines.

Results: 1717 patients were enrolled, 1694 were available for evaluation at baseline. Average age was 64.1 years and 52.5% was male. Baseline SBP and DBP were 158.3 +/- 14.7 mmHg and 92.5 +/- 9.3 mmHg. At 90D, SBP reduction was 18 mmHg and DBP 9 mmHg. At 180D, another 4mmHg and 2 mmHg reductions were observed (all p<0.001 vs preceding visit). BP control was 2.9% at baseline, 36.0% at 90D and 54.8% at 180 D (all p< 0.001 vs preceding visit). TCVR reduction was achieved in 44.3% at 90D and 56.3% at 180 D (all p<0.001 vs preceding visit). Determinants of BP control at 90 days were patient adherence and physician-judged accuracy of guidelines (positive effect). At 180D, patient adherence affected BP control positively, whereas the number of concomitant antihypertensive medications had a negative effect. TCVR reduction at 90D and 180 D was negatively affected by patient age and concomitant diabetes. Aliskiren+/- HCTZ was well tolerated.

Conclusion: In this study of clinical practice in Belgium, BP control and TCVR reduction was achieved by a regimen including aliskiren+/- HCTZ. Patient adherence was an important determinant of blood pressure control. Age and DM were the strongest negative determinants of TCVR reduction.

PP.01.33 HYPERTENSION AND INCREASED CARDIOVASCLUAR EVENTS IN ELDERLY PATIENTS WITH CORONARY ARTERY DISEASE: A CROSS-SECTIONAL, MULTICENTER SURVEY IN CHINA

J. Fan[1], X. Li[1], L. Wang[2], P. Yu[3], Z. Jian[4], X. Tuo[5], H. Xu[6]. *[1]General Hospital of Chinese PLA, Beijing, CHINA, [2]Second Affiliated Hospital of Tianjin Medical University, Tianjin, CHINA, [3]Beijing Hospital, Beijing, CHINA, [4]Xiangya Hospital, Changsha, CHINA, [5]Changhai Hospital, Shanghai, CHINA, [6]Xiyuan Hospital, Beijing, CHINA*

Objectives: The overall aging of the Chinese population, increasing survival of CAD, and high prevalence of hypertension in the elderly has created a great challenge for Geriatric Cardiologist. The current situation in China remains un-