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

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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 telangiectasia. 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 9.9±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 occurred. 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 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 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 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 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 significantly reduced.

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

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

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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.

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 (EnligHTN) developed by St. Jude Medical.

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.

<table>
<thead>
<tr>
<th>Month</th>
<th>Change in BP (mmHg)</th>
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<tr>
<td>1</td>
<td>Systolic -28, Diastolic -10</td>
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<tr>
<td>3</td>
<td>Systolic -27, Diastolic -10</td>
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<td>6</td>
<td>Systolic -26, Diastolic -10</td>
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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.
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±0.8 V, 100 Hz, and 0.510 ms. 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 pressure response 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

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

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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±2 yrs; BMI 33±1 kg/m²) and 32 RH-MOX patients (age 61±2 yrs; BMI 33±1kg/m², mean±SEM). MSNA was available from 18 RH-MOX and 13 RH-MOX at baseline, 3 month follow-up.

Results: Baseline BP was 171/94±3/2 mmHg 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 months (19.2±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±3 RH-MOX vs. -5.2±2 bursts/min RH-MOX) and 6 months (-5.3±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 response” (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 ENHANCED BLOOD PRESSURE RESPONSE TO RENAL DENERVATION IN PATIENTS WITH RESISTANT HYPERTENSION

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Objective: Activity of the enzyme angiotensin II converting enzyme (ACE) is essential to maintain blood pressure in the kidney (K). ACE inhibition reduces blood pressure by blocking the effect of angiotensin II on the renal microcirculation. Whether orally active aminopeptidase A inhibitors (APA) reduce blood pressure by blocking the activity of the brain renin-angiotensin system (RAS) is unknown. We therefore examined whether orally active aminopeptidase A inhibitors (APA) reduce blood pressure and whether the effect of APA is enhanced in patients receiving the centrally acting sympathetic agent moxonidine. Our observation of a similar baseline MSNA in both groups may be indicative of either a “central moxonidine response” (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.06 SUSTAINED BLOOD PRESSURE REDUCTION AND SYMPATHETIC INHIBITION ONE YEAR AFTER RENAL DENERVATION IN PATIENTS WITH RESISTANT HYPERTENSION

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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, 12 months following RDN in 21 patients (age 59±11 years, BMI 32±5 kg/m², mean±SD) with RH.

Results: Office BP averaged 171±22/94±16 mm Hg despite the use of an average of 4.6±2 antihypertensive drugs. Baseline MSNA was 50±11 bursts/min (79±17 bursts/100 heartbeats), 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±5.7, 11.1±3.3 and -25.0±5.0, 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 reinervation, 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 INCCLUSION CRITERIA

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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 trials.

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 (193±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 effectiveness 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

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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=25), 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 program 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.
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**

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**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 monitoring was performed before RDN and after 1, 3 and 6 months. In a subgroup of patients, ambulatory central BP pre-denervation 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 pre-denervation 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±0.8, 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=0.0696), 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 antihypertensive 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**

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**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% vs 40.2 %, 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 comorbidities (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 7D**

**KIDNEY AND RENIN-ANGIOTENSIN SYSTEM**

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

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**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 AT2-gonost Compound 21 (C21; 1µM), TNFα (10ng/ml; served as technical control) or vehicle. Some cells were additionally pre-stimulated for 60 min with the AT2R-blocker PD123.219 (30µM) 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**


**Objective:** Increasing evidence supports a role for the angiotensin (Ang) II-Ang II type 1 receptor (AT1R)-TGFβ axis in atherosclerosis development. Countering 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 atherosclerotic homoygous Fibulin-4/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 aneurysms 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-4/R mouse. Postnatal treatment with losartan or aliskiren similarly reduced hemodynamic stress, and increased the lifespan of Fibulin-4/R mice (which normally die at ~120 days) to >160 days. Elastic fiber fragmentation was not rescued in established atherosclerotic mice by either drug, although aliskiren reduced atherosclerosis in adult mice. Postnatal treatment with losartan or aliskiren markedly affected cardiac structure, but dramatically improved cardiac function with increased ejection fraction of 2-fold.

**Conclusion:** In established aortic atherosclerosis neither losartan nor aliskiren prevents aortic media degeneration, although aliskiren did reduce atherosclerotic area. Both drugs independently 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 atherosclerosis 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**

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The AT1R/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**

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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), glomerulosclerosis-index were assessed. Proliferative and pro-inflammatory pathways were assessed via qPCR. A [3H]-thymidine-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 ml/min;p<0.05). BP increase was to a greater 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; P2Y2R-KO vs. WT: 113±6 vs. 150±6 µg/g;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 the pro-inflammatory 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**

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**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 hyperfiltrators 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 hypertensive normofilterers (Group 1) and 47 controls (Group 2), who had normal CrCl at baseline (true normofilterers, Group 1) whereas 47 subjects had a baseline CrCl >150 ml/min/1.73m2 (former hyperfiltrators, Group 2). Participants of Group 2 had higher age-and-sex-adjusted systolic blood pressure (p<.007) than those of Group 1. In addition, 24-h cumulative epinephrine (p<.001), heart rate (p=.05), ambulatory night-time BP fall (p=.008), and left ventricular end-systolic stress (p=.01) were higher in Group 2. During the follow-up, subjets 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% of Group 2 (p<.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<.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**

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**Backgrounds:** We previously cloned a molecular interaction 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 aortic 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 HYPERFILTRATION AND VASCULAR FUNCTION IN WILD TYPE BUT NOT IN ENOS-KO MICE**

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In the regulation of vascular tone, the vasoconstrictor response of Ang 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. Systolic blood pressure did not differ between 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 infarcted 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.
Direct Angiotensin Type 2 Receptor Stimulation Inhibits T-Lymphocyte Recruitment to the Central Nervous System and Modulates T-Cell Differentiation


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The angiotensin type 2 receptor (AT2R) acts anti-inflammatory in models of neuronal injury. Here we identified 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 (EAE), a 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.

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.
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

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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 diamicN IR 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 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 RRs 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 TRAIL

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Objective: To evaluate the effects of amloidpine-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 amloidpine + diuretics (group A) or low-dose amloidpine + 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 +/- 7.1)/(78.1 +/- 6.4) 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 GENOTYPE INFLUENCE WHEN SELECTING THE BEST COMBINATION OF ANTIHYPERTENSIVE DRUGS?

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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, serum 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 BSRAs+CA.
7E.04 LACK OF DIFFERENCE BETWEEN NEBIVOLOL/HYDROCHLOROTHIAZIDE AND METOPROLOL/HYDROCHLOROTHIAZIDE ON CENTRAL WAVE AUGMENTATION AND BLOOD PRESSURE


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-vasodilating 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/HCTZ on wave augmentation and cBP.

Methods: We used a randomized double blind crossover design to compare nebulol/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 wash-out 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. Nebivolol/HCTZ or 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. AIx@hr75 was 23.7±5.8, cBP was 145±18/93±10 mmHg. At baseline AIx was 30.3±6.8 %, AIx@hr75 was 20.9±8.3 % for nebivolol/HCTZ and 21.9±8.5 % for metoprolol/HCTZ. 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

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

Methods: The non-interventional 3A Registry included outpatient in whom the physician 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 patients with diabetes and/or heart failure at baseline were prospectively followed for three years.

Results: Overall 312 patients (68 % with aliskiren, 18 % with ACE-I/ARB, 14 % without RAS-blockade) recruited by 899 physicians 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


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+amilodipine 5 mg, were randomised either to SNB (i.e.,prolinolactone 25 mg, then +euroxide 20-40 mg, then +amilodipine 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 (Ir) concentration (HPLC); (ii) urinary AcSDKP/creatinine ratio (UR) to evaluate ramipril inactivation (HPLC); (iii) delay of last medication intake before visit (LMI); and (iv) pill count (PC, %). One point of MA score was attributed to trough Irb >20ng/ml, UR >10nmol/mmol, LMI <24h and PC >80%. MA was defined as low (MA, score <2), intermediate (MA, 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 N.S.). MA 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] vs [-9,-2] mmHg, p<0.001/p=0.0025), favoring SNB, whereas in LMA pts the difference between the two groups did not reach significance (-6 [-19,7] vs [-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 allowed 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

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Objective: The DISTINCT I (reDefining Intervention with Studies Testing Innovative Nifedipine GITS – Candesartan Therapy I) trial 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, multinational 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, and NC in combination both contributed significantly to SBP/DBP reductions (P<0.001 [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 in 8 days (12.5 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.

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%. Non-dose dependent hypotensive events were very rare.

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

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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 prospectively designed, 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 27.2±1.470 mmHg in the N30+V80 group and by 27.0±1.648 mmHg with N60 group compared to 14.3±1.661 mmHg 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, -4.5±8.17% with N60, and -2.4±8.56% with V160. The decrease in the N60 group was statistically significant compared to V160 alone (P=0.046). Pulse pressure (PP) amplification was significantly increased from 1.2±1.0 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

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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 titration-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 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. Non-significant 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.
SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF QGC001, A CENTRALLY ACTIVE AMINOPEPTIDASE INHIBITOR, IN HEALTHY VOLUNTEERS

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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. 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.
ORAL SESSION

ORAL SESSION 8A

CARDIOVASCULAR RISK FACTORS

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

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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. Fast- ing 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, anti-hypertensive 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 [122.6] and 116.4 mm Hg and diastolic BP 78.6 and 74.1 mm Hg, respectively. Smoking modified the relation of caffeine levels (ng/ml) with systolic blood pressure (p=0.05) but not with diastolic (p=0.09). Smoking modified the relation of caffeine levels with blood pressure in a population-based family study, taking smoking status into account.

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

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Objective: We showed that a nocturnal non-dipping 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 Pres- sure (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). 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

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Objective: The aim of the present study was to compare the predictive role of arterial stiffness and augmented left ventricular mass index (LVMl) 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 echo-cardiographic study for estimation of LVMl, 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), LVMl (123.7±22.9 vs 107±24.2 g/m², 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 LVMl (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 LVMl predicts future development of CAD, whereas high baseline PWV exhibits no independent prognostic
value. These findings suggest 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


**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-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


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

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**Purpose:** Potassium has important functions in the body including specific cellular functions and interactions in the Renin-Angiotensin-Aldosterone System. Less is known about the prognostic impact of mild hypokalemia in an apparently healthy population. We hypothesized that incidental mild hypokalemia 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 mEq/L (mean: 3.4 mEq/L; range 3.7-5.4) versus a normokalemic group (mean: 4.0 mEq/L; 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 mHg (26.1) vs. 154.6 mHg (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 adjust and 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 week 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

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**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 hypothermia 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
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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 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**

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**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=0.13 (p<0.05) and left ventricular mass index (LVMI) (r=0.547, p<0.001). At multivariate analysis LA volume was independently correlated to LVMI (beta=0.358, p<0.001), BMI (beta=0.36, p<0.001), male gender (beta=0.275, 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=0.12, 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.

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

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**Objective:** Ventricular-arterial interaction (V Al) 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 V Al 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 AIs 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 V Al otherwise undetected by Ea/Ees.

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

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**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.

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**Abstract 8B.02**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Condition: mean (SD)</th>
<th>Baseline 1</th>
<th>GTN</th>
<th>Baseline 2</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>49 (6)</td>
<td>49 (5)</td>
<td>48 (5)</td>
<td>47 (4)</td>
<td></td>
</tr>
<tr>
<td>MAP</td>
<td>81 (5)</td>
<td>82 (6)</td>
<td>82 (6)</td>
<td>83 (7)</td>
<td></td>
</tr>
<tr>
<td>ESP</td>
<td>94 (12)</td>
<td>88 (12)**</td>
<td>93 (13)</td>
<td>95 (13)*</td>
<td></td>
</tr>
<tr>
<td>Ees(mmHg/ml)</td>
<td>1.15 (0.31)</td>
<td>1.10 (0.25)</td>
<td>1.17 (0.27)</td>
<td>1.22 (0.27)</td>
<td></td>
</tr>
<tr>
<td>Es(mmHg/ml)</td>
<td>1.98 (0.42)</td>
<td>1.95 (0.42)</td>
<td>1.91 (0.58)</td>
<td>1.86 (0.41)</td>
<td></td>
</tr>
<tr>
<td>TTPreflected wave (ms)</td>
<td>242.09 (27.79)</td>
<td>227.73 (19.84)*</td>
<td>244.00 (27.71)</td>
<td>246.55 (24.85)</td>
<td></td>
</tr>
<tr>
<td>TTP longitudinal strain (ms)</td>
<td>381.25 (36.45)</td>
<td>400.67 (39.50)*</td>
<td>418.99 (46.90)</td>
<td>424.70 (56.11)</td>
<td></td>
</tr>
<tr>
<td>TTP apical systolic circumferential strain rate (ms)</td>
<td>1.78.10 (26.25)</td>
<td>201.78 (28.22)*</td>
<td>188.84 (23.62)</td>
<td>191.55 (25.12)</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.001
Methods: Intervventional study. Inclusion: 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), HR (heart rate), SVSVRI (Stroke Systemic Vascular Resistance Index) and TFC (Thoracic Fluids Conductivity). Patients were divided in: control group (office BP >140/90 and 24h ABP <130/80) and case group (office BP >140/90, and 24h ABP >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). Posttreatment BP decreased to 130.6 ± 18.4 (pre vs posttreatment p<0.001). Similar results were found for daytime and nighttime BP. 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 posttreatment (table 1). We found differences in hemodynamics patterns for SSVR (control group vs posttreatment 229.8 ± 78.5 vs 175.6 ± 55 p<0.04, and pre and posttreatment 210.4 ± 80.3 vs 175.6 ± 55 p=0.04). The treatment suggested by the specialists vs HOTMAN study was similar in 6 of 21 cases (28.5%).

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

PREVALENCE OF ECHOCARDIOGRAPHIC LEFT ATRIAL ENLARGEMENT IN HYPERTENSION: A SYSTEMATIC REVIEW OF RECENT CLINICAL STUDIES

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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”, “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 2-5) 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).

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.

RIGHT VENTRICULAR MORPHO-FUNCTIONAL REMODELING IN NEVER TREATED MILD HYPTERTENSIVES: ROLE OF AORTIC PRESSURE AND BIVENTRICULAR PARAMETERS

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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 echocardiology according with LV-RV ASE/AEAE 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 PWW were higher in hypertensives (124±11mmHg vs 116±16, P=0.013; 7.1±2 vs 6.2±1m/s P=0.04).

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±3c/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.
HAEMODYNAMICS ARE ASSOCIATED WITH VARIANTS OF THE OBESITY ASSOCIATED (FTO) GENE IN AN OMANI ARAB PEDIGREE

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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 (CNSys, 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 0.003) 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 significance levels. Of the ABPM parameters only sleep BP dip was significantly associated with the FTO gene variants. 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 may help in the understanding of the genetic link between blood pressure, obesity and T2D.

PREVALENCE AND CLINICAL PROFILE OF PATIENTS WITH TAKO-TSUBO CARDIOMYOPATHY AND HISTORY OF SYSTEMIC HYPERTENSION

R. Citro1, P. Predotti1, A. Silverio2, M. Di Maio2, R. Giudice2, C. Prota1, L. Soriente1, R. Ascoli1, B. Palumbo1, R. Pietrofeso1, F. Silvestri1, F. Piscione1. 1Heart Department, A.O.U. San Giovanni e Ruggi, Salerno, ITALY. 2Medical-Surgical Department, 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.
BC.01 ANGIOTENSIN-(1-7) MODULATES RENAL VASCULAR RESISTANCE THROUGH INHIBITION OF MITOGEN-ACTIVATED PROTEIN KINASE P38 IN APOLIPROTEIN E DEFICIENT MICE

S. Pothoff1, M. Fähling2, T. Clasen1, Y. Mori1, S. Sivritas1, A. Patzak2, J. Bohlender, B. Gudo. 

The objective of our study was to investigate the role of Ang-(1-7) in mediating renal vascular resistance. We used a transgenic rat model with selective soluble adenylate kinase (sAK) deficiency to induce early kidney fibrosis and hypertension. By comparing sAK deficient (sAK−/−) and wild-type (WT) mice, we observed that sAK−/− mice develop a more severe renal phenotype with increased fibrosis and inflammation. These findings highlight the potential protective role of sAK in the regulation of kidney fibrosis and hypertension.

Results: In sAK−/− mice, we observed a significant increase in renal fibrosis as compared to WT controls. Histological analysis revealed more extensive interstitial fibrosis and glomerulosclerosis in sAK−/− kidneys. Furthermore, gene expression analysis using microarrays showed upregulation of genes associated with inflammatory and fibrotic responses. These results suggest a role for sAK in the modulation of renal fibrosis and inflammation.

Conclusion: Our findings suggest that sAK plays a critical role in the regulation of renal fibrosis and inflammation. Further studies are needed to elucidate the molecular mechanisms underlying this effect.

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

J. Bohlander, B. Guido. 

University of Bern, Institute 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 Ang-N and sAK concentrations, comparing L-nitroarginine methyl ester (L-NNAME) 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 (p<0.05 all) and plasma aldosterone 1.5-times (p<0.05) higher, and uK 0.6-times (p<0.05) and REN-mRNA expression 0.35-times lower in TGR vs. CTR without differences for the other genes (p=NS). L-NNAME increased BP by 36% vs. 25% (p<0.05), HW/BW 16% vs. 15% (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 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-NNAME-induced hypertensive response and cause early increased cardiac and renal end-organ damage compared to normal plasma Ang-N levels.
**Improvement of Vascular Remodeling and Endothelial Function in Transglutaminase 2 Knock-Out Mice Infused with Angiotensin II**

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**Objective:** Transglutaminase 2 (TG2) induces cross-linking of proteins. This is positively related to 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 relaxations were assessed by dose-response tests to acetylcholine (1 nM to 100 μM) and L-NAME (10 μM) and sodium nitroprusside (10 nM to 1 mM) respectively, in mesenteric arteries precontracted 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 acetycholine-induced relaxation in all the groups except for Ang II-treated WT, suggesting an impairment of NO production only in this group. Endothelium independent relaxations was similar in all the groups. TG2-K/O presented reduced M/L as compared to WT (4.8±0.3% vs. 6±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 remodeling 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.

**Pressure, Echocardiographic, Histological and Molecular Effects of Stent Implantation in the Aortic Isthmus in a Growing Animal Model**

T. Fiaschi, F. Magherini, T. Gamberti, 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.

**Design and methods:** Cultured rat ventricular fibroblasts (3rd passage, >99% purity) were cultured to serum free for 24 h, were stimulated with Ang II (100 nM) after 24 h incubation with normal glucose (NG, 5 mM), or high glucose (HG, 25 mM) buffer. JAK2 and STAT3 phosphorylation and SOX2 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-Tyr phospho-STAT3 phosphorylation in cardiac fibroblasts.

**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.

**Effective of High Glucose on Ang II Induced JAK2/STAT3 Tyr-phosphorylation in Cardiac Fibroblasts**


**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.

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**Results:** Ang II enhances JAK2 and phospho-Tyr-Tyr phospho-STAT3 phosphorylation in cardiac fibroblasts.

**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.
Conclusions: Present findings indicates that HG concentration enhances intracellular ANG II synthesis in cardiac 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 BC.07

![Graph showing HG (25 mM) and LG (5 mM) with P-Tyr and JAK2/STAT3 phosphorylation](image)

BC.08 A SUSTAINED RELEASE OF S-NITROSOGlutathIONE HAS A LONGER IMPACT ON PULSE THAN ON MEAN ARTERIAL PRESSURE

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Objective: Among NO-donors, S-nitrosoglutathione (GSNO) shows pleiotropic effects in the cardiovascular field especially vasodilatation 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 ed (30 mg/kg) ISI under transient isoflurane anesthesia to reduce stress. MAP and PAP after single administration in rats.

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).

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.

Abstract BC.09

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

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Introduction: Exendin-4 (ex4) 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 ex4 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 ex4 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, ex4 treatment significantly decreased diastolic contracture and increased left ventricle developed pressure. Liraglutide, but not ex4, 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 ex4 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 ex4 with increasing ischemia time and infarct size. This loss of response to PostC occurs earlier in hypertrophy hearts.
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. Wohlfahrt¹, A. Krajčoviečová², J. Seidlerova², O. Mayer², J. Filipovsky³, S. Laurent¹, R. Cifková¹, J. Cosin-Sales², J. Ruvira², J. Diago³, J. Aguilar⁴, B. Igual¹, M. Wohlfahrt¹, J. Filipovsky³, S. Laurent¹, P. Laeis², H. Rauer², P. Boutouyrie¹, Vm Study Collaboration.

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, arterial 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 -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 mHg) 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.02 EFFECT OF SYSTEMIC HYPERTENSION ON AORTIC DIMENSIONS. CARDIOVASCULAR MAGNETIC RESONANCE STUDY

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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±0.8cm²/m² vs N: 18.1±0.8cm²/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. Laurent¹, P. Laeis², H. Rauer², P. Boutouyrie¹, Vm Study Collaboration.

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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, arterial 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 mHg) 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 Lascio¹, E. Bianchini¹, V. Gemignani¹, R.M. Bruno¹, L. Ghiodoni², F. Faita¹, ¹Institute of Clinical Physiology, National Council of Research, Pisa, ITALY; ²Department 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 acceleration cPWV values (cPWVacc) were compared with ultrasound carotid stiffness (CS) measurements, relative distension (reID) 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. reID values were obtained by a contour tracking technique applied to ultrasound B-mode image sequences, while CS and DC ones were derived from reID 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 (R²=0.60), reID (exponential fit, R²=0.47) and DC ones (exponential fit, R²=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.06 EFFECT OF BARORECEPTOR FIELD STIMULATION ON SERUM ALDOSTERONE LEVELS ARE INDEPENDENTLY LOCAL AND REGIONAL AORTIC STIFFNESS: DIFFERENT MEASUREMENTS, RELATIVE DISTENSION (REID) AND DISTENSIBILITY VALUES (DC): RESULTS ARE PRESENTED.**

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**Abstract 8D.06**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ΔPWV (%)</th>
<th>ΔPamp (%)</th>
<th>ΔFF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>continuous field stimulation</td>
<td>-10.0±2.9</td>
<td>-58±44</td>
<td>-3.2±0.3</td>
</tr>
<tr>
<td>pulse field stimulation</td>
<td>-6.6±1.8</td>
<td>-79±58</td>
<td>-5.5±1.7</td>
</tr>
<tr>
<td>SNP infusion</td>
<td>-13.4±4.7</td>
<td>-183±159</td>
<td>-4.2±7.0</td>
</tr>
</tbody>
</table>

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

T. Quinaglia Silva1, M. Bensalah1,2, A. Rederrelli1,2, L. Macor1,2, E. Bollache2, N. Kachenoura2, P. Boutouyrie2,3, S. Laurent3,4, E. Mousseux2,3,1

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**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
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 (aapPWV) 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 (R²=0.08, p<0.001), BMI (R²=0.10, p<0.001), sex (R²=0.14, p<0.001) and brachial diastolic blood pressure (R²=0.05, p=0.005). In a stepwise multivariate regression analysis cfPWV and daPWV were strongly and independently correlated to M/V (partial R²=0.0715, p=0.0013; and partial R²=0.0745, p=0.0010, respectively) even after adjustment for age, sex, BMI and brachial DBP. When challenged together, both cfPWV and aapPWV were independently associated with M/V, with 5% of explained variance each. Although to a lower extent, daPWV (Partial R²=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**

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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±10%) 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

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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.

<table>
<thead>
<tr>
<th>Different definitions of MH</th>
<th>MH</th>
</tr>
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<tbody>
<tr>
<td>BP measurements</td>
<td></td>
</tr>
<tr>
<td>Clinic BP</td>
<td>Day ABP</td>
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<tr>
<td>Day MH (clinical definition)</td>
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<tr>
<td>Day MH only</td>
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<td>Day and night MH</td>
<td>low</td>
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<tr>
<td>Night MH only</td>
<td>low</td>
</tr>
<tr>
<td>Night-MH only (clinically relevant)</td>
<td>low</td>
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</tbody>
</table>

9A.02 PREVALENCIA 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-Bastos2, L. Barbosa, J. Silva1, S. Ribeiro1. 1Faculdade Medicina Porto e Unidade Hipertensao H. Pedro Hispano, Porto, PORTUGAL, 2Universidade 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 ABP i.e. 24-h BP < 130/80, daytime BP < 135/85, and nighttime BP < 120/70 mmHg), 24h BP 116/71±6 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 117/70±7/5 mmHg, 56±17 years, BMI 27±8 Kg/m2, 60% female, 39.8% of ND and 43/8 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 PREVALENCIA DE POSTPRANDIAL HYPOTENSION IN ELDERLY HYPERTENSION PATIENTS DETECTED BY HOME BLOOD PRESSURE MONITORING


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 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.

Conclusion: PPH is highly prevalent among elderly hypertensive subjects. HBPM could be a valuable tool to evaluate its presence.
OUT OF OFFICE BLOOD PRESSURE AND TARGET ORGAN DAMAGE IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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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 (HBPI) 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-I) 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-I, 28% refux 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 0.44), as well as between diastolic ABP and urinary albumin excretion (UAE) (6 studies, n=355, age 13.1 years, 42% diabetes type-I, 28% refux 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 0.44), as well as between diastolic ABP and urinary albumin excretion (UAE) (6 studies, n=355, age 13.1 years, 42% diabetes type-I, 28% refux 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 0.44), as well as between diastolic ABP and urinary albumin excretion (UAE) (6 studies, n=355, age 13.1 years, 42% diabetes type-I, 28% refux 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 0.44), as well as between diastolic ABP and urinary albumin excretion (UAE) (6 studies, n=355, age 13.1 years, 42% diabetes type-I, 28% refux nephropathy) with pooled r 0.32 (95% CI 0.05, 0.58).

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. Scent 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 HBPI monitoring.

CLINICAL IMPLICATION OBTAINED FROM WITHIN-VISIT BLOOD PRESSURE VARIABILITY IS TO CAPTURE “TRUE” BLOOD PRESSURE

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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.

ACUTE EFFECTS OF THE EXPOSURE TO DIFFERENT TYPES OF MUSIC ON BLOOD PRESSURE MEASUREMENT

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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.

<table>
<thead>
<tr>
<th></th>
<th>Silence</th>
<th>Mozart</th>
<th>Queen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP ± SD</td>
<td>144.6 ± 10.3</td>
<td>137.8 ± 8.1</td>
<td>148.3 ± 10.8</td>
</tr>
<tr>
<td>Diastolic BP ± SD</td>
<td>83.9 ± 9.8</td>
<td>80.1 ± 10.7</td>
<td>85.8 ± 11.9</td>
</tr>
<tr>
<td>Heart Rate ± SD</td>
<td>73.2 ± 10.9</td>
<td>71.4 ± 7.9</td>
<td>80.6 ± 12.1</td>
</tr>
<tr>
<td>Respiratory Rate ± SD</td>
<td>15.8 ± 2.9</td>
<td>14.7 ± 1.9</td>
<td>18.2 ± 3.2</td>
</tr>
</tbody>
</table>

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 antihypertensives/low 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**

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**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 to 14 cm 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 129 mmHg and diastolic 84 mmHg. 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 ones had been used.

**Results:** AC average increased from 23.8 cm in 1983 to 27.5 cm 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 (ps 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 29 cm. 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**

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**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 (BPe), evening - 21.00-23.00 (BPm), morning - 6.00-9.00 (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), SBPs (F=5.04, p<0.01), SBPw (F=9.98, p<0.002), SBPf (F=11.29, p<0.001 respectively), SBP values were higher (F=5.73, p<0.02), DBPd (F=5.17, p<0.02); 2) IV scale scores (the negative emotional level) for SBPp (inverse relationship, F=4.33 p<0.05); 3) age for SBPd (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 SBPp 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?**

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**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 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**

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**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 (BMI > 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 (LVM). 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 onsets 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**

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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**

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1UMDNJ-Robert Wood Johnson Medical School, Cardiovascular Institute, New Brunswick, NJ, USA, 2Rutgers University, Biostatistics, Piscataway, NJ, USA, 3Harvard Medical School, MGH, Cardiology, Boston, MA, USA, 4Centers for Disease Control and Prevention, Atlanta, GA, USA, 5Tune University School of Public Health and Tropical Medicine, New Orleans, LA, USA, 6Wake Forest School of Medicine, Biostatistical Sciences, Winston-Salem, NC, USA, 7Johns 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 were 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.
CHANGES IN HYPERTENSION STATUS ASSOCIATED WITH PHENTERMINE AND TOPIRAMATE EXTENDED-RELEASE OVER 108 WEEKS

J. Jordan1, K. Narkiewicz2, W.W. Day3.

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 $\geq 2$ 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 $<120/80\text{ mmHg}$ without antihypertensive medication use), prehypertension (n=113; SBP/DBP 120-139/80-89mmHg without antihypertensive medication use), and hypertension (n=490; SBP/DBP $\geq 140/90\text{ mmHg}$, 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<0.005 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<0.01 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 naso-pharyngitis.

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.

Abstract 9B.04

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

<table>
<thead>
<tr>
<th>LS Mean Change</th>
<th>Subjects With Normotension at Baseline</th>
<th>Subjects With Prehypertension at Baseline</th>
<th>Subjects With Hypertension at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (n=24)</td>
<td>Placebo (n=33)</td>
<td>Placebo (n=170)</td>
</tr>
<tr>
<td></td>
<td>7.5/46 (n=12)</td>
<td>7.5/46 (n=32)</td>
<td>7.5/46 (n=109)</td>
</tr>
<tr>
<td></td>
<td>15/92 (n=36)</td>
<td>15/92 (n=48)</td>
<td>15/92 (n=211)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>-0.7</td>
<td>-3.1</td>
<td>-3.1</td>
</tr>
<tr>
<td></td>
<td>-9.4*</td>
<td>-10.0*</td>
<td>-10.8*</td>
</tr>
<tr>
<td></td>
<td>-9.3*</td>
<td>-12.6*</td>
<td>-11.9*</td>
</tr>
<tr>
<td>Weight, %</td>
<td>-1.2</td>
<td>-2.8</td>
<td>-2.8</td>
</tr>
<tr>
<td></td>
<td>-10.1*</td>
<td>-9.7*</td>
<td>-10.6*</td>
</tr>
<tr>
<td></td>
<td>-9.6*</td>
<td>-12.2*</td>
<td>-11.5*</td>
</tr>
<tr>
<td>Subjects progressing to hypertension, %</td>
<td>12.5</td>
<td>18.2</td>
<td>--</td>
</tr>
<tr>
<td>Subjects achieving normotension, %</td>
<td>--</td>
<td>30.3</td>
<td>3.5</td>
</tr>
<tr>
<td>Percentage of subjects with a net change* in antihypertensive medications use, %</td>
<td>12.5</td>
<td>12.1</td>
<td>0.6</td>
</tr>
</tbody>
</table>

*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

ALISKIREN, BUT NOT LISINOPRIL, REDUCES RENAL VASCULAR RESISTIVITY IN HYPERTENSSIVE PATIENTS WITH METABOLIC SYNDROME AND MICRONALBUMINURIA


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 lirvls of sCr, K+, Uric acid,glucose,lipidic profile and 24 -h. UAER.

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 (mg/dl): 1,09 to 1,07 (ns) and 1,05 to 1,18 (p<0.001); eGFR (ml/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+ (mm/L) 4,16 to 4,23 (ns) and 4,24 to 4,38 (p<0.001).

CONCLUSION: In hypertensive patients with MS and microalbuminuria long-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.

9B.05
**9B.06** VISCERAL OBESITY IS A “NEW” MARKER OF ENDOTHELIAL DYSFUNCTION AMONG SUBJECTS AFFECTED BY CHRONIC KIDNEY DISEASE

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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) ultrasonographic evaluation of flow mediated dilation of the brachial artery (FMD). Renal function was assessed by measured creatinine clearance (mCrCl), CKD-EPI (eGFR) and Cockroft-Gault (eCrCl) formulae. Albuminuria was 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 distributed 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 which main CV risk factors and indices of renal function were the independent variable, waist circumference was maintained as the only modifiable 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

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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 ORs 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: 1.1-1.6) and 1.2 for hyperlipidemia (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 PRORENIN RECEPTOR BLOCKER HANDLE REGION PEPTIDE IN ALISKIREN-TREATED DIABETIC TRANSGENIC (MREN2) 27 RATS**

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**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-antigens in 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 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**

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**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 diabetest, MetS and insulin resistance, respectively. Moderate heterogeneity was found between 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**

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**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.

<table>
<thead>
<tr>
<th>Age</th>
<th>ZDF</th>
<th>ZDF+C21</th>
<th>ZDF+Losartan</th>
<th>ZDF+C21+Losartan</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 week</td>
<td>0.066±0.008</td>
<td>0.093±0.004</td>
<td>0.082±0.010</td>
<td>0.065±0.007</td>
</tr>
<tr>
<td>11 week</td>
<td>0.308±0.013</td>
<td>0.236±0.015*</td>
<td>0.102±0.021*</td>
<td>0.077±0.021*</td>
</tr>
<tr>
<td>20 week</td>
<td>0.344±0.026</td>
<td>0.329±0.016</td>
<td>0.284±0.026</td>
<td>0.215±0.021*</td>
</tr>
</tbody>
</table>

**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**

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A reduced insulin sensitivity (IS) is considered a primary pathophysiological mechanism underlying a cluster of metabolic abnormalities (hyperinsulinaemia, hyperglycaemia, dyslipidaemia, 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 46.4±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.

Abstract 9C.05

AORTIC STIFFNESS AND WAVE REFLECTIONS IN PREGNANCIES COMPROMISED BY GESTATIONAL DIABETES MELLITUS: A LONGITUDINAL STUDY

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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 (cPWV) 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 cPWV and AIX@75 is displayed in the Figure. Compared to women with normal pregnancies, women with gestational diabetes had a significantly higher cPWV (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, cPWV 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.06

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

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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. 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 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**

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**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 streptozotocin injection, tail cuff systolic blood pressure was measured before each rat was anaesthetised (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>0.15). 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 differences 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**

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**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 overexpression of wild-type SIRT2 in HepG2 cells caused an antihypertensive effect, we aimed to determine whether SIRT2 increases oxygen consumption, stimulating both mitochondrial respiration and sensitivity 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.

**Abstract 9C.07**

<table>
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<th>control</th>
<th>control + telmisartan</th>
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<td>414±32***</td>
<td>579±46</td>
<td>543±40</td>
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<tr>
<td>blood glucose (mmol/L)</td>
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<td>30±4***</td>
<td>7±2</td>
<td>6±2</td>
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<tr>
<td>systolic blood pressure (mmHg)</td>
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<td>127±9</td>
<td>146±17**</td>
<td>112±12</td>
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<tr>
<td>vein diameter (mm)</td>
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<td>0.21±0.02**</td>
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<tr>
<td>artery diameter (mm)</td>
<td>0.13±0.02</td>
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<tr>
<td>artery to vein ratio</td>
<td>0.59±0.07</td>
<td>0.58±0.10</td>
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</table>

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

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**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±8y). PWV, ACR, GFR (MDRD), and ischemic heart disease prevalence 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 48.96% 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±1.9m/sec; ACR: 134.5±6.99mg/g and GFR: 61.4±1.3ml/min) or DBT (PWV: 10.4±0.5m/sec; ACR: 89.0±15.0mg/g and PWV: 47.0±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 = -0.801, 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 PWV in either GI (r = -0.731, p<0.01; PWV: r = -0.76, p<0.01) or DBT (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.
9D.01 THE NEW RENIN INHIBITOR VTP-27999 ALTERS RENIN IMMUNOREACTIVITY AND DOES NOT BIND NATIVE PRORENNIN

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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 t½1/2, 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 renin-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 immunosays 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

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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 hydrochlorothiazide 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

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Background: Beta-blockers (BBs) with different pharmacological properties may have heterogenous 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 (Alx75HR75) 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 (3.9±4.19 ms/mmHg) was higher than that in the atenolol group (2.6±3.78 ms/mmHg), although not statistically significant (P>0.05). BRS was stable when HR 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 have 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

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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 cerebral vascular 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 an average of 67 and 133 patients who would have had 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.

OLMESARTAN PLUS AZELNIDIPINE VERSUS DIURETIC IN HYPERTENSIVE PATIENTS WITH DIABETES AND ALBUMINURIA

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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 amlodipine 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 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 antihypertensives 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 groups, 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.

ANTIHYPERTENSIVE DRUG THERAPY IN SOUTH ASIAN PATIENTS: A SYSTEMATIC REVIEW

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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.

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

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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 ubiquitous 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 – Rationale and Design of the Early Hypertension Registry” (EARLY) 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 in comparison to those of other ARB treatment with placebo treatment or single Drug Treatment With Other Single Drug Treatment.
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 VENTRICULAR DIASTOLIC FUNCTION AFTER SURGICAL REMOVAL OF A PHEOCHROMOCYTOMA**

D. Hering1, K. Kunicka1, E. Swierbelska1, W. Kucharska1, L. Obolonczyk2, M. Siekierska-Hellmann1, K. Sworczak2, K. Narkiewicz2.

**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/m², 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 adrenergic uptake are sustained over time warrant further examination.

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


**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/m², 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 adrenergic uptake are sustained over time warrant further examination.

<table>
<thead>
<tr>
<th>Abstract 9D.08</th>
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<th>At 1 month follow-up</th>
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<td>Office DBP (mmHg)</td>
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<td>Office HR (bpm)</td>
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<td>79±4</td>
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<td>MSNA (burst/min)</td>
<td>52±3</td>
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<td>MSNA (Over/100s [arbitrary])</td>
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<td>59±5</td>
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<tr>
<td>Plasma Adrenalin (pg/ml)</td>
<td>289±110</td>
<td>138±42</td>
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<tr>
<td>Plasma Noradrenalin (pg/ml)</td>
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<tr>
<td>Urine metanephrine (µg/24h)</td>
<td>1599±621</td>
<td>55±10</td>
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<tr>
<td>Urine normetanephrine (µg/24h)</td>
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<td>251±59</td>
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<tr>
<td>IVSd (mm)</td>
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<td>54.6±4.7</td>
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<tr>
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<tr>
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<td>5.9±0.5</td>
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</table>

**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.
Objective: It is generally accepted that acute cigarette smoking increases sympathetic tone 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 analyze. 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 (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.
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 of 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 respective-

ly: 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**

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 18-80 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 urine sample was collected for UNa+, UK+ and creatinine excretion. HT was defined as a mean systolic BP ≥ 140 or diastolic BP ≥ 90 mmHg and/or use of antihyper-
tensive 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 hy-
pertensive 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) and 11.9 g/day in 2005 and UK+ was 76.2±0.4 mmol/day. UNa+ cor-
related with systolic BP (r=0.06) and BMI (r=0.01) 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 im-
proved 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**

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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 im-
balanced 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-eff-
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 cardiovas-
cular 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% reduction of myocardial infarctions (outcome 1) (95%CI: 0.80-0.90, dif-
ference between groups in achieved systolic/diastolic BP: 13.4/7.1 mmHg); by 32% RR reduction of stroke (outcome 2) (0.63-0.75, 13.7/7.7 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, 15.8/8.1 mmHg); by 17% RR reduction of car-
diovascular mortality (outcome 6), (0.76-0.90, 13.7/7.7 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 asso-
ciated with the achieved between 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 VENTRICAL REMODELING IN TYPE 2 DIABETES WITH OLMESARTAN IN THE ROADMAP STUDY: ECG-LVH RESULTS**

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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, mul-
ticenter, 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 re-
modeling 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 base-
line, the prevalence of patients in the highest quartile (ie. >200 mV*msec) increased from 26% to 25.6% 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 ven-
tricular remodeling in patients with type 2 diabetes independent of differences in blood pressure. Thus, olmesartan delayed not only the onset of microalbu-
murina (NEJM 2011), but also ECG signs of cardiac structural adaptation in type 2 diabetes.
Low Sodium Intake Induces Functional Capillary Recruitment and Influences Endothelial Surface Layer Dimensions in Healthy Male Subjects

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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 pressure under control.

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.

Prevalence of Arterial Hypertension in Serbia - Pahis Study

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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 48.9±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 102 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.

Long-term Telemetry Recordings Demonstrate Increased Renal Sympathetic Nerve Activity and Blood Pressure in Rats with Chronic Kidney Disease

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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 method: 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.
POSTER SESSION

POSTER SESSION P01

EPIEMIOLOGY 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

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Objectives: 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 most common 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 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%), whereas for nurses 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


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 blood 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.

<table>
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<td>BP diastolic</td>
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<tr>
<td>Normal</td>
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<td>76.9</td>
<td>82.1</td>
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<tr>
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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 first, second and third respectively were: 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 1st 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

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Object: Masked hypertension(isolated ambulatory hypertension) is normoten-sive by clinic measurement but proves to be hypertensive by 24 hour Ambula-tory Monitoring 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.

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

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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 mmHg 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: β = 0.278, p<0.001. In contrast, diastolic BPc decreased with increasing age: β = -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 hypertensive and 79% of treated patients were not controlled. These patients had a greater number of peaks (≥ 180 mmHg for systolic and / or ≥ 110 mmHg for diastolic BPc) 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.

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

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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 in 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 731 patients (pts) (465 men and 295 women, mean age 61.2 years) who were already being followed by primary care centers for hypertension, from blood pressures (BP) were <140/90 mmHg and who were receiving DHP CCB drugs as either monotherapy or in combination were analyzed. Among these pts, 1658 (23%) had diabetes, 157 (2.4%) had renal disease, 1403 (19%) had coronary heart disease, 2774 (4%) had previous stroke, and 625 (9%) had peripheral artery disease. Any kind of cardiovascular disease was present at 1750 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 monother-apy 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.
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 with hypertensive 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 5,266 (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.

**Complex Evaluating of the Effectiveness of Cardiovascular Risk Self-Assessment Among Physicians and Their Awareness of Clinical Practice Guidelines**

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**Aim:** To evaluate cardiovascular risk factors self-assessment 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 work was 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 internists, 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 assessment, 251 patients had had SCORE less than 5%.

**Conclusions:** 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 the own health.

**Prevalence of Prehypertension and Metabolic Disorders in Young People of the Altai Region**

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**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%), in 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.

**Cardiovascular Morbidity and Mortality in Hypertensive Patients and the Associated Cardiovascular Risk Factors**

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**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 all 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.
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. Hoffmann1, P. Matyjaszczyk2, W. Byle3, 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 in 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 substantially higher mean systolic (men:143.9±12.0 vs. 82.8±7.0 mmHg, p<0.05; women: 135.4±18.8 vs. 72.6±10.8 mmHg, p<0.05) and diastolic blood pressure values (men:89.4±12.0 vs. 82.8±7.0 mmHg, p<0.05). They had a larger body mass (men:88.8±15.0 vs. 78.7±15.6 kg, p<0.05; women:73.7±15.6 vs. 70.6±13.4 kg, p<0.05), BMI (men:28.7±4.5 vs. 27.7±4.5 m²/m², p<0.05; women:27.8±4.5 vs. 25.8±4.7 kg/m², p<0.05) and hip circumference (men:98.5±11.5 vs. 95.0±9.2 cm, p<0.05; women:88.8±9.2 vs. 82.7±11.6 cm, 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% vs. 23.1%, p<0.05). In younger group 69 patients had active lifestyle, whereas in older group 111 patients (25.6% vs. 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% vs. 23.6%, p<0.05) and between younger and older male patients (15.9% vs. 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 significantly more often declared active lifestyle was the health beneficial behaviour.

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


Objective: Analyze the magnitude of diagnostic inertia in non-diabetic 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? (n = 10 075,3%); male (1.740), age (1.038), atrial fibrillation (0.991), 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**


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: 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.

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Conclusions: Diagnostic Inertia demonstrates a new problem that is easily solved through alarm systems in the computerized record of the patient’s history.
CARDIOVASCULAR RISK FACTORS MANAGEMENT IN TYPE 2 DIABETES MELLITUS PATIENTS IN PRIMARY CARE IN SPAIN

V. Giner1, E.M. Gil2, J. Martinez2, A. Palacios Del Cerro2, D.F. Stancu2, C. Andres3, V. Blanes3, M.C. Nicolau1, M.J. Esteban1, M.M. Reig1, 1Hypertension Unit, General Internal Medicine Department, Verge dels Lliris Hospital, Alcoy, SPAIN, 2Primary Care Centers, Alcoy Health Department, Alcoy, SPAIN, 3Primary Care Centers, Elda Health Department, Elda, SPAIN

Objective: To describe the prevalence of cardiovascular risk factors (CVRF) and their management in patients with type 2 diabetes mellitus (T2DM) in Primary Care in Spain.

Design and method: Multicentric, observational, cross-sectional study including 211 T2DM patients (54.5% men aged 68.4±9.7 yrs. with 10.1±7.6 yrs. of evolution) from 9 Primary Care Centers 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 59.2%, and <7.0% in 43.1%. Among 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 antidiabetic, 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.

MANAGEMENT OF HYPERGLYCEMIA IN TYPE 2 DIABETES MELLITUS IN THE UsUAL CLINICAL PRACTICE IN SPANISH PRIMARY CARE CENTERS


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 excluded in 9 PCCs in the province of Alicante (Spain).

Results and conclusions: 211 T2DM patients (54.5% men aged 68.4±9.7 yrs.; with 10.1±7.6 yrs. of evolution; by 3.1±1.8 laboratory tests/patient) were included. Averages of 5.7±2.7 drugs/patient/day were taken, with 89.6% of the patients having oral antidiabetics, 70.6% antihypertensives, 63.0% hypolipidemians, 26.1% insulins, 19.0% antiinflammatory 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 was made at the PCC; Mean HbA1c was 7.2±1.2%. Well-controlled pa-

RENAL FUNCTION IN HYPERTENSION:

V. Giner1, A. Genoves2, A. Cuco2, M.L. Campoy2, R. Pastor3, I. Boix2, T. Quilis2, M.J. Esteban1, M.M. Reig1, S. Martinez2, 1Hypertension Unit, General Internal Medicine Department, Verge dels Lliris Hospital, Alcoy, SPAIN, 2Primary Care Centers, Elda Health Department, Elda, SPAIN, 3Primary 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 included in 9 PCCs 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% of patients during the 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. 21.3% patients had nephropathy, retinopathy, or nephropathy, 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 comparison of TOD prevalence before (Known) and after (Actual) evaluation at the inclusion:

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.

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 method: 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.
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 1 gr. 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.

### PP01.19 ASSSESSMENT AND THERAPEUTIC MONITORING OF HYPERTENSIVE PATIENTS IN A MEDICAL CONSULTATION IN UNIVERSITY HOSPITAL IN BLIDA, ALGERIA

A. Bachir Cherif1, A. Taleb1, A. Bouamra2, A. Benetos3, S. Benkhedda4, A. Chibane5, M. Temmar1, M. Bouafia1, 1Cardiology Department University Hospital, Blida, ALGERIA, 2Department Epidemiology University, Blida, ALGERIA, 3Geriatric Department of University Hospital, Nancy, FRANCE, 4Cardiology Department University Hospital, Alger, ALGERIA, 5Internal Department University Hospital, Ain Taya, ALGERIA, 5Cardiology 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 Bilia 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<80mmHg, 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 ARAS 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 ARAS + 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.

**Abstract PP01.20**

**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 %.

**Abstract PP01.21**

**HYPERTENSION CONSULTATION: 18 MONTHS OF EXPERIENCE**

A. Serafin, 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-
MANAGEMENT OF ARTERIAL HYPERTENSION
BLOOD PRESSURE CONTROL AND MULTIPROFESSIONAL APPROACH OF HYPERTENSIVE TEMPORAL TRENDS IN MANAGEMENT

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 a multidisciplinary approach.

Conclusions:

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 efficacy 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 on the management of hypertension 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:
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.

Objective: Diabete 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 with them. Our objective was to analyse the results of a multiprofessional approach in the treatment of diabetic hypertensive patients from 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, glycermia, Hb1C, lipids profile and body mass index – BMI). Patients with only one visit were excluded. Statistical analyses were conducted with the software 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).

Table – Comparison of BP, Glycermia, Hb1C, Lipids profile and BMI between V1 and V2

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Conclusion: Multiprofessional intervention was effective in improving most cardiovascular risk factors in our group of hypertensive diabetic patients.

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<thead>
<tr>
<th>Variable</th>
<th>V1</th>
<th>V2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>140.1±9.8</td>
<td>133.5±19.2</td>
<td>0.002**</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>87.8±12.5</td>
<td>79.6±11.5</td>
<td>0.002**</td>
</tr>
<tr>
<td>Glycermia (mg/dL)</td>
<td>159.8±67.0</td>
<td>147.7±55.6</td>
<td>0.834</td>
</tr>
<tr>
<td>Hb1C (%)</td>
<td>7.9±1.7</td>
<td>7.3±1.0</td>
<td>0.001**</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>206.9±52.1</td>
<td>175.7±45.7</td>
<td>0.000**</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>121.9±43.3</td>
<td>100.4±38.0</td>
<td>0.000**</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>42.1±10.4</td>
<td>43.2±10.4</td>
<td>0.185</td>
</tr>
<tr>
<td>TRIGLYCERIDES (mg/dL)</td>
<td>220.8±141.6</td>
<td>176.4±133.4</td>
<td>0.001**</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.8±5.4</td>
<td>30.5±4.8</td>
<td>0.409</td>
</tr>
</tbody>
</table>

* * *

Conclusion: Multiprofessional intervention was effective in improving most cardiovascular risk factors in our group of hypertensive diabetic patients.
Design and methods: In 2012, a survey on 9544 treated hypertensive patients (male 42%, age 66.6±10.6 years) followed by 200 general practitioners was carried out in Bulgaria using BP-CARE design. CV risk assessment was based according to 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 TOWARDS HEALTHY LIFESTYLE CHANGES IN HYPERTENSION: DIFFERENCES AMONG SPECIALTIES**

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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 lifestyle factors by a Likert scale from 1 to 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 lower (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 importance 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 (4.45 and 4.50) scored highest for stress management and healthy diet respectively. Physicians were asked to score importance of lifestyle factors by a Likert scale from 1 to 5.

**PP.01.27 BLOOD PRESSURE CONTROL IN NIGERIAN HYPERTENSIVE PATIENTS: A REVISIT**

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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 “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±73.1 mm Hg systolic and 99.2±17.2 mm Hg 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**


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 DYSLIPOHAEMIA**

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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 devices for lipid screening compared with laboratory lipid test results in healthy subjects and patients with dyslipidaemia.

Design and methods: 2 CardioChek PA Analyzers (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 (ChexMate) and PTS Panel Quality Control materials. Fasting venous samples from 50 subjects were analysed on both
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 of hypertensive patients amounted to 12.3% of the representative sample. The respondents were re-examined in representative sample in 2007. Losses related to determinants of hypertensive patients. 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 effect of the treatment of hypertensive patients does not change even complications of hypertension: stroke, acute myocardial infarct, chronic heart failure and kidney failure, 46.2% indicates patients suffering from complications. 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

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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 pharmacoepidemiologic study of daily clinical practice in Belgium from November 2009 till January 2011. According to study protocol, inform patients about any complications. The study protocol, inform patients about any complications.

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 and DBP reductions were observed (all p<0.001 vs preceding visit). BP control was 2.9% at baseline, 36.8% 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 65.9% at 180D (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+/- 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.

PP.01.33 HYPERTENSION IN RUSSIAN POPULATION: MULTICENTER SURVEY IN CHINA

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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-