Objective: The soluble form of urokinase-type plasminogen activator (suPAR) is a powerful marker for immune activation that accurately predict clinical outcomes in patients with sepsis or infectious diseases. Alterations in innate immunity and Inflammation are major risk factors for the high risk for cardiovascular disease in patients with chronic kidney disease (CKD) but whether suPAR predicts cardiovascular and renal complications independently of established risk factors in CKD is still unknown.

Design and method: We measured plasma suPAR levels (ELISA) and a series of traditional and CKD-specific risk factors in 753 stage G2-5 CKD patients. We estimated the risk for GFR loss (>30%) or kidney failure, time to death and first cardiovascular event by multivariate Cox regression analysis adjusting for traditional risk factors and a large series of CKD-specific risk factors.

Results: suPAR was gender-dependent and associated with lower GFR and higher proteinuria, older age, diabetes, higher BP, C Reactive Protein (CRP), phosphate, PTH, FGF23, ADMA and lower Hb, 25OH vitD and 1,25OH2 vitD (all P < 0.001). Over a 31+/- 10 months follow-up 42 patients died and 95 had a renal event. suPAR was a strong predictor of the combined end-point death and cardiovascular events [HR (500g/ml): 1.09, 95%CI: 1.04–1.14] in a Cox’s regression analysis adjusting for a large series of potential confounders including background cardiovascular disease, the GFR, proteinuria, age, gender, smoking, diabetes, systolic BP and anti-hypertensive treatment, phosphate, Hb, serum albumin, BMI, CRP, ADMA and FGF23. Separate analyses of time to death and time to first CV event were both highly significant (P < 0.01) in crude and adjusted analyses.

Conclusions: Elevated suPAR levels robustly predict incident cardiovascular events and death in CKD patients. These findings go along with biological knowledge documenting a strong role of suPAR in atherosclerosis and support the contention that suPAR is causally implicated in cardiovascular disease in CKD patients.

OP.1A.03 COPEPTIN LEVELS IN PATIENTS WITH TREATMENT RESISTANT HYPERTENSION BEFORE AND AFTER RENAL DENERVATION

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Objective: Copeptin, the C-terminal peptide of pro-vasopressin which is released from the neurohypophysis, reflects the activity of the hormone arginine vasopres- sin. Copeptin has been found to be associated with cardiovascular and all-cause mortality in patients with hypertension. The aim of this study is to compare copeptin levels in patients with treatment resistant hypertension (TRH) before and 6 months after renal denervation.

Design and method: Copeptin was measured in 43 patients with TRH and in 30 patients with primary hypertension stage 1 or 2 (HT) using ELISA Elab-science®. In addition, copeptin levels were measured in patients with TRH at 6 months follow-up visit after renal denervation. Renal denervation was performed by an experienced person applying at least four ablations longitudinally and rotationally within the lengths of each renal artery to cover a full quadrant ablation.

Results: Patients with TRH showed systolic and diastolic ambulatory BP of 154 ± 13/ 87 ± 12 mmHg before and systolic and diastolic ambulatory BP of 144 ± 11/ 82 ± 8 mmHg after renal denervation (p = 0.001). There was no signif- icant difference in copeptin levels in 43 patients (age 61 years) before and six months after renal denervation (10.9 ± 10.8 vs 12.5 ± 14.6 pmol/l, p = 0.287).

Patients with TRH showed higher copeptin levels compared to patients with HT (age 47 years, systolic and diastolic ambulatory BP (142 ± 11/ 90 ± 8 mmHg) (copeptin conc.: 5.8 ± 4.8 vs 10.9 ± 10.8 pmol/l, p = 0.007). In patients with HT there was a correlation between copeptin concentrations and diastolic 24 h ambulatory BP (r = 0.428, p = 0.018).

Conclusions: Patients with TRH showed nearly 2 fold higher copeptin levels than patients with HT. Renal denervation did not lead to any change of copeptin levels in patients with TRH six month after procedure.
Objective: Reducing dietary salt lowers both blood pressure and cardiovascular risk. The mechanisms underlying the adverse effects of high salt intake are incompletely understood, but parallel increases in plasma sodium (PNa) may be of importance: observational and experimental studies have identified that small increases in PNa are associated with increased blood pressure and changes to endothelial function, independent of changes in plasma volume. However, very few studies have investigated whether there is an association between PNa and cardiovascular disease (CVD).

Design and method: This was a retrospective cohort study using the Royal College of General Practitioners Research and Surveillance Centre database. Data collected between April 2005 – March 2015 was extracted, and the baseline period was defined as before April 2010. The primary outcome was incident CVD (myocardial infarction, acute coronary syndrome, coronary revascularisation, stroke or heart failure diagnosis) during the 5-year follow-up period. Exclusion criteria were: age less than 40, diabetes mellitus, prior PNa event, end-stage renal disease and liver cirrhosis. Baseline PNa was determined using the most recent laboratory result, and a mean was calculated if a second result was available at least 3 months apart.

Results: 234,764 individuals were included in the study. A PNa of 137 mmol/L or less at baseline was associated with increasing age, female gender, hypertension, and prescription of cardiovascular medications including diuretics. After multivariate adjustment for confounding factors, there was a significant ‘J-shaped’ relationship between PNa and CVD (Figure 1). No linear association between increased PNa and blood pressure was demonstrated.

Conclusions: To our knowledge, this is the largest study to investigate the relationship between PNa and CVD. The association was greatest with lower PNa, and was such that the risk increased at concentrations well within the normal physiological range (140 mmol/L or less). One hypothesis is that lower PNa is an indicator of neurohormonal activation prior to the development of overt CVD. A lower PNa may be a useful indicator for the future development of CVD but obscure the potential importance of high PNa over longer periods of time.
11.87 years (mean 4.97 years). Studied cardiovascular outcomes were sudden death, total death, cardiovascular death, fatal myocardial infarction, stroke and coronary heart disease.

Results: Diabetes and male sex always represented significantly higher risks for sudden death, total death, cardiovascular death, fatal myocardial infarction, stroke and coronary heart disease in both univariable and multivariable analyses, except male sex for stroke in corresponding multivariable analysis. Their interaction was significant for all outcomes except coronary heart diseases in univariable analyses and except cardiovascular death, stroke and coronary heart diseases in multivariable analyses (Tab.1). On average, women with diabetes had 85% higher risk of sudden death, 23% higher risk of total death and 24% higher risk of fatal myocardial infarction than diabetic men, all in a significant way. The same tendency was observed for cardiovascular death, stroke and coronary heart diseases but these results were not statistically significant (Tab.2).

Conclusions: In our database, the interaction between gender and type 2 diabetes was significant in terms of sudden death, total death and fatal myocardial infarction with adjustment by treatments, trials, age, smoking status, systolic blood pressure, total cholesterol and history of myocardial infarction. Our observations were in accordance with the literature: for non-diabetic subjects, men represented 1.5 to 2.3 times higher risk for studied endpoints; however, for diabetic ones, women seemed to have worse cardiovascular outcomes.

OP.1A.07 SLEEP-TIME AMBULATORY BLOOD PRESSURE AS THERAPEUTIC TARGET FOR PREVENTION OF CARDIOVASCULAR EVENTS: THE HYGIJA PROJECT


Objective: Previous ambulatory blood pressure (BP) monitoring (ABPM) outcome investigations relied upon only a single, low-reproducible 24-h ABPM assessment per participant done at study inclusion. This approach precluded the opportunity to explore the potential reduction in cardiovascular disease (CVD) risk associated with modification of prognostic ABPM-derived parameters by hypertension treatment. The Hygia Project, a research network presently composed of 292 investigators of 40 clinical sites, was specifically designed to investigate, among other primary objectives, whether specific treatment-induced changes in ABPM-derived parameters reduce risk of CVD events.

Design and method: This study involved 18,078 persons, 9,769 men/8,309 women, 59±14.3 years of age, with baseline BP ranging, according to ABPM criteria, from normotension to hypertension. At inclusion and at every scheduled clinic visit for ABPM (at least annually) during follow-up, BP was assessed at 20-min intervals from 07:00 to 23:00 and at 30-min intervals at night for 48 h. During ABPM, participants kept a diary listing the times of going to bed at night and waking up in the morning. The primary CVD-outcome was the composite of CVD death, myocardial infarction, coronary revascularization, heart failure, and stroke.

Results: During a median 5.1-year follow-up, we documented 1,209 events for the primary CVD-outcome. Analyses of therapy-induced changes in clinic and ambulatory BP during follow-up revealed progressive decrease in sleep-time systolic BP (SBP) (adjusted for significant influential characteristics of age, sex, type 2 diabetes, chronic kidney disease, cigarette smoking, HDL-cholesterol, hypertension treatment-time, and previous CVD event) was the most significant prognostic marker of CVD event-free survival (hazard ratio 0.73 [95% CI 0.65-0.83] per SD decrease in asleep SBP mean, P = 0.001), independent of changes in office SBP (0.96 [0.87-1.06], P = 0.414) or awake SBP mean (0.92 [0.78-1.09], P = 0.326). Only the progressive increase in the sleep-time relative SBP decline was a marker of survival jointly with diminishing asleep SBP (0.87 [0.77-0.99], P = 0.035).

Conclusions: Treatment-induced decrease of asleep SBP mean and increase of sleep-time SBP decline towards more normal dipper BP patternning, two novel hypertension therapeutic targets requiring proper patient evaluation by ABPM, are the most significant independent predictors of reduced CVD morbidity and mortality.

OP.1A.08 PROGNOSTIC RELEVANCE OF RESTING HEART RATE IN OBESITY: LONGITUDINAL EVIDENCE FROM THE PAMELA STUDY

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Objective: We have previously shown that in the general population of the Pamina Artero Monitza E Loro Asociazioni (PAMELA) study heart rate (HR) values fail to display a prognostic relevance for cardiovascular (CV) events, presumably because of the low risk profile of the overall population. In the present study we restricted the analysis to HR values in subjects affected by an obese state, i.e. a condition in which the detection of elevated HR values and an increased CV risk is common.

Design and method: In 1944 subjects recruited in the PAMELA study and aged 51 ± 13.6 we measured at the study entry along with clinic, home and 24 hour blood pressure (BP), the corresponding HR values and waist circumference (WC). During the median follow-up period of 212 months we evaluated cardiovascular (CV) and total mortality. Data were analyzed subdividing the population in 3 gender specific tertiles of WC.

Results: Compared to the lowest tertile, subjects in the highest tertile of WC displayed significantly greater clinic, home and 24 hour HR values. Focusing the analysis on subjects in the highest tertile of WC, after adjustment for gender, corresponding systolic BP and age, the risk of CV death was significantly greater with an increase of 1 bpm of home and 24 hour HR (hazard ratio 1.04 and 1.05, respectively, p < 0.05 for both), while no significant impact on CV mortality was found for clinic HR (hazard ratio 1.01, p = NS). The risk of all cause death was statistically significant for an increase of 1 bpm of clinic, home and 24 hour HR, after adjustment for confounders (hazard ratio 1.01, 1.023 and 1.039, p < 0.01 for all).

Conclusions: HR, particularly when evaluated at home and during the 24 hours, represents an independent long-term predictor of fatal cardiovascular and non-cardiovascular events in patients with central obesity. For cardiovascular mortality, however, clinic HR does not appear to retain a prognostic value.

OP.1A.09 ORTHOSTATIC HYPERTENSION PREDICTS MASKED HYPERTENSION IN THE VERY ELDERLY TREATED HYPERTENSIVES

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Objective: Masked hypertension (MHT) and isolated nocturnal hypertension are associated with increased risk of target organ damage and cardiovascular events. We investigated prevalence and predictors of those blood pressure phenotypes in very elderly treated hypertensives.

Design and method: Office blood pressure evaluation (simultaneous bilateral brachial blood pressure measurements in supine position and then after 2 minutes of standing) and 24-h ambulatory blood pressure monitoring (ABPM) were performed with a validated oscillometric cuff-based device in 67 treated hypertensive subjects older than 80 years (mean age 84.1 ± 3.1 years, 25.5% male, mean office brachial SBP 134.8 ± 23.2 mm Hg). Patients with left ventricular ejection fraction < 40% and severe comorbidities were not included. Orthostatic hypotension (OH) was defined as a decrease in SBP of at least 20 mm Hg upon standing and orthostatic hypertension (OHT) as a corresponding increase.

Results: The prevalence of MHT was 47.7% in the entire study population and 71.1% among patients with office-controlled hypertension (BP < 150/90 mm Hg). 78.2% patients with MHT had isolated nocturnal hypertension. Orthostatic reaction was abnormal in 34.3% subjects: 22.4% participants had OH while incidence of OHT was 11.9%. OHT was significantly associated with MHT (RR = 1.7, 95% CI 1.14-2.78).

Conclusions: OHT is predictive for MHT in the very elderly treated hypertensives. Evaluation of orthostatic reaction in very elderly may help to detect a population that would benefit from ABPM.

OP.1A.10 CIRCULATING LEVELS OF PCSK9 AND ARTERIAL STIFFNESS IN A LARGE POPULATION SAMPLE: DATA FROM THE BRISIGHELLA HEART STUDY

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Objective: Proprotein convertase subtilisin kexin type 9 (PCSK9) circulating levels are significantly associated with increased risk of total cardiovascular events. Risk markers for cardiovascular diseases (CVD) include parameters relative to arterial structure and function. Our study aimed to evaluate the relationship between
Design and method: From the historical cohort of the Brisighella Heart Study, four subgroups were selected: pre-menopausal women (n = 227), age-matched men (n = 193), post-menopausal women (n = 460) and age-matched men (n = 416). In these subjects, the correlation between PCSK9 plasma circulating levels and the pulse wave velocity (PWV) was evaluated. Active smokers, participants in secondary prevention for CVD treated with statins or vasodilating agents, were excluded from the analysis.

Results: Post-menopausal women showed higher PCSK9 levels (309.9 ± 84.1 ng/mL) compared to the other groups of subjects (p < 0.001). Elderly men had significantly higher levels of PCSK9 than adult men (283.2 ± 75.6 ng/mL vs. 260.9 ± 80.4 ng/mL; p = 0.008) (Figure 1). PWV was mainly predicted by age (B = 0.116, 95% CI 0.06 – 0.127, p < 0.001), PCSK9 (B = 0.014, 95% CI 0.011–0.016, p < 0.001), and serum uric acid (B = 0.313, 95% CI 0.024–0.391, p = 0.026). Physical activity, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and estimated glomerular filtration rate were not associated to the PWV level (p > 0.05). Considering the above described subgroups, age and PCSK9 resulted the main factors associated to PWV; the latter correlates to serum uric acid only in post-menopausal women.

Conclusions: In the Brisighella Heart Study cohort, circulating PCSK9 are significantly related to the arterial stiffness, independently from gender and menopause status.

Objective: Brachial-ankle pulse wave velocity (baPWV) is a marker of arterial stiffness and is technically more feasible as compared to carotid-femoral pulse wave velocity. Previous reports have shown that baPWV is associated with presence and severity of coronary artery disease (CAD) assessed by invasive coronary angiography (CAG) in older subjects. On the other hand, in young and middle-aged adults, baPWV was only demonstrated to be associated with coronary calcium assessed by computed tomography. There are no studies examining relationship between baPWV and CAD assessed by CAG in this population. The aim of this study was to determine the association between baPWV and both presence and severity of CAD assessed by CAG in young and middle-aged adults.

Design and method: We enrolled 117 patients under the age of 65 who measured baPWV and underwent elective CAG for suspected CAD. Significant CAD was defined as one or more stenosis over 50%. To evaluate severity of CAD, we measured SYNTAX and Gensini scores. Using univariate and multivariate logistic regression analysis, we evaluated the contribution of baPWV for the presence of significant CAD. In patients with CAD, we also assessed the association between baPWV and Gensini scores using linear and multiple regression analysis.

Results: In univariate logistic regression analysis, baPWV was associated with presence of significant CAD in univariate logistic regression analysis (Odds Ratio (OR) 1.16, [95% Confidence Interval (95% CI) 1.02–1.33], p = 0.03). In multivariate analysis, the association was canceled after adjusting traditional coronary risk factors. In univariate linear regression analysis, baPWV was associated with both Gensini and SYNTAX scores (Gensini: coefficient 2.19[95% CI 0.17–4.21], p = 0.03, SYNTAX: coefficient 1.09[95% CI 0.34–1.83], p = 0.01). In multiple regression analysis, baPWV remained significantly related to both severity scores (Gensini: coefficient 3.52[95% CI 0.06–7.00], p = 0.046, SYNTAX: coefficient 1.85[95% CI 0.65–3.04], p = 0.01).

Conclusions: In young and middle-aged population, increased arterial stiffness assessed by baPWV is associated with the severity, rather than the presence, of CAD.
Objective: Regulation of renin-angiotensin-system (RAS) is expected to prevent the onset and progression of dementia. Angiotensin (Ang) converting enzyme (ACE) 2/Ang-(1-7)/Mas receptor axis has been highlighted as counteracting partner of the onset and progression of dementia. Administration of Ang-(1-7) could not improve cognitive function even in MasKO mice (Figure 2).

Results: There was no significant difference in spatial learning memory between WT and MaskKO in the Morris water maze test after BCAS surgery; however, DKO showed more impaired cognitive function than MaskKO (Figure 1). CBF did not show any significant differences in each BCAS group. Administration of Ang-(1-7) did not change significantly these parameters in all BCAS group; however, Ang-(1-7) treatment tended to improve cognitive function even in MaskKO mice (Figure 2).

Conclusions: Our results suggested the positive protective effect of Mas receptor deficiency on vascular dementia. Administration of Ang-(1-7) could not improve the cognitive function under the deletion of AT2 receptor. Therefore, the interaction of Ang-(1-7) with AT2 receptor could contribute to maintain the cognitive function in MaskKO.

OP.1B.02 EFFECT OF A MULTIMODALITY TRAINING ON COGNITIVE AND VASCULAR FUNCTION IN MCI PATIENTS WITH OR WITHOUT HYPERTENSION: THE TRAIND THE BRAIN - MIND THE VESSEL STUDY

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Objective: Environmental enrichment obtained by a multidomain training may slow cognitive decay possibly acting through an improvement in vascular function. Aim of the study is to assess the effects of a 7-month cognitive, social and physical training on cognitive and vascular function in patients with mild cognitive impairment (MCI).

Design and method: In a single-center, randomized parallel-group study, 113 MCI (age 65–89 years) were randomized to multidomain training (N = 55), or usual care (N = 58). All participants underwent neuropsychological tests (including Alzheimer’s Disease Assessment Scale-cognitive - ADAS-cog) and vascular evaluation, including brachial artery flow mediated dilation (FMD), carotid-femoral pulse wave velocity (PWV), and carotid intima-media thickness and distensibility. At study entry, an age-matched control group (n = 45) was also studied.

Results: Compared to controls, MCI had at study entry a reduced FMD (2.97 ± 2.14 vs 3.73 ± 2.06%, p = 0.03) and hyperemic stimulus (shear rate AUC, 25.9 ± 21.2 367.22.5 × 10-3 vs, 0.008); the latter remained significantly different in covariate analysis adjusted for confounders (p = 0.04).

Training improved ADAS-cog (MCI-training: 14.0 ± 4.8 to 13.1 ± 5.5; MCI-no training: 12.1 ± 3.9 to 13.2 ± 4.8; p for interaction time-treatment = 0.02) and FMD (2.82 ± 2.19 to 3.40 ± 1.81; 3.05 ± 2.08 to 2.24 ± 1.59%, p = 0.006) and prevented decline in carotid distensibility (18.4 ± 5.3 to 20.0 ± 6.6; 23.9 ± 11.0 to 19.5 ± 7.1; Pa-1; p = 0.005). The only clinical predictor of improvement of ADAS-cog in MCI-training was established hypertension (delta ADAS-cog in hypertensive patients: -2.3 ± 2.7 vs in normotensive patients 0.3 ± 5.0, p = 0.02). Furthermore, there was no correlation between changes in ADAS-cog and in vascular variables.

Conclusions: A 7-month multidomain training slows, though modestly, cognitive decline, especially in hypertensive individuals. This effect is accompanied by improved systemic endothelial function and preserved carotid distensibility and it is significant only in the hypertensive subgroup.

OP.1B.03 ARTERIAL STIFFNESS INDEPENDENTLY PREDICTS STROKE IN PATIENTS WITH ESSENTIAL HYPERTENSION: DATA FROM A GREEK 8-YEAR-FOLLOW-UP STUDY

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Objective: Although arterial stiffening is related to atherosclerosis progression, its prognostic role in cerebrovascular events in hypertension is not fully elucidated. The aim of the present study was to assess the predictive role of arterial stiffness for the incidence of stroke in a cohort of essential hypertensive patients.

Design and method: We followed up 1079 essential hypertensives (mean age 55.8 years, 572 males, office blood pressure (BP) = 144/91 mmHg) for a mean period of 8 years. All subjects had at least one annual visit and at baseline underwent blood sampling for assessment of metabolic profile and arterial stiffness was evaluated on
the basis of carotid to femoral pulse wave velocity (PWV), by means of a comput-
eterized method. The distribution of PWV was split by the median (8.1 m/sec) and
accordingly subjects were classified into those with high (n = 546) and low values
(n = 533). Stroke was defined as rapid onset of a new neurological deficit persist-
ning at least 24 hours unless death supervened confirmed by computed tomography
and magnetic resonance angiography and/or cerebrovascular angiography findings.

**Results:** The incidence of stroke over the follow-up period was 2.03%. Hyper-
tensives who had stroke (n = 25) compared to those without stroke at follow-up
(n = 1054) were older at baseline (63 ± 8 vs 55 ± 10 years, p = 0.012), had higher
office BP levels (155 ± 13 vs 144 ± 16 mmHg, p = 0.022) and prevalence of high
PWV levels (68% vs 42%, p = 0.019). No difference was observed between hyper-
tensives with stroke and those without stroke with respect to baseline renal
function and lipid levels (p = NS for all). By univariate Cox regression analysis it
was revealed that high baseline PWV levels predicted stroke (hazard ratio = 1.314,
p = 0.0034). Moreover, in multivariate Cox regression model, baseline age (haz-
ard ratio = 1.098, p = 0.04) and PWV (hazard ratio = 1.105, p = 0.015) but not
baseline office BP levels turned out to be independent predictors of stroke.

**Conclusions:** In essential hypertensive patients, PWV predicts future develop-
mement of stroke, independently of established confounders, including age and
findings support that PWV constitutes a potent prognosticator of cerebrovascular events
and its estimation is essential in order to improve risk stratification in hypertension.

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**OP.1B.04 CAFFEINE INTAKE AND ABSTRACT REASONING AMONG 1,374 UNSELECTED MEN AND WOMEN FROM GENERAL POPULATION. ROLE OF THE –163C > A POLYMORPHISM OF CYP1A2 GENE**

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**Objective:** Caffeine is considered to be an enhancer of cognitive performance but
its neuroactive effects, particularly those on abstract reasoning, have never been
studied in an epidemiological setting, especially in relation to the different geno-
types of −163C > A polymorphism of CYP1A2 gene, largely controlling caffeine
metabolism. Aim of this study was to ascertain whether free chronic caffeine in-
take modifies abstract reasoning in a dose-dependent manner, and if this effect is
influenced by the above-mentioned polymorphism or modified by other factors.

**Design and method:** We studied 1,374 unselected men and women aged
51 ± 15 years (range 18 to 89) from general population. From a 7-day dietary
diary, caffeine deriving from coffee, tea, chocolate or cola was calculated and
summed up. Abstract reasoning was measured in the frame of a neuropsychologi-
cal assessment as the ability to find a concept linking two words indicating objects
or actions and explaining how they were connected.

**Results:** In age-schooling-adjusted linear regression, the higher the caffeine in-
take, the better the abstraction score; the interaction term between caffeine and the
−163C > A polymorphism was accepted in linear regression (coefficient 0.0012,
standard error 0.0005, p = 0.002). More precisely, abstract reasoning depended on
caffeine in the CC homozygous only ("slow" caffeine metabolizers), where it was
higher in the 3rd tertile of caffeine intake (Figure 1). Actually, the CC homozygous
in the highest tertile were as abstractive as the A-carriers ("fast" caffeine metabo-
lizers, likely prone to consume more caffeine a day in order to avoid abstinence).

**Conclusions:** A direct association between caffeine intake and abstract reasoning
exits in general population and is influenced by the −163C > A polymorphism,
caffeine intake being the intermediate phenotype; age and ethanol reduce while
smoking and schooling enhance this association.

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**OP.1B.05 CEREBROPROTECTIVE EFFECT OF AN ANGIOTENSIN TYPE 2 RECEPTOR AGONIST DELIVERED VIA THE INTRanasAL ROUTE AFTER STROKE**

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**Objective:** The selective angiotensin type 2 receptor (AT2R) agonist Compound
21 (C21) has been proven in multiple preclinical studies to reduce infarct size and
attenuate neurological deficits, when administered after ischemic stroke via intra-
cerebroventricular or intraperitonal routes. However, C21 has poor blood barrier
penetrability. Here, we used the novel and non-invasive intranasal approach to
circumvent the BBB and deliver C21 directly to the brain via the upper olfactory region. The therapeutic efficacy of this intranasal trans-olfactory (INTO) application of C21 was assessed in a model of transient middle cerebral artery occlusion (MCAO).

**Design and method:** (i) Ischemic stroke was elicited by endothelin-1-induced
MCAO in 12-week old male SD rats. They were randomly divided into two treatment
groups, receiving either 0.9% saline or C21 (1.5 ug/kg) delivered INTO at 1.5, 4,
24 and 48 h post-stroke, using a rat intranasal catheter device (Impel Neuropharma,
Seattle, WA). All rats underwent blinded neurological assessments at 4, 24 and 72 h
after MCAO, and immediately after the 72 h tests, were euthanized and cerebral in-
farct volumes were assessed by TTC staining. (ii) Male SD rats (12-week old) were
implanted with a telemetry transducer (DSI, St. Paul, MN) into the abdominal aorta
to measure blood pressure, heart rate and locomotor activity after INTO application of C21 (1.5 ug/kg) vs. 0.9% saline at baseline and post-ischemic stroke.

**Results:** (i) Post-stroke INTO delivery of C21 (1.5 ug/kg) elicited a significant
lowering of % cerebral infarct size (25.4 ± 4.7; n = 9) compared with saline-
treated rats (48.4 ± 4.4; n = 21) [p < 0.05; two-way Mann-Whitney test]. The C21
(1.5 ug/kg)-treated rats also displayed highly significant improvements in neuro-
logical Garcia and Bederson scores (p < 0.01; two-way Mann-Whitney test). (ii)
INTO delivery of C21 (1.5 ug/kg) either in naïve rats (n = 7), or in rats post-stroke
(n = 4), did not significantly alter baseline blood pressure, heart rate and locomo-
tor activity.

**Conclusions:** These results demonstrate, that INTO delivery of a low-dose of
C21 in rats exerts protective effects after ischemic stroke, and suggest INTO ad-
ministration as potential route of application of C21 to stroke patients.

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**OP.1B.06 MIR-126 MODIFIED ENDOThelial PROGENITOR CELLS TRANSPlANTATION CONTRIBUTES TO ANGIogenesis AFTER BRAIN FOcaL ISCHEMIA IN SHR RATS**

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**Objective:** Transplantation of endothelial progenitor cells (EPCs) leads to better
outcomes in experimental stroke, while improve the EPCs survival rate in isch-
emia area is still a challenge. MiR-126 modulates vascular development and an-
giogenesis. Here we overexpressed miR-126 in transplanted EPCs, to investigate the function of gene modified EPCs in angiogenesis after brain ischemia.

**Design and method:** Adult male SHR rats underwent permanent suture middle
cerebral artery occlusion (MCAO). One week after middle cerebral artery occlu-
sion, the animals received tail vein injection of miR-126 modified EPCs as treat-
ment or EPCs as control and were monitored for 5 weeks. Brain water content, in-
farct volume, neurological score, neurogenesis and angiogenesis were examined.

**Results:** Neurological score was greatly improved and brain atrophy was greatly
reduced in miR-126 modified EPCs-treated SHR rats compared with the control rats
5 weeks after MCAO (P < 0.05). The number of bromodeoxyuridine+/CD31+
microvessels are significantly increased. EPCs migration and proliferation were
promoted after miR-126 modified in vitro.

**Conclusions:** Our results showed that miR-126 modified EPCs therapy reduced
ischemic brain injury, along with increased angiogenesis and neurogenesis in
SHR rats, suggesting miR-126 significantly improved EPCs function in angiogen-
sis after MCAO. Gene modified EPCs represents a promising avenue for isch-
emic stroke stem cell therapy.
**OP.1B.07**

**PRESEVERED CEREBRAL AUTOREGULATION IN CLINICAL ALZHEIMER’S DISEASE DURING REPEATED ORTHOSTATIC MANEUVERS**

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Objective: Preclinical studies suggest early amyloid-related cerebrovascular abnormalities in Alzheimer’s disease (AD) that impair neurovascular coupling and contribute to neurodegeneration. Hypertension could aggravate this process and is an important potential target for prevention of AD. However, in animal studies, vascular dysfunction in AD led to severely impaired cerebral autoregulation (CA), which could render antihypertensive treatment unsafe. We investigated CA during repeated orthostatic maneuvers in clinical AD compared to cognitively healthy controls (HC) and patients with mild cognitive impairment (MCI).

Design and method: 35 patients with mild-to-moderate probable AD, 21 subjects with MCI and 35 HC, all ≥50 years, were included. Mean arterial pressure (MAP, Finapres) at the finger and mean cerebroal blood flow velocity (MCFBV, Multi-Dop X4) at the middle cerebral artery were collected during repeated sit-to-stand maneuvers at a frequency of 0.05 Hz for 5 minutes. CA was quantified in the frequency domain by transfer function analysis (CARMNet Matlab script version 1, 2016), and in the time domain by calculating the maximal change in MAP and MCFBV for each sit-to-stand maneuver expressed as absolute values and as percentage of mean MAP and MCFBV. Groups were compared using ANOVA (p < 0.05).

Results: MCFBV was lower in AD (39.6 cm/s) compared to HC (45.1 cm/s, p = 0.033), with MCI subjects in between (41.1 cm/s). The repeated orthostatic maneuvers caused similarly large perturbations in MAP (22.4 mmHg for HC, 18.7 mmHg for MCI subjects and 20.7 mmHg for AD patients, p = 0.161). The absolute and relative changes in MCFBV were larger for HC (15.1 cm/s and 33.1%) compared to MCI subjects (9.7 cm/s and 23.7%, p = 0.002), but not compared to AD patients (11.7 cm/s and 29.9%). For TFA, the normalized gain was similar in HC (1.42%/mmHg), MCI (1.17%/mmHg) and AD (1.31%/mmHg, p = 0.053).

Conclusions: In this study we found no evidence for impaired cerebral auto-regulation in AD patients for large (≥20%) changes in MAP. This would suggest antihypertensive treatment to be safe in AD.

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**OP.1B.08**

**PREVALENCE AND COVARIATES OF UNCONTROLLED HYPERTENSION IN YOUNG AND MIDDLE-AGED ISCHEMIC STROKE SURVIVORS – THE NORWEGIAN STROKE IN THE YOUNG STUDY**


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Objective: Hypertension is the most important modifiable risk factor for stroke. Few data are available on control of hypertension in younger ischemic stroke survivors.

Table 1. Characteristics of the study population according to blood pressure control.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Body mass index (kg/m²)</th>
<th>Carotid plaque (%)</th>
<th>PWV (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&lt;142)</td>
<td>64.5±11.5</td>
<td>51.9±9.1</td>
<td>12.2±6.9</td>
</tr>
<tr>
<td>Controlled (HT &lt;140)</td>
<td>24.8±1.1</td>
<td>27.3±4.2</td>
<td>29.2±7.3</td>
</tr>
<tr>
<td>Uncontrolled (HT &gt;140)</td>
<td>1.4±15.1</td>
<td>15.1±21</td>
<td>15.6</td>
</tr>
<tr>
<td>Uncontrolled (HT &gt;140)</td>
<td>0.9±1.3</td>
<td>0.9±1.7</td>
<td>1.6±2.1</td>
</tr>
</tbody>
</table>

HT, hypertension; *P* <0.05; †P <0.01 versus normal control; ‡P <0.01 versus controlled HT.

Design and method: We assessed clinic and ambulatory blood pressure (BP) measurements of 318 patients aged 15–60 years included in the Norwegian Stroke in the Young Study. Controlled hypertension was defined as clinic BP <140/90 mmHg and ambulatory BP <130/80 mmHg. Carotid-femoral pulse wave velocity (PWV) was measured by applanation tonometry. Carotid plaque was considered present if intima-media thickness >1.5 mm.

Results: At hospital discharge, 57% of patients received antihypertensive treatment. At the 3-month follow-up visit, 45% of these had controlled hypertension. Furthermore, 10% were diagnosed with new-onset hypertension during follow-up. Patients with uncontrolled hypertension were older, had higher body mass index and PWV and more likely to have diabetes and carotid plaques compared to other groups (all p < 0.001) (Table 1). In multivariable logistic regression, presence of uncontrolled hypertension was independently associated with higher PWV and body mass index, carotid plaque, and less use of antihypertensive treatment (all p < 0.05).

Conclusions: Uncontrolled hypertension was highly prevalent in ischemic stroke survivors < 60 years and associated with obesity and functional and structural arterial damage. Our results highlight the unmet potential of optimization of hypertension diagnosis and management in order to prevent recurrent vascular events in ischemic stroke survivors.

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**OP.1B.09**

**NT-PROBNP IS AN INDEPENDENT PREDICTOR OF STROKE IN JAPANESE WITH CARDIOVASCULAR RISK FACTORS**

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Objective: NT-proBNP is a strong prognostic marker in advanced stages of cardiac diseases like heart failure or coronary artery disease (CAD) in Western population. However, little is known whether Asian subjects differ from Western subjects in the prognostic power of NT-proBNP for cardiovascular outcome. We hypothesized that NT-proBNP would be an independent predictor for stroke and CAD events in Asian population considering the reported differences in the rates of cardiovascular events compared with Western population.

Design and method: The J-HOP (Japan Morning Surge-Home Blood Pressure) study included 4310 Japanese with a history of and/or risk factors for cardiovascular disease. We analyzed 3619 patients (mean age 65.0 ± 10.6 years, male 46.1%) who had been measured NT-proBNP at baseline of 4310 patients.

Results: During a mean follow-up of 4.0 ± 2.1 years, 60 stroke and 69 CAD events occurred. When we divided NT-proBNP into quartiles, the incidence of stroke were significantly higher in the highest quartile (NT-proBNP > 97.38 pg/ml; hazard ratio [HR] 6.87; 95% confidence interval [CI] 1.57 to 30.7; P = 0.01) and in the second highest quartile (NT-proBNP 50.48–97.37 pg/ml; HR 4.76; 95% CI 1.07 to 21.24; P = 0.04) compared with the lowest quartile (NT-proBNP < 25.48 pg/ml) after adjusted for conventional cardiovascular risk factors. However, these associations were not found in the incidence of CAD.

Conclusions: NT-proBNP is an independent predictor of future stroke events in Japanese with cardiovascular risk factors. For detecting heart failure, NT-proBNP level >125 pg/ml has been accepted. The slight elevation of NT-proBNP in the current normal range might predict the incidence of stroke in Asian population.

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**OP.1B.10**

**INTRACRANIAL STENOSIS IN FIRST-GENERATION CHINESE MIGRANTS WITH NEWLY DIAGNOSED DIABETES**

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Objective: Ethnic differences might influence the value of current approach to cardiovascular risk stratification. Intracranial atherosclerotic disease was indeed reported as a common cause of ischemic stroke among patients of Asian ancestry and stroke incidence in China is high. However, no study investigated the prevalence of intracranial stenosis (ICS) in Chinese migrants with newly diagnosed DM and the screening of vascular lesions is still mainly focused on the more accessible extracranial carotid artery. Present survey was thus performed to determine the prevalence of intracranial stenosis in Chinese migrants with newly diagnosed diabetes.

Design and method: A cross-sectional community-based survey enrolled Chinese first generation migrants (n = 1200) and native Italians (n = 291) aged 35–59 years. Hypertension was diagnosed according to ESH guidelines. Diagnosis of DM was based on fasting plasma glucose criteria (more than 125 mg/dl confirmed by repeat testing), and/or current treatment with glucose-lowering drugs. Chinese patients with newly diagnosed diabetes were screened for intracranial stenosis using Doppler ultrasound. ICS (any degree of stenosis) was diagnosed when the peak flow velocity at Transcranial Doppler (TCD) was higher than: 120 cm/s for anterior cerebral arteries (ACA); 155 cm/s for middle cerebral arteries (MCA); 100 cm/s for posterior cerebral arteries (PCA); 100 cm/s for basilar artery (BA); 90 cm/s for intracranial vertebral arteries (VA).

Results: DM was diagnosed in 168 (14.0%) and 21 (7.3%) participants in the Chinese and Italian cohorts respectively (age- and gender adjusted OR 2.29; 95% C.L. 1.41 to 3.72). Difference was not reduced when obesity and socioeconomic indexes were included in the model. Ninety-six Chinese patients with newly diagnosed DM accepted to undergo the screening of cerebral vascular lesions. No patient had carotid stenosis of any degree whereas per-person prevalence of intracranial stenosis was 18.2%. Nine out of the 17 patients with any intracranial stenosis (52%) had more than 1 intracranial lesions.

Conclusions: The high prevalence of asymptomatic intracranial stenosis in Chinese patients with newly diagnosed diabetes emphasizes the importance of paying attention to intracranial vessels in this minority group.
ORAL SESSION 1C:
BLOOD PRESSURE VARIABILITY

OP.1C.01 INCREASED BLOOD PRESSURE VARIABILITY PREDICTS ALL-CAUSE MORTALITY IN PATIENTS WITH DIABETES FREE OF CARDIOVASCULAR DISEASE AND NOT ON ANTIHYPERTENSIVE DRUGS

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Objective: Blood pressure variability has been associated with risk of cardiovascular events in observational studies, independently of mean blood pressure (BP) levels. BP variability is typically summarized as the standard deviation (SD), coefficient of variation (CV), or variation independent of mean (VIM), of blood pressure over multiple office blood pressure readings, days apart.

Design and method: Using data from a Swedish primary health care cohort of patients with diabetes, we identified 12,179 patients (2,321 with and 9,858 without pre-existing cardiovascular disease, CVD), who had at least two BP measurements within the first year, did not change BP-lowering treatment during the observation period, and had >0 for calculated variability measures. Patients were followed for a median of four years. Associations of variability measures (SD, CV, VIM) with mortality, adjusting for other risk factors (Framingham Risk Score variables - including mean BP), of blood pressure variability were similar but with wider confidence intervals, when allowance was made for competing causes of mortality. Importantly, addition of the variability measures did not markedly alter the results (Table).

Conclusions: Our results suggest that three measurement days are sufficient for the reliable assessment of morning day-to-day home blood pressure variability.

OP.1C.02 THE NUMBER OF MEASUREMENT DAYS NEEDED TO RELIABLY ASSESS HOME BLOOD PRESSURE VARIABILITY – THE FINN-HOME STUDY

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Objective: Increased home blood pressure variability, and especially morning day-to-day variability, has been recognized as an independent predictor of cardiovascular morbidity and mortality. However, the optimal measurement protocol for assessment of home blood pressure variability is unknown. Our aim was to study how many days of measurement are needed to reliably assess day-to-day morning home blood pressure variability.

Design and method: We studied a population sample of 1736 Finnish adults (mean age: 56 ± 8 years; 54% women). The participants underwent a clinical examination and self-measured their blood pressure at home twice in the morning during seven consecutive days in 2000–2001. Day-to-day variability of morning home blood pressure was calculated based on the mean of the two morning measurements of each day. We used standard deviation as the variability index. We calculated the standard deviation of home morning blood pressure based on two through seven measurement days.

We studied the association between systolic/diastolic blood pressure variability and adverse cardiovascular events using Cox regression models. The primary endpoint was a combination of stroke, hospitalization for heart failure, and major coronary heart disease event, whichever occurred first. Follow-up ended on December 31, 2007. The models were adjusted for age, sex, smoking status, diabetes status, use of antihypertensive treatment, presence of hypercholesterolemia, history of cardiovascular disease, and systolic/diastolic home blood pressure level.

Results: 169 adverse cardiovascular events occurred during follow-up. Systolic and diastolic home blood pressure variability became significantly associated with cardiovascular events after the third measurement day (Table). Hazard ratios for three-day systolic/diastolic blood pressure variability were 1.04/1.06 (confidence interval 1.02–1.07; p = 0.0005/1.01–1.11; p = 0.01) and hazard ratios for seven-day variability were 1.08/1.08 (confidence interval 1.01–1.08; p = 0.01/1.04–1.12; p = 0.03), respectively. The use of more than three measurement days did not markedly alter the results (Table).

Conclusions: Our results suggest that three measurement days are sufficient for the reliable assessment of morning day-to-day home blood pressure variability.

OP.1C.03 DISPERSION OF VENTRICULAR REPOLARIZATION IN RELATION TO BLOOD PRESSURE VARIABILITY IN ARTERIAL HYPERTENSION

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Objective: To evaluate T peak - T end (Tpe) interval and Tpe/QT ratio in relation to blood pressure variability values in hypertensive patients.

Design and method: 57 consecutive patients with mild to moderate hypertension, without coronary heart disease, 45.6% men, mean age 55 ± 12 years, were included and evaluated simultaneously by Holter electrocardiography and ambulatory blood pressure monitoring (ABPM) for 24 hours. Holter ECG monitoring was performed with a true 12 lead continuous recording device and used for manual measuring of the dispersion of ventricular repolarization parameters. Tpe was defined as the interval between the peak and end of the T wave and was measured in the precordial leads. The end of the T wave was measured by the method of the tangent to the steepest slope of the descending portion of the T wave. Tpe was corrected for heart rate using Bazett formula. Mean and maximum Tpe and Tpe/QT ratio were calculated. Blood pressure variability was assessed using the 24 hours, daytime and nighttime standard deviation (SD) of the systolic (SBP) and diastolic blood pressure (DBP) values measured by ABPM.

Results: Mean Tpe was 69.2 ± 9.8 ms, maximum Tpe was 81.4 ± 13.4 ms. Mean Tpe/QT was 0.17 ± 0.02, maximum Tpe/QT was 0.20 ± 0.02. Mean 24 hours SBP SD was 14.9 ± 4.2 mm Hg, mean 24 hours DBP SD was 13.5 ± 5.2 mm Hg. Daytime SBP SD was 14.3 ± 4.7 mm Hg, daytime DBP SD was 13 ± 6.6 mm Hg. Nighttime SBP SD was 10.6 ± 3.4 mm Hg, nighttime DBP SD was 8.8 ± 3.7 mm Hg. Nighttime DBP SD showed significant correlations with mean Tpe (r = 0.41, p = 0.001) and mean Tpe/QT ratio (r = 0.40, p = 0.001).

Conclusions: Nighttime diastolic blood pressure variability correlates with Tpe interval and Tpe/QT ratio, well known noninvasive markers of arrhythmic risk.
Objective: The mechanisms underlying the associations between (pre)diabetes and cardiovascular disease (CVD) are incompletely understood. We hypothesize that greater blood pressure variability (BPV) may underlie this association, as greater BPV is associated with (incident) CVD. However, data on BPV in (pre)diabetes is scarce. Therefore, we investigated the association between (pre)diabetes and within-visit, 24-hour and 7-day BPV.

Design and method: Cross-sectional data from The Maastricht Study (N = 3451, 1924 with normal glucose metabolism [NGM], 511 with prediabetes and 516 with type 2 diabetes [T2D], 51% men, aged 60 ± 8 years), an observational population-based cohort study enriched with individual cardiovascular risk factors, was analyzed. In T2D, the average systolic/diastolic values of within-visit, 24-hour and 7-day BPV were: 4.8/2.6, 10.5/7.3, and 10.4/6.5 mmHg, respectively and in prediabetes and NGM, 5.0/2.6, 10.3/7.0, and 10.4/6.5 mmHg, respectively. We additionally analyzed 24-hour BPV divided into day (09:00 h–21:00 h) and night (01:00 h–06:00 h). Differences in BPV as compared to NGM were assessed with multiple linear regression, adjusted for age, sex, mean systolic or diastolic blood pressure, smoking status, alcohol use, body mass index, prior CVD, lipid profile, use of lipid-modifying and antihypertensive medication, and estimated glomerular filtration rate.

Results: In T2D, the average systolic/diastolic values of within-visit, 24-hour and 7-day BPV were: 4.8±2.6, 10.5±7.3 and 10.4±6.5 mmHg, respectively and in prediabetes and NGM, 5.0±2.6, 10.3±7.0 and 10.4±6.5 mmHg, respectively. Adjusted analyses showed that T2D was associated with greater nocturnal systolic BPV (AR V = 0.42 mmHg [95% CI: 0.05–0.80]) and greater 7-day systolic BPV (SD 0.76 mmHg [0.35–0.65]) as compared to NGM. Prediabetes was associated with greater within-visit systolic BPV only (SD 0.35 mmHg [0.06–0.65]) as compared to NGM.

Conclusions: Both prediabetes and T2D are associated with greater very-short to mid-term BPV. Nevertheless, the slightly greater BPV seen in both prediabetes and T2D as compared to NGM suggest that very-short to mid-term BPV may explain not only a small part of the increased CVD risk associated with glucose metabolism status. These findings do not detract from the fact that very-short to mid-term BPV is substantial and important in individuals with and without (pre)diabetes.
**Design and method:** In 1997 all adult population of Didima, Argolida, Greece was invited to participate in a study involving office (2 visits, 6 readings) and home (3 days, 12 readings) BP measurements. Cardiovascular morbidity and mortality were assessed after 19.0 ± 1.4 years (2016). Standard deviation (SD) and coefficient of variation (CV) of home and office BP were used to quantify BPV.

**Results:** 665 participants (age 54.4 ± 17.7 years, 42% men) were analyzed. During follow-up 216 deaths (124 cardiovascular) and 146 cardiovascular events (fatal and non-fatal) were documented. In Cox regression models, all indices of systolic home BPV were predictive of cardiovascular risk, even after adjustment for all available cardiovascular risk factors (adjusted HR 1.05 for 1% increase in systolic home BPV and 1.06 for 1% increase in percentage CV; all p < 0.05). The HR for SD (but not CV) of diastolic home BPV significantly predicted cardiovascular outcome, yet it lost statistical significance after adjustment for several cardiovascular risk factors (adjusted HR 1.03 for 1% increase in BPV, p = NS). For office BP, only unadjusted indices of BPV were predictive of cardiovascular risk (adjusted HR 1.01/1.03 for a 1% SD increase in systolic/diastolic BPV and 1.02/1.02 for 1% increase in percentage CV, all p = NS). In Cox model including CVs of both home and office systolic BP as independent variables, CV of home BP remained a significant predictor of cardiovascular outcome independent of office BPV.

**Table.** Cox regression models with variability indices of home and office BP measurements (Hazard ratios unadjusted/adjusted, *p* < 0.05; *p* < 0.01).

<table>
<thead>
<tr>
<th>Variable</th>
<th>SD</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic home BPV</td>
<td>1.13/1.05</td>
<td>1.10/1.06</td>
</tr>
<tr>
<td>Systolic office BPV</td>
<td>1.10/1.01</td>
<td>1.09/1.02</td>
</tr>
<tr>
<td>Diastolic home BPV</td>
<td>1.06/1.03</td>
<td>1.02/1.02</td>
</tr>
<tr>
<td>Diastolic office BPV</td>
<td>1.09/1.03</td>
<td>1.05/1.02</td>
</tr>
</tbody>
</table>

**Conclusions:** In this long-term general population outcome study, both home and office BPV independently predicted cardiovascular events, with indices of home systolic BPV exhibiting superior prognostic ability.

**OP.1C.08 RELATIONSHIP BETWEEN WITHIN-VISIT BLOOD PRESSURE VARIABILITY AND SKELETAL MUSCLE MASS**

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**Objective:** Sarcopenia, defined as loss of skeletal muscle mass and function with age, is an important health issue in aging society. Although, hemodynamic factor is considered to be an important contributor in the development of sarcopenia, there have been very few studies regarding this topic. Thus, we tried to investigate the relationship between blood pressure variability and skeletal muscle mass in nation-wide large population cohort.

**Design and method:** This cross-sectional study was based on data acquired in the Korea National Health and Nutrition Examination Survey (KNHANES), conducted from 2009 to 2011 by the Korean Centers for Disease Control & Prevention. We included 14,482 participants (male 6,392, aged 20 years or older) for the analysis who had both blood pressure and whole-body dual energy X-ray absorptiometry (DXA) scan data. As an intra-individual within-visit blood pressure variability index, we calculated standard deviation (SD), coefficient of variation (CV), and maximum minus minimum BP difference (MMD) of systolic and diastolic blood pressure, which was measured 3 times. Appendicular skeletal muscle mass (ASM) was the sum of lean masses of both arms and legs. We adjusted ASM by height^2, weight, and body mass index.

**Results:** Significant inverse relationship was observed between blood pressure variability index (SD, CV, and MMD) and adjusted ASM. Blood pressure variability index were significantly higher in the lowest ASM quintile group both in male and female participants (p < 0.001). In multivariate analysis, blood pressure variability index were significantly associated with ASM, even after adjusting confounding factors (p < 0.001).

**Conclusions:** Using the national representative database, we showed significant inverse relationship between within-visit blood pressure variability and skeletal muscle mass in Korean population. Considering the underlying mechanism of increased blood pressure variability, hemodynamic influence may play an important role in the development of sarcopenia.
**OP.1C.11**

INITIAL ORTHOSTATIC HYPOTENSION ASSOCIATED WITH THE USE OF ANTIHYPERTENSIVE DRUGS IS HIGHLY PREVALENT IN PATIENTS WITH UNEXPLAINED SYNCOPE

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2Department of Internal Medicine; Maastricht University Medical Centre, Maastricht, The Netherlands
3Department of Cardiology; Maastricht University Medical Centre, Maastricht, The Netherlands

**Objective:** The prevalence of initial orthostatic hypotension (IOH) as a cause of syncope is unknown. IOH is defined as a transient decrease in blood pressure (BP) within 15 seconds after standing of >40 mmHg systolic and/or >20 mmHg diastolic, with symptoms of cerebral hypoperfusion, but without suspect alternative diagnosis. Two patients did not meet the BP criteria, but history taking also indicated IOH. Thus, 17 patients (10.8%) were diagnosed with IOH, of whom 59% used antihypertensive drugs (mostly beta-blockers). The squatting-to-standing test (n = 107) did not increase the number of patients diagnosed with IOH.

**Results:** Beat-to-beat-BP data were available for 157 patients (mean age 61.1 ± 18.6 years, BP 137 ± 18/83 ± 10 mmHg, 57% female). Clinical diagnoses for the cause of syncope are shown in the Table. Upon active standing, 78 patients (49.7%) met the BP criteria for IOH (mean -47.2 ± 14.5/29.0 ± 11.6 mmHg within 15 seconds after standing). Of those 78 patients, 15 patients had sustained orthostatic hypotension, 29 did not report symptoms of hypoperfusion, and in 19 patients history or additional tests revealed an alternative diagnosis. Two patients did not meet the BP-criteria, but history taking also indicated IOH. Thus, 17 patients (10.8%) were diagnosed with IOH, of whom 59% used antihypertensive drugs (mostly beta-blockers). The squatting-to-standing test (n = 107) did not increase the number of patients diagnosed with IOH.

**Conclusions:** IOH is highly prevalent in patients with unexplained syncope and is associated with the use of antihypertensive drugs in the majority of patients.

---

**Table:** Causes of syncope

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflex syncope</td>
<td>53 (32.5%)</td>
</tr>
<tr>
<td>Initial orthostatic hypotension</td>
<td>17 (10.8%)</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>35 (9.6%)</td>
</tr>
<tr>
<td>Locomotor abnormalities (no syncope)</td>
<td>13 (8.3%)</td>
</tr>
<tr>
<td>Heart rhythm /structural cardiac abnormalities</td>
<td>8 (5.1%)</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>6 (3.8%)</td>
</tr>
<tr>
<td>Psychogenic /hyperventilation</td>
<td>5 (3.2%)</td>
</tr>
<tr>
<td>Vestibular dysfunction</td>
<td>4 (2.5%)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Autonomic dysfunction</td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Other/multifactorial</td>
<td>15 (9.6%)</td>
</tr>
<tr>
<td>Unexplained</td>
<td>17 (10.8%)</td>
</tr>
</tbody>
</table>

Diagnosis in 157 outpatients with previously unexplained syncope after evaluation in a multidisciplinary syncope unit in a tertiary health care centre.

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**Design and method:** We prospectively collected data from all outpatients that were evaluated in our syncope-unit between September 2015 and November 2016. All patients were evaluated by two syncope-experts (a cardiologist and either a neurologist or an internal/vascular medicine specialist) and underwent a standard diagnostic protocol, including echocardiography, electrocardiography, and laboratory testing, as well as a beat-to-beat BP measurement using a Nexfin device (BMEYE, The Netherlands). We measured hemodynamic changes after active standing, first after lying supine for >5 minutes and then after squatting for 30 seconds. Symptoms of cerebral hypoperfusion were noted. If considered clinically indicated long-term rhythm-monitoring, cardiac exercise test, head-up-tilt-table-testing, electroencephalography, or additional imaging was performed.

**Results:** Beat-to-beat-BP data were available for 157 patients (mean age 61.1 ± 18.6 years, BP 137 ± 18/83 ± 10 mmHg, 57% female). Clinical diagnoses for the cause of syncope are shown in the Table. Upon active standing, 78 patients (49.7%) met the BP criteria for IOH (mean -47.2 ± 14.5/29.0 ± 11.6 mmHg within 15 seconds after standing). Of those 78 patients, 15 patients had sustained orthostatic hypotension, 29 did not report symptoms of hypoperfusion, and in 19 patients history or additional tests revealed an alternative diagnosis. Two patients did not meet the BP-criteria, but history taking also indicated IOH. Thus, 17 patients (10.8%) were diagnosed with IOH, of whom 59% used antihypertensive drugs (mostly beta-blockers). The squatting-to-standing test (n = 107) did not increase the number of patients diagnosed with IOH.

**Conclusions:** IOH is highly prevalent in patients with unexplained syncope and is associated with the use of antihypertensive drugs in the majority of patients.

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**OP.1C.12**

VISIT-TO-VISIT BLOOD PRESSURE VARIABILITY IS RELATED TO SYMPATHETIC NEURAL DRIVE AND BAROREFLEX SENSITIVITY IN HYPERTENSIVE PATIENTS

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**Objective:** Neurogenic mechanisms have been shown to regulate not only absolute blood pressure levels but also blood pressure variability during the short-term 24 hour period. No information are available on whether visit-to-visit blood pressure variability is related to sympathetic and baroreflex function.

**Design and method:** 61 untreated essential hypertensive patients aged 56.1 ± 2.5 years (mean ± SEM) underwent 3 clinic BP measurements on 3 occasions during a 6 weeks period. In each patient we assessed muscle sympathetic nerve traffic (MSNA, microneurography), spontaneous MSNA-baroreflex sensitivity according to Kienbaum method, and blood pressure variability of systolic and diastolic BP, quantified as coefficient of variation (CV) and as standard deviation (SD) of the BP values.

**Results:** Patients were subdivided into CV and SD quartiles. Quartiles matched for age and gender. For each quartile a relationship was sought with CV and SD quartiles. Compared with the patients in the lowest systolic BP CV quartile, patients in the highest quartile showed significantly greater MSNA (62.5 ± 4 vs 48.2 ± 3 bursts/100 heart beats, P < 0.02) and significantly lower baroreflex sensitivity values (1.23 ± 0.2 vs 2.09 ± 0.2 a.u., P < 0.03). This was the case also when BP variability was expressed as SD. When diastolic BP was considered, no significant difference between quartiles was found.

**Conclusions:** These data provide the first demonstration that in hypertension a greater visit-to-visit blood pressure variability is associated with greater levels of sympathetic activation and more pronounced baroreflex dysfunction. The relationship appears to be valid particularly for the systolic BP component. Thus sympathetic and reflex mechanisms contribute not only to the short-term but also to the long-term BP variability phenomenon.

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**Table:** Causes of syncope

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflex syncope</td>
<td>53 (32.5%)</td>
</tr>
<tr>
<td>Initial orthostatic hypotension</td>
<td>17 (10.8%)</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>35 (9.6%)</td>
</tr>
<tr>
<td>Locomotor abnormalities (no syncope)</td>
<td>13 (8.3%)</td>
</tr>
<tr>
<td>Heart rhythm /structural cardiac abnormalities</td>
<td>8 (5.1%)</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>6 (3.8%)</td>
</tr>
<tr>
<td>Psychogenic /hyperventilation</td>
<td>5 (3.2%)</td>
</tr>
<tr>
<td>Vestibular dysfunction</td>
<td>4 (2.5%)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Autonomic dysfunction</td>
<td>3 (1.9%)</td>
</tr>
<tr>
<td>Other/multifactorial</td>
<td>15 (9.6%)</td>
</tr>
<tr>
<td>Unexplained</td>
<td>17 (10.8%)</td>
</tr>
</tbody>
</table>

Diagnosis in 157 outpatients with previously unexplained syncope after evaluation in a multidisciplinary syncope unit in a tertiary health care centre.

---

**Design and method:** We prospectively collected data from all outpatients that were evaluated in our syncope-unit between September 2015 and November 2016. All patients were evaluated by two syncope-experts (a cardiologist and either a neurologist or an internal/vascular medicine specialist) and underwent a standard diagnostic protocol, including echocardiography, electrocardiography, and laboratory testing, as well as a beat-to-beat BP measurement using a Nexfin device (BMEYE, The Netherlands). We measured hemodynamic changes after active standing, first after lying supine for >5 minutes and then after squatting for 30 seconds. Symptoms of cerebral hypoperfusion were noted. If considered clinically indicated long-term rhythm-monitoring, cardiac exercise test, head-up-tilt-table-testing, electroencephalography, or additional imaging was performed.

**Results:** Beat-to-beat-BP data were available for 157 patients (mean age 61.1 ± 18.6 years, BP 137 ± 18/83 ± 10 mmHg, 57% female). Clinical diagnoses for the cause of syncope are shown in the Table. Upon active standing, 78 patients (49.7%) met the BP criteria for IOH (mean -47.2 ± 14.5/29.0 ± 11.6 mmHg within 15 seconds after standing). Of those 78 patients, 15 patients had sustained orthostatic hypotension, 29 did not report symptoms of hypoperfusion, and in 19 patients history or additional tests revealed an alternative diagnosis. Two patients did not meet the BP-criteria, but history taking also indicated IOH. Thus, 17 patients (10.8%) were diagnosed with IOH, of whom 59% used antihypertensive drugs (mostly beta-blockers). The squatting-to-standing test (n = 107) did not increase the number of patients diagnosed with IOH.

**Conclusions:** IOH is highly prevalent in patients with unexplained syncope and is associated with the use of antihypertensive drugs in the majority of patients.
ORAL SESSION 2A:
GENETICS, GENOMICS, PROTEOMICS, METABOLOMICS

OP.2A.01 IMPACT OF A 29 SNPS-BASED GENETIC RISK SCORE FOR HYPERTENSION ON AORTIC DISEASE

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Objective: A genetic risk score (GRS) based on 29 SNPs associated with high blood pressure (BP) was shown to be associated with future development of hypertension, stroke and cardiometabolic events. Aim of the present study is to evaluate the impact of this polygenic BP component on the occurrence of aortic disease, namely aortic dissection (AD), thoracic aorta aneurysm (TAA), abdominal aorta aneurysm (AAA), including possible events (either rupture or need of surgical correction).

Design and method: More than 27,000 people in the Swedish Malmo Diet and Cancer Study had at least 24 valid SNPs and were followed up for a median of more than 18 years. The number of BP elevating alleles of each SNPs, weighted by their effect size in the discovery studies, was summed into a BP-GRS.

Results: In Cox regression models, adjusted for traditional cardiometabolic risk factors (TRF) including hypertension, we found a significant associations of the BP-GRS, prospectively, with incident TAA (hazard ratio 1.32; 95% confidence interval (CI) 1.06–1.24 comparing the third vs. first tertile; P=0.015) but not with either AAA or aortic dissection. Calibration, discrimination and reclassification analyses did not show any improvement in prediction using the BP-GRS in addition to the model which used only the TRF.

Conclusions: A GRS for hypertension associates with TAA suggesting a link between genetics determinat of BP and aortic disease. The effect size is small but the addition of more SNPs to the GRS could improve its discriminatory capability.

OP.2A.02 FURTHER REDUCTION OF THE WIDTH OF STROKE-SUSCEPTIBILITY QUALITATIVE TRAIT LOCI AND IDENTIFICATION OF CANDIDATE GENES IN THE STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RAT

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Objective: In the previous study, we identified two major quantitative trait loci (QTLs) for stroke susceptibility on chr 1 and 18 in the stroke-prone spontaneously hypertensive rat (SHRSP). Most of difference in stroke susceptibility between SHR and SHRSP was explained with these two QTLs. In this study, we attempted to narrow down the QTL regions, and to identify candidate genes in the target regions.

Design and method: Sixteen subcongenic and double subcongenic strains were established to cover the QTLs on chr 1 and 18. Stroke susceptibility was evaluated by stroke latency under 1% salt loading. Sequence variations in coding regions of established to cover the QTLs on chr 1 and 18. Stroke susceptibility was evaluated by stroke latency under 1% salt loading. Sequence variations in coding regions of genes were analyzed on whole-genome sequence data of SHRSP and SHR, and confirmed with direct sequencing. Comprehensive gene expression analysis was performed on the complete genome sequence data suggested that 2 genes in this candidate region harbored a missense variant between SHR and SHRSP. In contrast to the QTL on chr 1, it was difficult to narrow down the QTL on chr 18.

Conclusions: In conclusion, we successfully narrowed down the QTL on chr 1 and identified several candidate genes in the region. The QTL on chr 18 might harbor multiple causative genes that made the analysis difficult.

OP.2A.03 PROTEOMIC ANALYSIS REVEALS ALTERED PATHWAYS FROM EARLY STAGES OF THE DEVELOPMENT OF HYPERTENSIVE NEPHROPATHY IN SHR

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Objective: Hypertensive nephropathy, a leading cause of declining kidney function is a multi-factorial process not well understood. Therefore system biology approaches should be adopted for a better understanding of the molecular pathways involved.

Design and method: Proteomics studies were performed using the renal parenchyma of spontaneously hypertensive rats (SHR) and their normotensive counterparts (Wistar Kyoto (WKY) rats. Animals were sacrificed at early time intervals (6, 13, and 20 weeks after birth), renal tissue extracts were subjected to two-dimensional gel electrophoresis, differentially expressed proteins were identified and altered pathways were evaluated by using Ingenuity Pathway Analysis.

Results: The SHR group of animals reached and maintained mean BP of approximately 160–170 mmHg at all time intervals, while the WKY animals remained normotensive. As seen in the following Table, proteomic analysis revealed numerous spots with altered expression at 6, 13 and 20 weeks. Protein characterization followed by pathway analysis revealed that different processes are affected at different age.

Conclusions: Proteomic analysis followed by pathway analysis revealed that in the SHR model of hypertensive nephrosclerosis, early changes follow a pattern of progression from oxidative stress, mitochondrial dysfunction and receptor function to apoptosis pathways and alterations in cellular junctions. This work was supported from an ARISTEIA II grant (number 4045) to D. Vlahakos from the General Secretariat of Research and Technology of the Greek Ministry of Education.

OP.2A.04 EPIGENETIC REGULATION OF HYPERTENSION: STRAIN-SPECIFIC SILENCING OF A RAT ANGIONTENSINOGEN TRANSGENE IN MICE

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Objective: Understanding the mechanisms of hypertension requires a comprehensive understanding of how genetic susceptibility affects the development of the disease. The angiotensinogen gene (AGT) is one such gene, which is implicated in the pathogenesis of hypertension. The aim of this study is to investigate the epigenetic regulation of AGT in two different mouse strains, SHR and WKY, in order to identify strain-specific differences in the gene expression.

Design and method: The study involved the analysis of gene expression in the kidneys of SHR and WKY mice using microarray analysis. The data was then analyzed to identify strain-specific differences in gene expression.

Results: The results of the microarray analysis showed that there were significant differences in gene expression between the two strains. The analysis also showed that there were strain-specific differences in the expression of AGT, which is consistent with the hypothesis that AGT plays a role in the development of hypertension.

Conclusions: The results of this study provide evidence for the epigenetic regulation of AGT in the development of hypertension. Future studies could further investigate the role of AGT in hypertension, and the potential for epigenetic interventions to treat the disease.
Objective: The renin-angiotensin system (RAS) is the most important system regulating blood pressure and, therefore, the major target for the treatment of hypertension. Angiotensinogen (AOGEN) is the only precursor of all peptides of the RAS. The role of epigenetic factors in AOGEN regulation still remains unclear.

Design and method: In 1992, Kamura and colleagues generated a transgenic mouse overexpressing rat AOGEN under the control of its own promoter (TGM(rAOGEN)123). These mice exhibit increased angiotensin II levels, and, consequently, high blood pressure and end-organ damage as early as at 8 weeks of age. We backcrossed this mouse, originally generated on the outbred genetic background, NMRI, to two distinct genetic backgrounds, FVB/N and C57BL/6. Similar to the NMRI background, 123FVB/N mice showed a drastic increase in blood pressure (158 ± 3.2 mmHg in FVB/N wildtype). However, 123C57BL/6 mice lost the hypertensive phenotype and showed only a mild increase in blood pressure (113.2 ± 0.3 mmHg in C57BL/6 wildtype mice), indicating that the C57BL/6 background has a protective effect.

Results: Analysis of the rat AOGEN mRNA levels revealed a drastic downregulation of transgene expression on the C57BL/6 background. To understand the mechanisms leading to transgene silencing we studied epigenetic modifications of the transgenic mouse. Indeed, several CpG islands in the 800 bp regulatory region of the rat AOGEN gene were hypermethylated on the C57BL/6 background compared to FVB/N. A genome-wide association study in an F2 generation intercross of the two transgenic mouse strains revealed a 6.4 Mb locus containing 66 genes, on chromosome 13 with significant linkage to the hypertensive phenotype.

Conclusions: These data indicate that hypermethylation of the rat AOGEN gene promoter leads to downregulation of its expression and the loss of the hypertensive phenotype on the C57BL/6 background. Further studies are in progress to identify the gene(s) on chromosome 13 responsible for the protective effect.

OP.2A.05 LANOSTEROL SYNTHESE GENE POLYMORPHISMS IMPACT THE DECLINE IN RENAL FUNCTION AMONG HYPERTENSIVE PATIENTS


Objective: Cholesterol is an essential component of mammalian cell membranes and serves as a precursor for bile acids and various steroid hormones. Lanosterol, the first committed intermediate in cholesterol biosynthesis, is coded by the Lanosterol Synthase gene (LSS) with a missense polymorphism that affects E0 biosynthesis in adrenocortical cells. Recently, we reported that the LSS AA genotype is associated with salt-sensitive hypertension. Exposure to increased circulating E0 causes glomerular damage, and is a risk factor for acute kidney injury. In this report, we explore the importance of LSS in the progression of chronic kidney disease (CKD).

Design and method: A cohort of 338 naïve hypertensive patients (f 162, m 176, age 42.7 ± 8.41 years), were enrolled in a prospective follow-up study (5.32 ± 4.37 years) in which blood pressure values were kept at goal with ACEi plus diuretic and, when needed, a Ca2+ channel antagonist.

Results: Blood pressure values (SBP/DBP) after 4.6 years of follow-up were at target for all patients with no difference according to genetic polymorphism (LSS AA 138/85 AC 137/87 CC 137/87, respectively). The slope in eGFR (CKD-EPI) was 1.43 ± 0.47 ml/1.73m2/yr in the whole studied population. When analysed according to the LSS genotype, the decline in renal function was double in the AA homozygotes (LSS AA -2.01 ± 2.4 vs CC 2.23 ± 1.20 ml/1.73m2/yr; p = 0.024). The impact of such LSS polymorphism was also reflected in renal survival analysis (p = 0.001).

Conclusions: Our findings further support the role of LSS polymorphisms in the progression of CKD. This metabolic pathway may accelerate the decline in renal function via its effects on glomerular podocyte and tubular components.

OP.2A.06 QUANTIFICATION OF URINARY PROTEIN LEVELS OF PODOCYTE ASSOCIATED MOLECULES IN HYPERTENSIVE PATIENTS WITH MICROALBUMINURIA

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Objective: Microalbuminuria is an indicator of early renal and vascular disorders. Decrease in podocyte number is a critical determinant contributing to the development of proteinuria. We hypothesize that urinary protein levels of podocyte-associated molecules could be related with an early glomerular injury. Thus, the objective of this study was to quantify the protein and mRNA levels of podocalyxin and nephrin in urinary sediment of hypertensive patients with microalbuminuria.

Design and method: This prospective study analyzed 21 hypertensive patients with microalbuminuria (12 men and 9 women, mean age 52.7 ± 6.4 years), and 31 hypertensive patients without microalbuminuria (21 men and 10 women, mean age 53.2 ± 7.4 years). We quantified mRNA and protein levels of podocyte-associated molecules (podocalyxin and nephrin), and aquaporin-1, as renal tubular control, by quantitative PCR and immunoblot in the urinary sediment of these patients. Then, we correlated urinary protein levels with clinical parameters.

Results: Urinary protein levels of podocalyxin and nephrin were significantly augmented in microalbuminuric group compared to normalalbuminuric [3.0-fold change, p < 0.001; and 2.7-fold change, p < 0.001, respectively]. Whereas, mRNA levels of nephrin showed a significant decrease (2.9-fold change, p < 0.01) and podocalyxin mRNA values were similar in microalbuminuric patients. Aquaporin-1 values were not different between groups. Podocalyxin and nephrin protein levels were correlated with mRNA expression in microalbuminuric patients (r = 0.53, p < 0.01, and r = 0.74, p < 0.001, respectively). Further, urinary podocalyxin and nephrin protein levels were associated with urinary protein/creatinine levels in microalbuminuric patients (r = 0.74, p < 0.01; and r = 0.68, p < 0.05, respectively). Finally, mRNA nephrin levels were also correlated significantly with urinary protein/creatinine ratio (r = 0.73, p < 0.05).

Conclusions: Protein levels of podocyte associated molecules are higher in urinary sediment of hypertensive patients with microalbuminuria and mRNA expression were diminished, indicating a podocyte damage. Urinary podocalyxin and nephrin are correlated with clinical parameters such as proteinuria. Protein levels of podocyte associated molecules could be a valuable method for studying an early glomerular injury in these patients.

OP.2A.07 RNASEQ STUDY OF SALT STRESS PATHWAYS IN RENAL TUBULE REVEALS INCREASED EXPRESSION OF HEAT SHOCK GENES INVOLVED IN SALT SENSITIVE HYPERTENSION

L. Graham, A. Aman, D. Campbell, A. Dominiczak, S. Padmanabhan. University of Glasgow, Glasgow, United Kingdom

Objective: Among the environmental factors that contribute to hypertension, excessive salt intake is the most common and important risk factor. Although, the specific pathways involved in salt tolerance in the renal tubules is not well defined, metabolomic studies in bacteria, yeasts, and human cell lines report lower glycolysis, tricarboxylic acid cycle, branched-chain amino acid metabolism and heme biosynthesis responding to salt challenge. However, to date there are no studies on transcriptome response in renal tubules to salt stress. Here we aimed to delineate the hyperosmotic salt stress pathways in renal tubules.

Design and method: Tall Ascending Limb (TAL) tubules were isolated from s129 mice, and treated with NaCl (300mOsMol) or no treatment (n = 3 per group). Total RNA was isolated and RNA-Seq performed using the NextSeq 500 platform operating 2x75 bp paired end cycles (33 million reads per sample). Raw read files were adapter trimmed and quality filtered using Cutadapt, to produce reads with mean quality score no less than 20 using Sanger quality scores. Differentially expressed genes were identified using the DESEQ2 R package, and significant pathways identified using Gene Set Analysis (GSA). Genes for PIANO enrichment were accepted as differentially expressed if the adjusted p-values calculated using DESEQ2 were less than 0.01. Significant pathways were identified as those where the Benjamin-Hochberg adjusted p-values were below a threshold of 0.05, at a false detection rate of 0.1.
Results: Twelve genes were significantly associated with the salt stress treatment. Heat maps revealed an upregulation of heat shock genes and a down regulation of drug membrane transport genes during salt loading. Gene set enrichment revealed the greatest changes occurred in the expression of two heat shock genes: Hspa1a (Log2 fold change 4.35, p = 2.48e–12) and Hspa1b (Log2 fold change 4.05, p = 2.48e–12).

Conclusions: Our results are the first to show that hyperosmotic salt stress in renal tubules alters the transcriptome, leading to an over expression of heat shock genes in the kidney. These genes have been shown to increase NaCl reabsorption and urea content in the medullary region of the kidney, contributing to salt sensitive hypertension.

OP.2A.08
RELATIONSHIP BETWEEN SELECTED DNA POLYMORPHISMS AND CORONARY ARTERY DISEASE COMPLICATIONS

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Objective: Coronary heart disease (CHD) development is complex in origin, with contributions from well-defined lifestyle and not well-determined genetic risk factors. The aim of this study is to report the relationship between certain SNPs and the risk of cardiovascular (CV) complications in patients with CAD confirmed by coronary angiography.

Design and method: In the present study, 1345 subjects with CHD were included. The median follow-up period was 8.6 years. 19 SNPs were investigated for any association with Major Advanced CV Events (MACE), Acute Coronary Syndromes (ACS) and Revascularizations. We modelled the 19 SNPs as a multi-locus genetic risk score (GRS19).

Results: During follow-up period, 245 participants died; 114 due to CV causes. A fatal or non-fatal CV event occurred in 882 participants including 214 ACS, 578 revascularizations and 90 strokes. The alleles of the following SNPs: rs1746048 (CXCL12), rs9818870 (MRAS) and rs17114036 (PAP2B) were associated with a higher risk of MACE and the alleles of SNPs rs1746048 (CXCL12) and rs122608 (LDLR) were associated with a higher risk of revascularization. The alleles of rs12190287 (MRAS), rs121902287 (TCF21) and rs2259816 (HNF1a) were associated with a higher risk of ACS. Despite the lack of relationship between significant CAD and GRS19, in the top quartile of GRS19 there was significant relationship between GRS19 and combined endpoint, MACE, ACS, and revascularization.

Conclusions: The SNPs of CXCL12 and LDLR were associated with risk of revascularization and CXCL12, LPA, MRAS, PAP2B were associated with the risk of MACE. GRS19 determines CV complications in CAD patients with the highest genetic risk score values.

OP.2A.09
VARIABILITY OF LENGTH OF TELOMERES IN WOMEN WITH BREAST CANCER AND DIFFERENT HYPERTENSIVE STATUS DURING ANTICANCER TREATMENT

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Objective: to assess variability of the length of telomeres in leucocytes in women with breast cancer (BC) and different hypertensive status during anticancer treatment

Design and method: The study included 68 women aged 48.8 ± 10.1 years with triple negative BC. All participants underwent medical examination by oncolgist and cardiologist, including assessment of cardiovascular risk factors, clinical analyses, electrocardiogram, echocardiography, office blood pressure evaluation, ambulatory blood pressure monitoring with blood sampling for measuring the length of telomeres before (n = 68) and after (n = 46) anticancer treatment. The length of telomeres in leucocytes was measured by quantity RT-PCR method. The length of telomere repeat in each sample was measured three times. With 10% variations in one sample measurement repeated. The results are shown as percentage against calibrator. The length of telomeres was compared with the one in the group of clinically healthy women (142 persons) of different age groups. All women were prescribed chemotherapy for eight cycles, including paclitaxel, doxorubicin and cisplatin.

Results: Telomere repeats were initially lower by 22.4 ± 3.6% (p < 0.001) in patients with BC compared with women without hypertension (p = 0.003) compared with women without hypertension after chemotherapy.

Conclusions: Reduction in the relative length of telomeres is higher in patients with BC than in healthy women population of the same age group and can be associated with the presence of hypertension after chemotherapy.
Results: The survey included 6379 subjects and analysis based on 2370 treated hypertensives. The onset of treatment was less than 2 years in 7% of subjects and the median follow-up duration of treatment was 10 years. Perfect compliance was observed in 64% of subjects. Independent determinants of non-compliance are: male sex, young age, number of antihypertensive tablet, treatment for a metabolic disease (diabetes, dyslipidemia), presence of other chronic illness, secondary prevention of cardiovascular disease. To get the risk class of nonobservance a web page is available at http://www.comitehta.org/flahs-observance-hta/

Conclusions: The development of the FLAHS Compliance Test is a tool whose use is possible during an office visit. Its free availability for French doctor will be one of the actions undertaken as part of the “call for action for adherence in hypertension” proposed by the French Society of Hypertension in 2017.

Objective: The FLAHS surveys are carried out by self-questionnaire on a sample of the general population living in metropolitan France) sampling frame. In 2015, FLAHS was conducted in five regions of France. A random sample of 6,519 people was selected among which 5,074 participated (participation rate 77.6%). The survey included 6379 subjects and analysis based on 2370 treated hypertensives. The onset of treatment was less than 2 years in 7% of subjects and the median follow-up duration of treatment was 10 years. Perfect compliance was observed in 64% of subjects. Independent determinants of non-compliance are: male sex, young age, number of antihypertensive tablet, treatment for a metabolic disease (diabetes, dyslipidemia), presence of other chronic illness, secondary prevention of cardiovascular disease. To get the risk class of nonobservance a web page is available at http://www.comitehta.org/flahs-observance-hta/
drugs; meanwhile, polytherapy often results in poor therapeutic adherence, classified as “pseudo-resistant” hypertension. In this context, Therapeutic Drug Monitoring (TDM) of antihypertensive drugs, which consists in the measurement of drug concentration in biological matrices, may help to discern problems in drug pharmacokinetics/pharmacodynamics from cases of poor therapeutic adherence, also considering that not-pharmacological alternative consists in invasive surgery. It has been hence validated an UHPLC-MS/MS method for simultaneous TDM on plasma samples of ten antihypertensive drugs: amlopidine, atenolol, clonidine, chlortalidone, doxazosin, hydrochlorothiazide, nifedipine, olmesartan, ramipril and telmisartan.

Design and method: This method has been validated according to FDA guidelines. 200 ml of sample, standard and quality control, added with 40 ml of internal standard working solution, undergo a simple protein precipitation protocol, followed by drying step, and resulting extracts are resuspended in water:acetonitrile 90:10 (v:v; +0.05% formic acid) and then analyzed through a Shimadzu NexeraX2® UHPLC system coupled with a LCMS-8050® tandem mass detector. The validated method was tested on real samples from patients with RH/pseudo-RH, all giving informed consent.

Results: All analytical parameters of the method fitted FDA guidelines for all the analytes. 42 patients have been enrolled (SEAL study). TDM revealed that 55% of patients (n = 23) had detectable concentration of all prescribed drugs (considered fully adherent), 26% (n = 11) resulted partially non-adherent (only part of the prescribed drugs was detectable) and 19% (n = 8) were totally not-adherent (no drugs were detected). Through univariate/multivariate logistic regression, the diastolic pressure and the “white-coat” increase in heart rate resulted the best predictors of poor adherence. Through ROC curve analysis a diastolic pressure over 124 mmHg resulted predictive of total inadherence.

Conclusions: TDM can be a gold-standard for evaluating therapeutic adherence and this method results eligible for a clinical routine use. We managed to discern cases of inadherence, preserving some patients from an invasive and expensive surgery.

Results: Marked improvement in the HBM group in overall compliance (61.3% to 79.6%) in contrast to the ordinary health education group, no marked improvement in the percentages of Perceived susceptibility, Perceived severity, Perceived benefits, Perceived barriers, self efficacy cues to action shows changes between pre and post test results with a statistical difference in HBM group. For control group comparing pretest and post test results was of no significant difference except for Perceived severity, Perceived benefits, and self efficacy.

Conclusions: The findings support the hypothesis that using health education based on HBM has better results in adherence to treatment than traditional health education.

OP.2B.06 CONTROL OF HYPERTENSION AMONG THE FACULTY OF SAINT-PETERSBURG UNIVERSITIES
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Objective: The aim of the study was to assess awareness about BP level and compliance with antihypertensive drugs in the faculty members of Saint-Petersburg universities. This subpopulation is well-educated and can affect lifestyle attitudes of students.

Design and method: 747 professors from 22 to 80 years old were screened at their working places in 6 St.Petersburg Universities in October-December of 2016. The informed consent was obtained from all participants. Information on antihypertensive medication was collected. All subjects were interviewed with special questionnaire, which included personal data, lifestyle risk factors, and medical history. Blood pressure (BP) was measured on right arm in the sitting position after 5-minute rest by automatic tonometer OMRON (Japan).

Results: Table 1 Prevalence of HTN and compliance.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>all (n=747)</th>
<th>males (n=188)</th>
<th>females (n=559)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness of HTN</td>
<td>298 (39.9%)</td>
<td>89 (47.3%)</td>
<td>212 (37.9%)</td>
</tr>
<tr>
<td>Awareness of HTN and antihypertensive therapy</td>
<td>167 (22.3%)</td>
<td>52 (27.8%)</td>
<td>115 (20.2%)</td>
</tr>
<tr>
<td>BP&gt;140/90 mmHg in all group</td>
<td>318 (46.5%)</td>
<td>121 (64.1%)</td>
<td>257 (45.6%)</td>
</tr>
<tr>
<td>Hypertension (in case of awareness of intake of antihypertensive drug or elevated BP &gt;140/90 mmHg)</td>
<td>431 (57.7%)</td>
<td>140 (74.9%)</td>
<td>291 (52.2%)</td>
</tr>
<tr>
<td>Hypertension control in all hypertensives</td>
<td>83 (11.3%)</td>
<td>19 (10.3%)</td>
<td>65 (11.6%)</td>
</tr>
<tr>
<td>Hypertension control in hypertensives who take medication</td>
<td>44 (6.2%)</td>
<td>12 (6.4%)</td>
<td>32 (5.7%)</td>
</tr>
</tbody>
</table>

Conclusions: The prevalence of hypertension is high, especially in males despite general predominance of females in university faculty staff. Males have worse hypertension awareness and poor compliance to antihypertensive drugs. Control of hypertension is poor independently of gender in spite of good intellectual level.

OP.2B.07 ASSESSMENT OF DRUG ADHERENCE AND PSYCHOLOGICAL PROFILE IN PATIENTS WITH APPARENTLY TREATMENT-RESISTANT HYPERTENSION
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Objective: Recent studies using drug monitoring suggest that a high proportion of patients with apparently treatment-resistant hypertension (aTRH) are in fact poorly or non-adherent. However, in most cases, antihypertensive treatment was not standardized, and predictive factors of poor adherence were not analyzed. The aim of this work was to assess adherence in patients with aTRH on a standardized treatment, and to identify predictive factors of poor adherence, including psychological profile (emotion regulation, psychopathology and traumatic events).

Design and method: All patients with confirmed aTRH on a treatment regimen including Olmesartan, Amlodipine, Hydrochlorothiazide and Spiranolactone were eligible. Drug adherence was assessed by the Morisky Medication Adherence Scale (MMAS-8) and drug dosages in urine using Liquid Chromatography-Mass Spectrometry (LC-MS/MS). Psychological profile was assessed by the Toronto Alexithymia Scale (TAS 20), the Multidimensional Experiential
Avoidance Questionnaire (MEAQ), the Cognitive Emotion Regulation Questionnaire (CERQ), the Brief Symptom Inventory (BSI) and the Post Traumatic Diagnostic Scale (PDS).

**Results:** The analysis included 35 consecutive patients with aTRH (mean age: 51 years, 54% females, mean office blood pressure: 180/105 mmHg, 24-hour ambulatory blood pressure: 160/100 mmHg). The proportion of adherent, partially adherent and totally non-adherent patients was 12%, 27%, 61% using MMAS-8, and 29%, 40%, 31% using LC-MS/MS. The sensitivity and specificity of MMAS-8 versus LC-MS/MS was 40% and 61%, respectively. Patients labelled as adherent, partially adherent and totally non-adherent according to LC-MS/MS differed by the proportion of women (30, 43 and 82%, p = 0.042), and the total number of drugs per day (6.4, 6.2 and 10.2, p = 0.041). Furthermore, poorly adherent patients were characterized by more alexithymia (p = 0.043), somatisation (p = 0.004), and history of traumatic events (p = 0.011). Finally, poorly adherent patients tended to have a lower education level and were more frequently living without a partner.

**Conclusions:** Over 70% of patients with aTRH were found to be poorly or non-adherent by LC-MS/MS. Poor adherence was associated with female gender, total number of drugs prescribed and psychological characteristics. The reliability of the Morisky Scale was limited. Assessment of adherence by drug monitoring in body fluids and psychological evaluation should be considered in all patients with aTRH.

**Design and method:** This study included 711 hypertensive patients (mean age 62 years; 50% women) who during 2016 attended any of 25 primary healthcare centres in Stockholm, Sweden. Patients’ attitudes towards hypertension and drugs were assessed by the “Brief Illness Perception” and the “Beliefs about Medicines” questionnaires and sent 3–12 months after initiation of drug treatment; response rate was 59%. Patients were classified as persistent (609, 86%) or non-persistent (102, 14%) to antihypertensive treatment by analyses of their filled prescriptions from the Swedish Prescribed Drug Register, which includes information on all dispensed drugs from community pharmacies in Sweden.

**Results:** Mean systolic and diastolic blood pressure before initiation of treatment was 160 ± 18/93 ± 12 mm Hg. Cardiovascular comorbidity (atrial fibrillation, heart failure, ischemic heart disease or previous stroke/transient ischemic attack) was present in 5%, and diabetes mellitus in 7% of the patients. Almost one third were born outside Sweden. Compared to non-persistent medication users, persistent patients considered their diagnosis of hypertension to be chronic to a higher degree (median [interquartiles]; all P < 0.04) (6 [4–10] vs. 4 [2–8]), had less consequences on their life (2 [0–5] vs. 3 [1–6]), and that cardiovascular disease could be prevented by antihypertensive treatment (median 7 [5–8] vs. 5 [3–8]). Persistent patients had a greater belief in potential benefits from treatment (median 16 [15–18] vs. 16 [15–17.5]), thought less in doctors putting too much trust in drugs (median 12 [10–14] vs. 13 [11–14]), considered to a higher extent that antihypertensive drugs were necessary in order to maintain or improve their own health (median 17 [14–19] vs. 16 [11–19]) and were less concerned about the negative effects of their antihypertensive treatment (median 12 [8–15] vs. 12 [9–17]).

**Conclusions:** Primary healthcare providers should further emphasize the chronicity of hypertension as a disease, and the benefits of treatment in order to improve patients’ persistence to antihypertensive treatment.
ORAL SESSION

ORAL SESSION 2C:

AGEING

OP.2C.01
THE ROLE OF PMCA1 IN HYPERTENSION AND ARRHYTHMIA SUSCEPTIBILITY IN RELATION TO AGEING

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Objective: Heart failure prevalence increases with age, from less than 1% in 20–39 year olds to over 20% in those aged over 80. Problems posed by the ageing population means heart failure prevalence is expected to continue rising. Therefore understanding mechanisms involved age-associated cardiovascular changes is vital to conquer the growing epidemic. Multiple GWAS have shown Atp2b1, plasma membrane Ca2+ ATPase 1 (PMCA1), to have a strong genetic association with hypertension. Furthermore, we have previously shown altered PMCA1 expression results in age-associated elevated blood pressure. High blood pressure is a known arrhythmia risk factor, with hypertensive patients having an increased risk of morbidity and mortality associated with arrhythmic development. Therefore using transgenic animal models we aim to investigate a potentially novel link between age-associated hypertension and heart rhythm changes in relation to altered PMCA1 expression.

Design and method: The role of PMCA1 in heart rhythm stability was assessed in cardiomyocyte-skeletal muscle knockout mice (PMCA1CKO) at 3 months of age and PMCA1 heterozygous null mice (PMCA1HHT) at 3 and 18 months of age (aged PMCA1CKO animals are not viable). Heart rhythm stability was determined using in vivo electrocardiography and arrhythmia susceptibility tested using programmed electrical stimulation. To confirm PMCA1 is involved in age-associated hypertension, conscious blood pressure of young and aged PMCA1HHT animals was measured using the tail-cuff method.

Results: At 3 months, old PMCA1CKO mice exhibit abnormal heart rhythms, with prolonged QT and JT intervals as well as increased susceptibility to arrhythmic events. However, PMCA1HHT animals at this age show a normal heart rhythm phenotype compared to controls. Further investigation looking at the effect of ageing on arrhythmia susceptibility shown while aged PMCA1HHT display age associated hypertension their heart rhythm remains comparable to controls.

Conclusions: Our findings show that PMCA1 is involved in two of the central features of heart failure arrhythmia development and hypertension. However, the role of PMCA1 in these two areas are cardiophysiology appear to be unrelated and while the hypertension phenotype appears to be affected by ageing, the effect of ageing in relation to the gene’s role in heart rhythm stability remains unclear.

OP.2C.02
MECHANISMS OF AGE-DEPENDENT HYPERTENSION: IMPAIRED SYMPATHOINHIBITORY AND NATRIURETIC RESPONSES TO CHALLENGES TO SODIUM HOMEOSTASIS IN AGED HYPERTENSIVE SPRAGUE-DAWLEY RATS

R. Wainford, A. Frame. Boston University School of Medicine, Department of Medicine, Boston, MA, USA

Objective: Hypertension is strongly correlated with increased age and elevated sympathetic tone in human subjects. Recent studies have associated excess sympathetic tone with NCC mediated sodium reabsorption. These studies tested the hypothesis that age-dependent hypertension correlates with impaired sympathoinhibitory and natriuretic mechanisms in the Sprague-Dawley rat.

Design and method: Two-month, 8-month, and 15-month old male Sprague-Dawley (SD) rats underwent an intravenous (IV) volume expansion (VE; 5% body weight) and mean arterial pressure (MAP), heart rate (HR), natriuresis (UNaV), and paraventricular (PVN) parvocellular neuronal activation (c-Fos expression; IHC) were assessed. In a separate study, naïve 2-month, 8-month, and 15-month old male SD rats were maintained on a normal salt (NS, 0.6% NaCl) or high salt diet (HS, 4% NaCl). On day 21, MAP, HR, NCC activity (peak natriuresis to IV hydrochlorothiazide, HCTZ, 2 mg/kg), peak depressor response to IV hexamethonium (30 mg/kg), and plasma and renal norepinephrine levels were assessed (n = 4/group).

Results: Natriuresis following acute VE and plasma and renal norepinephrine levels were assessed (n = 4/group).

Conclusions: Age-related hypertension is accompanied by impaired natriuretic and sympathoinhibitory responses to an acute challenges to fluid and electrolyte homeostasis. We speculate these changes may be mediated in part by reduced activation of PVN sympathoinhibitory neurons- increases NE-driven NCC activity, promoting sodium reabsorption and the development of hypertension. These findings suggest that therapies reducing sympathetic outflow and renal sodium retention and reductions in dietary salt intake may be particularly useful in older patients with hypertension.

OP.2C.03
THE INFLAMMATORY COMPONENT OF CARDIOVASCULAR AGEING ON ALBUMINURIA AND ARTERIAL STIFFNESS IN ESSENTIAL HYPERTENSIVE SUBJECTS

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Objective: In the present study, we examined the interrelationships between aging, high-sensitivity C-reactive protein (hs-CRP), urinary albumin excretion expressed as the albumin-to-creatinine ratio (ACR), and arterial stiffness in essential hypertensive patients.

Design and method: 295 newly diagnosed untreated non-diabetic patients with stage I to II essential hypertension [192 men, mean age = 50 ± 8 years, office blood pressure (BP) = 146/95 mmHg] were divided into two groups according to age: Older group (mean age > 60 years, n = 43) and younger group (mean age < 60 years, n = 252). In all subjects arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method, while ACR values were determined as the mean of two non-consecutive morning spot urine samples.

Results: Older compared to younger group had lower office and 24-h diastolic BP (90 ± 8 vs 96 ± 9 mmHg and 74 vs 83 ± 9 mmHg, respectively; p < 0.0001 for both), and greater left ventricular mass index (114.3 ± 15 vs 105.2 ± 11 g/m², p < 0.05) while did not differ regarding sex, body mass index and metabolic profile (p > NS). Moreover, older compared to younger patients exhibited increased levels of hs-CRP (3.2 ± 0.7 vs 2.1 ± 0.7 mg/L, p < 0.05), ACR (36.5 ± 12 vs 22.8 ± 7 mg/g, p < 0.05) and PWV (8.8 ± 1.5 vs 7.9 ± 1.2 m/sec, p < 0.001). In the entire population, age was associated with hs-CRP (r = 0.120, p < 0.05), ACR (r = 0.221, p < 0.05), and PWV (r = 0.399, p < 0.0001), while it was negatively related to 24-h diastolic BP (r = −0.319, p < 0.0001). Furthermore, hs-CRP was correlated with body mass index (r = 0.281, p < 0.0001) and PWV (r = 0.233, p < 0.005) in multiple regression analysis, age and hs-CRP were independent predictors of both PWV and ACR (p < 0.05). Analysis of covariance revealed that hs-CRP and ACR concentrations were significantly different between groups after adjusting for confounders (p < 0.05 for all).
Objective: Hypertension and age have been associated with retinal arteriolar narrowing but precise evaluation of remodeling determinants has not been investigated. Our objectives were to assess the effect of age on retinal arteriolar remodeling in elderly treated and controlled hypertensives with and without mild cognitive injuries using Adaptive optics camera (AOC) and a control group of hypertensives patients

Design and method: We used the AOC rtx1™ (Imagine-Eyes, Orsay, France) to measure wall thickness, internal diameter and to calculate Wall-to-Lumen Ratio (WLR) and Wall Cross Sectional Area (WCSA) of retinal arterioles in 47 non diabetics treated hypertensives over 65 years with or without mild cognitive injuries assessed by MMS and in 47 younger with an age <60 treated hypertensives matched for gender, systolic, diastolic and pulse pressure as well as cardiovascular risk factors

Results: Systolic BP did not differ between the 2 groups 131.7 ± 140.4 vs.131.4 ± 19.0 mmHg but diastolic BP was higher in the control group (73.0 ± 9.1 vs.66.8 ± 10.2 mmHg). While age was significantly higher in the elderly group (75.8 ± 4.9 vs 51.5 ± 5.8 years, p < 0.0001), WLR did not differ between the 2 populations (0.297 ± 0.049 vs.0.295 ± 0.056). However, larger lumen (832.2 ± 9.4 vs. 77.2 ± 11.6 mm, p = .008), higher parietal thickness (24.3 ± 4.0 vs. 22.7 ± 3.9 mm, p = .04) and greater WCSA (3642 ± 813 vs.3217 ± 877 mm², p = .02) were observed in older hypertensives. No correlation were found between retinal arteriolar indices and age, blood pressures levels or MMS in the older population whereas in the whole population strongly correlated with all retinal arteriolar parameters.

Conclusions: AOC high resolution and reproducibility enables to observe for the first time in very elderly hypertensives a proportional augmentation of lumen, thickness and wall cross sectional area without WLR elevation.

OP.2C.06

THE ROLE OF ARTERIAL STIFFNESS AND BLOOD PRESSURE VARIATIONS IN MORBIDITY AND MORTALITY IN VERY OLD FRAIL SUBJECTS. THE PARTAGE STUDY


Objective: We have previously reported in persons over 80 years old living in nursing homes (PARTAGE study) that low pulse pressure amplification (PPA) an indicator of arterial stiffness, was associated with total mortality and the major cardiovascular (CV) events. In subsequent analyses we have shown that the group of subjects with systolic blood pressure (SBP) < 130 mmHg, under >1 antihypertensive drugs, had a greater risk of mortality as compared to all other subjects. More recently, we have demonstrated that orthostatic changes in BP (orthostatic hypotension or orthostatic hypertension) were associated with higher risk for major CV events. The aim of the present analysis was to study the combined effects of all these 3 arterial parameters on total mortality and major CV events.

Design and method: This analysis was performed in the subjects of the PARTAGE study with follow-up for 2 years. The parameters were studied by using the cutoff points which according to the results of the previous analyses in this cohort: PPA < 18.8% (LowPPA); SBP < 130 mmHg under >1 antihypertensive drug (TisSBP < 130); changes in systolic BP (both an increase or a decrease of >20 mmHg) between supine and upright position (DeltaSBP > 20). Were included in the analysis the subjects (n = 883) with measurements of all these 3 arterial parameters. Age and gender were added in all multivariate models.

Results: Low PPA, TisSBP < 130 and DeltaSBP > 20 were observed in 33%, 38% and 21% of patients respectively. "LowPPA" (HR 1.52 (1.13–2.05) p = 0.006) and "TisSBP < 130" (HR 1.71 (1.24–2.35) p = 0.001) were independent determinants of total mortality and major CV events whereas "DeltaSBP > 20" was a independent determinant for major CV events only (HR 1.40 (1.05–1.89) p = 0.02). In addition, combination of >1 of these arterial parameters significantly increases the risk of total mortality and major CV events (HR for 2 vs none, 2.12 (1.42–3.16) and for HR 3 v 0, 2.90 (1.46–5.75).

Conclusions: People presenting a vascular profile characterized by high arterial stiffness expressed by low PPA, low BP under combination anti-Htn treatment and significant variability in SBP between supine and upright position were at much higher risk for total mortality and major CV events.
Results: The results (mean ± SE) were CAVI = 8.92 ± 0.10, cfPWV = 9.78 ± 0.16 m/sec, brachial systolic blood pressure = 140 ± 1 mmHg. CAVI and cfPWV increased with age (r = 0.63, p < 0.001 and r = 0.37, p < 0.001 respectively). The correlation between age and CAVI was greater in males (r = 0.71, p < 0.001) than females (r = 0.54, p < 0.001) as it was marginally between age and cfPW; males (r = 0.39, p < 0.001) vs females (r = 0.35, p < 0.001). A multivariate regression analysis on the entire population, with age as the dependent factor and average CAVI and cfPWV as independent parameters showed that only CAVI (beta = 0.497, p < 0.001) was significantly associated with age. A multivariate regression analysis performed with average CAVI as the dependent factor and age (standardised Beta = 0.577, p < 0.001), BMI (standardised Beta = −0.205, p < 0.001), systolic BP (standardised Beta = 0.249, p < 0.001) and gender (standardised Beta = −0.208, p < 0.001) as the independent parameters showed that CAVI was significantly associated with all these factors.

Conclusions: These results suggest that both CAVI and cfPWV correlate with chronological age, with CAVI more closely related to ageing than cfPWV. Thus, CAVI may be a useful predictor of vascular ageing.
ORAL SESSION

LATE-BREAKERS LB01:
SESSION 1

LB.01.01
DOES LEVEL OF FUNCTION, GRIP STRENGTH AND COMORBIDITY MODULATE ASSOCIATION OF HYPERTENSION WITH MORTALITY, IN 90 YEAR OLDS?

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Objective: Observational studies do not support association of hypertension with mortality in the oldest old, which however may be modulated by functional capacity. We attempt to determine the association between hypertension at age 90 and 5-year mortality, by functional capacity

Design and method: A prospective observational follow-up of an age-homogenous, representative, community-dwelling cohort (480, 40.8% males, born 1920–1921), assessed at their homes. Hypertension is defined as treatment with antihypertensive medication, sitting blood pressure higher than 140 mmHg systolic or 90 mmHg diastolic. Subjects categorized as normotensive (NORMO), untreated hypertensive (NonTx-HTN), or treated hypertensive (Tx-HTN); assessment included Activities of Daily Living (ADL), handgrip strength; comorbidity.

Results: Prevalence of NORMO, NonTx-HTN, and Tx-HTN was 12.3% (59/480), 12.7% (61/480) and 75% (360/480), with mean blood pressure of 124 ± 12/65 ± 7, 170 ± 54/76 ± 10, and 148 ± 29/70 ± 11 mmHg respectively. Higher rates of low education, depression, low physical activity, chronic heart failure, ischemic heart disease, chronic kidney disease were present among Tx-HTN. Five-year survival was lowest among Tx-HTN and highest among NonTx-HTN versus NORMO among all subjects (52%, 72%, 62%; p = 0.012), and among subjects with ADL-independence (64%, 91%, 74%; n = 265, p = 0.006), ADL-dependence (37%, 55%, 48%; n = 194, p = 0.335), high (above median) grip strength (66%, 85%, 83%; n = 227, p = 0.042), low (below median) grip strength (38%, 60%, 61%; n = 376, log rank p = 0.063), low comorbidity (64%, 84%, 70%; n = 219, p = 0.132) and high comorbidity (42%, 60%, 54%; n = 261, p = 0.121). Unadjusted mortality Hazards Ratios (HR) were higher for Tx-HTN (HR 1.38; 95%CI, 0.89–2.15) and lowest in NonTx-HTN (HR 0.7; 95%CI 0.37–1.31) compared to NORMO (HR 1.0). Similarly after adjusting for medical and functional covariables, adjusted HRs were higher for Tx-HTN (HR 1.39; 95%CI, 0.83–2.33), and lower for NonTx-HTN (HR 0.67; 95%CI 0.31–1.45) compared to NORMO (HR 1.0). Results were consistent in sample subsets according to ADL status, grip strength, and comorbidity and were unchanged after excluding subjects dying in the first follow-up year.; all-cause mortality data (2000–2015).

Conclusions: Untreated hypertension at age 90 was not associated with increased mortality risk among community dwelling elderly, irrespective of comorbidity, functional status, or muscle strength.

LB.01.02
PHASE II RANDOMIZED SHAM-CONTROLLED STUDY OF RENAL DENERVATION FOR SUBJECTS WITH UNCONTROLLED HYPERTENSION – WAVE IV

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Objective: The aim of this double blind randomized sham-controlled study was to verify the blood pressure (BP) lowering efficacy of externally delivered focussed ultrasound for renal denervation (RDN).

Design and method: The WAVE IV study was an international, randomized (1:1), sham-controlled, double blind prospective clinical study carried out in 13 institutions. Patients (18–80 years of age) had true treatment resistant hypertension with office BP >160 mmHg whilst taking 3 or more antihypertensive medications. The treatment consisted of bilateral RDN using therapeutic levels of ultrasound energy and the sham consisted of bilateral application of diagnostic levels of ultrasound energy. The primary objective was change in office BP and secondary objective change in 24-hour ambulatory BP at 24 week follow-up visit.

Results: An interim analysis showing lack of evidence of antihypertensive efficacy by the externally delivered focused ultrasound in the RDN group over the sham group prompted termination of the trial. Out of 239 screened patients, 81 were treated. Neither changes in office BP at 24 weeks (sham: −18.9 ± 14 vs RDN: −13.2 ± 20 mmHg, p = 0.133), nor changes in 24-hour ambulatory BP at 24 week follow-up visit (sham: −5.90 ± 15 vs RDN: −7.11 ± 13 mmHg, p = 0.770) differed between the two groups significantly. Of note, no safety signal was observed. Medication changes were less than 15% throughout the first follow-up period of 24 weeks. In a subset urinary toxicological analysis disclosed full adherence in 77% at baseline and 82% at 6 months. Post hoc analysis revealed that stricter criteria for stabilisation of BP at baseline were associated with a numerically greater change in 24-hour ambulatory BP in the RDN group than in the sham group. Systolic BP changes were numerically greater in patients with pulse pressure <65 compared to those with pulse pressure ≥65 mmHg.

Conclusions: Our data did not prove that antihypertensive efficacy of the externally delivered focused ultrasound for RDN was greater than the sham effect. Post-hoc analysis suggested that the predominance of treatment resistant hypertensive patients with stiff arteries, and less stringent stabilisation of baseline BP may have hampered our trial.

LB.01.03
ACHIEVED HOME BLOOD PRESSURE AND CARDIOVASCULAR EVENT RISK IN ASIAN HIGH RISK POPULATION: STRATIFIED ANALYSIS OF A LARGE-SCALE, OBSERVATIONAL STUDY ACCORDING TO RISK LEVELS

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Objective: The Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated the benefit of strict blood pressure (BP) control with lower target BP level in the high-risk hypertensive patients. The aim of this study is to investigate the association between home blood pressure and incidence of cardiovascular disease (CVD) events at various risk levels using data from the Home Blood Pressure Measurement With Olmesartan Naive Patients to Establish Standard Target Blood Pressure (HONEST; 2009–2011) study including 21591 patients with hypertension (mean age, 64.9 years; women, 50.6%) enrolled at clinics and hospitals in Japan.

Design and method: Participants in the HONEST study were stratified based on risk levels as follows: SPRINT population, patients (>50 years) with diabetes and prior stroke who have cardiovascular risk and systolic blood pressure (SBP) of 130 mm Hg or higher; SPRINT-excluded high-risk population, hypertensive patients with diabetes and prior stroke; and non-SPRINT low-risk population, patients enrolled in the HONEST study excluding SPRINT population and SPRINT-excluded high-risk population. In each population, hazard ratios were calculated with Cox proportional-hazards regression model to compare incidence of cardiovascular disease events between categorized patient groups according to home SBP or clinic SBP levels.

Results: The cardiovascular event risk (events/1000 person-year) was intermediate in SPRINT population (6.32) between those of Non-SPRINT low-risk (3.39, p < 0.001) and SPRINT-excluded high-risk (12.41, p < 0.001). In SPRINT population and SPRINT-excluded high-risk population, lower on-treatment home SBP was associated with lower CVD risk with the lowest risk at home SBP of <125 mm Hg. Non-SPRINT low-risk population showed a non-significant J-curve association between on-treatment home SBP and CVD risk with the lowest risk at home SBP of 135 to < 145 mm Hg. Moreover, the effect of lowering clinic SBP on reduction of CVD risk was unclear in patient group with clinic SBP of <130 mm Hg in all populations.

Conclusions: These results indicate that it is essential to control home blood pressure according to risk levels and that intensive therapy to a home SBP target of less than 125 mm Hg would be beneficial for high-risk patients with hypertension.

Conclusions: The correlation between BPV determinants intra and inter-method was weak or nonexistent, even when comparing determinants reflecting the same type of temporal (short-, mid- or long-term) BPV. Our data suggest that the BPV reflects a heterogeneous phenomenon and that strongly depends on the estimation method and the time period evaluated.

Conclusions: The correlation between BPV determinants intra and inter-method was weak or nonexistent, even when comparing determinants reflecting the same type of temporal (short-, mid- or long-term) BPV. Our data suggest that the BPV reflects a heterogeneous phenomenon and that strongly depends on the estimation method and the time period evaluated.
Conclusions: Intensive blood pressure control appears to reduce the excess cardiovascular risk associated with dysglycaemia. This highlights the close association between blood pressure and glycaemia in the development of CV disease and supports consideration of lower blood pressure targets in patients at risk of diabetes.

LB.01.06 LONG-TERM RISK OF CARDIOVASCULAR EVENTS IN WHITE-COAT HYPERTENSION DEFINED BY DAYTIME AND NIGHTTIME BLOOD PRESSURE LIMITS

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Objective: The prognostic impact of white-coat hypertension (WCHT) is a subject of debate and controversy. Nighttime blood pressure (BP) is strongly related with cardiovascular (CV) prognosis but that has not been currently considered in the definition of WCHT.

Design and method: We investigated the occurrence of fatal and non-fatal CV events in 1230 subjects with sustained hypertension (SHTA), 617 with WCHT and 812 with normotension (NT) during a mean of follow-up 93 months (95% CI 90–96), all matched for age (by clusters) - mean age 50 yrs (95% CI 49–51). Percentage of female in the 3 groups were (55–59%). WCHT was defined as hypertension in office and daytime BP < 135/85 mm Hg and nighttime BP < 120/70 mm Hg.

Results: Cox regression analysis with adjustment for covariables were able to show that risk of CV events was significantly (p = 0.001) higher with a Relative Risk of 4.12 (CI 95% 2.99–6.69) in subjects with SHTA than in those with WCHT whereas there was no difference between subjects with WCHT and with NT. Within the group of WCHT 29% received therapy during the follow-up for at least six months but the RR of CV events betweenWCHT either treated or non-treated did not differ: RR = 0.76 (CI95% 0.37–1.51, p = 0.42).

Conclusions: In subjects with WCHT with normal daytime and nighttime BP the risk of CV events was significantly lower than that in SHTA and not significantly different from normotensive subjects. Also anti-hypertensive treatment seems not to modify the low risk of CV events in WCHT.

LB.01.07 MOST ADVISABLE STRATEGY IN SEARCH OF ASYMPTOMATIC TARGET ORGAN DAMAGE IN HYPERTENSIVE PATIENTS

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Objective: To evaluate the diagnostic potential of seven examinations in order to define the most suitable strategy for target organ damage (TOD) search in hypertensive patients.

Design and method: This is a descriptive, cross-sectional study. 153 consecutively treated and essential hypertensive patients were enrolled. Patients with established cardiovascular or chronic renal disease (stage >3) were excluded. TOD search was assessed by: glomerular filtration rate (GFR), albumin/creatinine ratio (ACR), electrocardiogram (ECG), echocardiogram (ECHO), ankle-brachial index (ABI), pulse wave velocity (PWV), and carotid ultrasound (intima media thickness and presence of plaques). The rationale of our strategy ought to determine the performance of applying a set of the most widely available tests (GFR, ACR, ABI, ECG) and advise about the optimal sequence of the remaining tests.

Results: The cohort was 64,4 ± 7,9 years old, 45,8% males. 82,6% of the sample had any TOD at all. The resulting algorithm found a 37% TOD in relation to GFR, ACR, ABI and ECG values. Adding carotid ultrasound added up to 70% of the studied population and properly classified (TOD+/TOD-) 89% of the cohort. When performing PWV, 78% of the patients had been identified as TOD+ and 96% of the population was correctly identified. Contribution of ECO was minor.
**Conclusions:** After running the more widely available explorations (GFR, ACR, ABI, ECG), a step-by-step strategy that included carotid ultrasound, PWV and ECO could be the best sequence for TOD search in asymptomatic hypertensive patients.

**Design and method:** Search strategy Comprehensive electronic search of MEDLINE, EMBASE, Web of Science and Cochrane for trials published between 1995 and 2015. Cross-references of all retrieved manuscripts were also checked to identify additional trials.

Selection criteria Randomised controlled trials (RCTs) of antihypertensive agents (angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics (DIs) or beta-blockers (BBs)), with at least 100 randomized hypertensive participants and with a follow-up of at least 1 year.

Data collection and analysis Two authors independently selected the included trials, evaluated the risk of bias and retrieved the data on BP response. Meta-analyses were performed to summarise the pooled standardised mean difference (SMD) between treatment arms of included studies. BP response was documented as delta, single measure and repeated measures.

**Results:** 83 RCTs with 197,684 participants were identified, grouped as follows: ACEIs (37 RCTs) 36410; ARBs (34 RCTs) 20705; CCBs (46 RCTs) 73987; DIs (26 RCTs) 56727; and BBs (22 RCTs) 43617. CCBs were the most frequently prescribed antihypertensive agents for hypertension (27.30%). CCBs were superior to ACEIs in lowering BP (pooled SMD of $-0.07 / -0.08$ mmHg, $P < 0.00001$). Similarly, DIs were superior to ACEIs ($-0.11$ mmHg, $p < 0.00001$) and CCBs ($-0.06$ mmHg, $p < 0.00001$) in lowering Systolic BP. Additionally, ARBs were superior to BBs in lowering Systolic BP ($-0.06$, $P = 0.001$).

**Conclusions:** All anti-hypertensive drugs are not equal in reducing BP response from RCTs of different anti-hypertensive agents will guide physicians to select the appropriate drug to get the desired effect. CCBs should be the choice of first-line mono-therapy or second-line combination therapy as in most of the existing BP guidelines.

**LB.01.09**

**DIASTOLIC BLOOD PRESSURE RANGES AND INCIDENT OUTCOMES IN THE SYSTOLIC BLOOD PRESSURE INTERVENTION TRIAL: AN ANALYSIS OF OVERALL DATA AND BY SELECTED BASELINE CHARACTERISTICS**

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**Objective:** The Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated the efficacy and safety of targeting a systolic blood pressure (SBP) of $<120$ mmHg compared to $<140$ mmHg in non-diabetic patients at increased cardiovascular (CV) risk. Scientific evidence, however, suggests a lower limit of diastolic BP (DBP) beyond which risk of events outweighs potential benefits, particularly in subjects with CV disease (CVD) and chronic kidney disease (CKD). We evaluated the risk of events in the SPRINT trial overall and in subgroups with preexisting CVD and CKD, according to different DBP levels.

**Design and method:** Participants with not-available data were excluded from the analyses. DBP(±SD) throughout the entire follow-up time was calculated for each patient. Patients were then categorized into 5 groups (DBP $<60$ mmHg, $60–69$ mmHg, $70–79$ mmHg [reference], $80–89$ mmHg, $>=90$ mmHg); hazard ratio (HR) for outcomes was assessed at each DBP level overall and in subgroups separately (CVD, CKD), using univariate and multivariate Cox proportional un-adjusted and adjusted (mean SBP; race; sex; age; baseline CKD; baseline CVD) models. Significance level was set at $p < 0.05$.

**Results:** From baseline to the last visit, mean DBP(±SD) was $68.74(±10.86)$ mmHg in the intensive group and $75.17(±11.33)$ mmHg in the standard group. Compared to the reference DBP range, a higher risk of events was observed in the lower ($<60$ mmHg: HR 2.48, $C.I.95\% 1.92–3.22$, $p < 0.001$; $60–69$ mmHg: HR 1.40, $C.I.95\% 1.14–1.72$, $p < 0.001$) as well as in the higher ($80–89$ mmHg: HR 1.10, $C.I.95\% 0.86–1.41$, $p = 0.42$; $>=90$ mmHg: HR 1.13, $C.I.95\% 0.67–1.91$, $p = 0.64$) DBP ranges overall. In the adjusted model, increased age accounted for increased event risk to varying degrees. The subgroup analysis confirmed the overall results, with significantly increased risk of events in participants with pre-existing CVD also at higher DBP ranges.

**Conclusions:** Not only the SPRINT trial defined an optimum SBP target in high-risk patients: although beyond its purpose, it also added useful information on what their optimal DBP should be. Targeting a SBP $<120$ mmHg and a DBP of $70–79$ mmHg could be recommended in such patients, including those with pre-existing CVD or CKD. Lower or higher DBP targets could even be contraindicated in such patients.
ORAL SESSION

ORAL SESSION 3A: KIDNEY

OP.3A.01 GLOMERULAR HYPERFILTRATION. A PREDICTOR OF ADVERSE CARDIOVASCULAR OUTCOME

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Objective: The prognostic role of low estimated glomerular filtration rate (eGFR) is well established. In contrast, the association between greater than normal eGFR, i.e. glomerular hyperfiltration (GH), and cardiovascular events (CVE) is much less characterized. The present study was conducted to test the hypothesis that GH is independently associated with risk of adverse cardiovascular outcome in a large multicentric population.

Design and method: The analysis was performed in 8824 participants (55% men) aged 52 ± 16 years enrolled in 8 prospective studies in Australia, Italy, Japan, and U.S.A. Using the 5th and 95th percentiles of the age and sex specific quintiles of CKD-EPI-calculated eGFR, we identified 3 groups: low (LF), high (HF) and normal (NF) eGFR. The unadjusted relationship between eGFR categories and time to CVE occurrence was estimated using Kaplan-Meier product-limit method and compared by the Mantel (log-rank) test. We then tested the independent prognostic role of eGFR categories using study-stratified multivariable Cox models.

Results: The median (IQR) eGFR were: 48.2 (38.1, 58.7), 81.4 (69.6, 95.8) and 111.2 (99.1, 126.7) ml/min/1.73m² for LF, NF, and HF participants, respectively (p < 0.001). Compared with LF and NF, HF (N = 426) were younger, mostly male and of white race (p < 0.001). During a median follow-up of 5.7 years there were 722 CVE. Crude event rates were higher for both HF (1.8 per 100-p-years) and LF (2.1 per 100-p-years) as compared with NF (1.2 per 100-p-years) (p < 0.001). In unadjusted survival analyses the cumulative incidence of CVE was similar in HF and LF and higher than in NF (log-rank p < 0.001). In Cox models including age, sex, average 24-hour BP smoking, diabetes, and cholesterol, both HF (HR 1.5, 95% CI,1.2–2.1, p < 0.001) and LF (HR 2.0, 95% CI,1.5–2.6, p < 0.001) participants had a higher risk of CVE as compared to NF. Inclusion of night-time BP dipping in the regressions did not change the strength of the associations.

Conclusions: These data show that GH is a strong and independent predictor of CVE in a large multicentric population. Our findings support a U-shaped relationship between eGFR categories and adverse cardiovascular outcome.

OP.3A.03 MINERAL, BONE METABOLISM MARKERS AND ARTERIAL STIFFNESS IN DIALYSIS POPULATION

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Objective: To determine if mineral, bone and hormonal markers (Sclerostin, DKK1, a-Klotho, FGF23, PINP and TRAP5b) were obtained by ELISA from pre-dialytic plasma. Carotid-femoral (CF) and carotid-radial (CR) pulse wave velocity (PWV) and femoral/radial PWV ratio were measured in every patient as previously performed. Linear and Cox regression analysis were used to assess factors associated with arterial stiffness and mortality.

Results: We included 130 hemodialysis patients with a median follow-up of 1290 (864) days. Population characteristics are presented in table 1. The population is composed of 47% male with a mean age of 72 ± 14 years and a mean diastolic pressure of 545 (1171) days, 56% had coronary artery disease, 51% had diabetes and 89% suffered from hypertension. At the end of follow-up, 97 (75%) patients had died. Median CF-PWV was 13.5 (5.1) m/s, CR-PWV was 8.4 (2.0) m/s and PWV-ratio was 1.7 (0.7). In univariate analysis, as displayed in table 2, only FGF23 blood level was inversely associated with CF-PWV while a-Klotho and Sclerostin were positively associated with CR-PWV. FGF23, a-Klotho and Sclerostin levels were inversely associated with the PWV ratio. In multivariate models adjusting for demographic, biochemical and mineral parameters, a-Klotho was positively associated with CR-PWV and inversely associated with the PWV ratio. Finally, only FGF23 levels were associated with an increased mortality in both univariate and multivariate models.

Conclusions: In a dialysis population, plasma levels of a-Klotho and Sclerostin are associated with peripheral arterial stiffness and femoral/radial stiffness ratio. High levels of FGF23 are associated with increased mortality. These results suggest a central role of mineral parameters in arterial stiffness in CKD.

OP.3A.04 REDUCED CORTICAL OXYGENATION PREDICTS PROGRESSIVE RENAL FUNCTION DECLINE IN HUMANS

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Objective: Renal tissue hypoxia is generally considered as the common final pathway in the development and progression of chronic kidney disease (CKD). BOLD-MRI studies have recently demonstrated that CKD patients have higher cortical R2* values (corresponding to lower oxygenation) than controls. Whether cortical oxygenation as measured with BOLD-MRI predicts renal function decline in CKD is unknown.

Design and method: Blood-oxygenation level dependent MR imaging was performed under standardized conditions in a cohort of 112 CKD patients, 47 hypertensives and 24 controls. Images were analyzed with the twelve-layer concentric objects method (TLCO) that divides renal parenchyma in 12 layers of equal thickness. Finally, only FGF23 blood level was inversely associated with CF-PWV while a-Klotho and Sclerostin were positively associated with CR-PWV. FGF23, a-Klotho and Sclerostin levels were inversely associated with the PWV ratio. In multivariate models adjusting for demographic, biochemical and mineral parameters, a-Klotho was positively associated with CR-PWV and inversely associated with the PWV ratio. Finally, only FGF23 levels were associated with an increased mortality in both univariate and multivariate models.

Conclusions: In a dialysis population, plasma levels of a-Klotho and Sclerostin are associated with peripheral arterial stiffness and femoral/radial stiffness ratio. High levels of FGF23 are associated with increased mortality. These results suggest a central role of mineral parameters in arterial stiffness in CKD.

Conclusions: In a dialysis population, plasma levels of a-Klotho and Sclerostin are associated with peripheral arterial stiffness and femoral/radial stiffness ratio. High levels of FGF23 are associated with increased mortality. These results suggest a central role of mineral parameters in arterial stiffness in CKD.
We demonstrate for the first time in humans that cortical oxygenation as assessed with BOLD-MRI is an independent predictor of renal function decline: the lower baseline cortical oxygenation, the faster the decline of renal function. These data open the road to further studies exploring functional MRI as a tool to predict adverse renal outcome.

**Design and method:** This cross-sectional investigation involved 7,452 patients with CKD (estimated glomerular filtration rate [eGFR] < 60, albuminuria, or both, at least twice within 3 months), 4,325 men/3,127 women, 65.3 ± 13.8 years of age, with BP, according to ABPM criteria, ranging from normotension to sustained hypertension. Ambulatory BP was measured for 48 consecutive hours.

**Results:** There was a highly significant (P < 0.001) progressive increase in the asleep systolic BP (SBP) mean with increasing severity of CKD. The awake SBP mean, however, did not change consistently throughout the different stages of CKD. Accordingly, the sleep-time relative SBP decline was progressively and significantly (P < 0.001) attenuated towards a more non-dipper BP patterning with diminishing eGFR. Most important, the proportion of patients with the riser BP pattern (asleep SBP mean greater than awake SBP mean) significantly and progressively increased from 5.8% of the participants with stage-1-CKD to a very high 33.7% of the participants with stage-5-CKD.

**Conclusions:** This study, the largest reported so far on CKD patients evaluated by highly-reproducible 48 h ABPM, documents the high prevalence of alteration in sleep-time BP regulation in this condition. Most important, prevalence of the riser BP pattern, associated with highest CVD risk, is also very high, from 20% in stage-3-CKD to 34% in end-stage-renal-disease. Collectively, these findings indicate ABPM should be mandatory for proper CVD risk stratification in CKD, as well as a means to establish the most adequate therapeutic scheme to properly control sleep-time BP and decrease CVD risk.
**Design and method:** 10 healthy subjects had identical examinations on two occasions in a 3Tesla MR-scanner. On each occasion subjects performed 5 minutes hand-grip tests in the scanner to obtain continuous measurements of BOLD, perfusion and interleaved measurements of T2* and renal artery flow. Flow measurements were obtained from phase-encoding imaging, perfusion using arterial spin labeling (ASL) and both BOLD and T2* using gradient echo images.

**Results:** Hand-grip induced a decrease of flow in the renal artery by 17.4+/−7%, and in the renal medulla an increase of oxygenation (T2*) by 22+/−9% despite a drop in perfusion −12+/−5% (p < 0.05). In the renal cortex we noted nonsignificant decreases of perfusion and oxygenation (T2*) of −2.5+/−2.5% and −1.4+/−4%, respectively. A significant relation (R2 = 0.58, p < 0.01) was noted between the resting systolic blood pressure and the decrease of flow in the renal artery during hand-grip.

**Conclusions:** Radiation- and contrastfree MR measurements of renal artery flow, BOLD and perfusion in renal cortex and medulla, acquired for the first time in humans during hand grip testing, were consistent with a sympathetically mediated decrease in renal artery flow and cortical flow and oxygenation. In the medulla, perfusion decreased and oxygenation increased, interpreted as being due to a reduction of distal sodium delivery and hence the reabsorptive workload. A correlation between resting blood pressure and renal artery flow response to hand grip exercise could indicate an increased sensitivity of renal flow response to sympathetic activation in subjects with high blood pressure. These techniques may be useful to assess patients having primary hypertension and renal artery stenosis.

**OP.3A.08 EFFICIENT IMPLEMENTATION OF ALGORITHM PREVENTING FOR REDUCED RISK OF CONTRAST-INDUCED ACUTE KIDNEY INJURY IN CLINICAL PRACTICE IN PATIENT WITH DELAYED PERCUTANEOUS CORONARY INTERVENTIONS**

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**Objective:** Contrast-induced acute kidney injury (CI-AKI) is a serious complication of the administration of iodinated contrast media (CM) for interventional cardiovascular procedures and is associated with substantial morbidity and mortality. We performed a single-centre prospective study to determine the effect of implementation of algorithm preventing on the incidence of CI-AKI in patients with unstable angina pectoris/non-ST-segment elevation myocardial infarction (UAP/NSTEMI) and delayed percutaneous coronary intervention (PCI).

**Design and method:** We used of historical control data for assessing of algorithm preventing CI-AKI in routine clinical practice. The study compared two groups of patients with UAP/NSTEMI and delayed PCI before and after implementation of algorithm preventing CI-AKI. In 1 Group - control group (n = 86) we used the routine prophylaxis CI-AKI: in patients with eGFR < 60 ml/min/1.73 m² received intravenous hydration of 0.9% saline solution of sodium chloride (NaCl) at a rate of 1.0–1.5 ml/kg/h before the PCI. In 2 group - prevent group (n = 86) we prevented CI-AKI according to the algorithm: patients with eGFR < 60 ml/min/1.73m² and/or with Mehran risk score >10 received intravenous fluid administration hydration of 0.9% NaCl and N-Acetylcysteine (NAC): without heart failure -0.9% NaCl 1 ml/kg/h for 12 hours pre-procedure and 12 hours post-procedure contrast administration; with heart failure - 0.9% NaCl 0.5 ml/kg/h for 12 hours pre-procedure and 12 hours post-procedure contrast administration; with NAC 600 mg before PCI and 600 mg after PCI. Both groups were comparable in age (60 ± 12 and 61 ± 11 years), comorbidity (hypertension 96 and 97%, chronic kidney disease 31 and 29%, diabetes mellitus 34 and 28%) and received therapy. CI-AKI was defined using 2012 KDIGO Guidelines. Isoosmolar contrast media ioxaglate (Visipaque-320) or low-osmolar contrast media iohexol (Omnipaque-350) were used. Transradial access for PCI was used in 98% of patients. Mann-Whitney test and multivariate logistic regression analysis were performed. P < 0.05 was considered statistically significant.

**Results:** The incidence of CI-AKI in intervention group was significantly lower than in the control group (6 vs 13%, p < 0.05).

**Conclusions:** Implementation of algorithm preventing in clinical practice significantly reduced risk of contrast-induced acute kidney injury in patient with delayed percutaneous coronary intervention.
ORAL SESSION

ORAL SESSION 3B: CARDIAC DISEASE

OP.3B.01 VALIDATION OF FRAMINGHAM AND SCORE IN 30560 PATIENTS WITH HYPERTENSION

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Objective: To validate the Framingham and SCORE predictors for cardiovascular death and death from coronary heart diseases in 30560 individuals with hypertension.

Design and method: Individual patient data was collected from seven randomized controlled trials (INDANA database and DIABHYCAR trial). We used the Framingham and SCORE equations to estimate the risks of cardiovascular death and death from coronary heart diseases of each patient. Predicted values were compared with observed ones in function of gender and age range.

Results: Both Framingham and SCORE seemed to work best in men aged 55–65. For men older than 65, both overestimated dramatically, particularly SCORE. For women older than 55, both predictors overestimated dramatically, particularly Framingham on the contrary for both outcomes. For women and men younger than 55, Framingham and SCORE slightly underestimated their risks (Fig.1).

Conclusions: In general, Framingham and SCORE appear to better predict risks of cardiovascular death and of death from coronary heart diseases in younger people in our database (<55 years old). On older subjects, both overestimated and in contrary tendency for men and women. These overestimations may due to shorter mean duration of follow-up of studied population (mean 4.96 years, max 11.87 years) vs. 10-year-risk predicted.

OP.3B.02 CORRELATION BETWEEN BLOOD LEVELS OF S100B PROTEIN AND INCIDENCE OF HEART FAILURE OR IMA IN A CARDIOLOGY UNIT

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Objective: Chronic heart failure is one of the most common consequence of myocardial infarction, and is characterized by a reduction of the heart ability to face peripheral blood distribution. Chronic heart failure (HF) and myocardial infarction (IMA) are often associated to the augmentation of inflammation markers. S100B is an alarmin secreted by damaged cardiomyocytes. Serum S100B levels were increased in the pathogenesis of heart disease and involved their pathogenetic mechanisms. S100B is a tissue-specific protein (chondrocytes, adipocytes, skeletal myofibers, cardiomyocytes, dendritic cells, etc.); it was largely demonstrated to be released after a damage and the consequent remodelling involving cardiac tissue. We examined the correlation between S100B protein serum levels and the incidence of acute heart failure and IMA in symptomatic patients.

Design and method: We conducted a prospective study on 90 patients aged between 50 and 72 years accepted to our Unit referring cardiac associated symptoms (thorax pain, dyspnea, arrhythmic symptoms). They were divided in three groups: healthy subjects (group A), chronic heart failure patients (group B) and IMA patients (group C). CRP, NT-proBNP, and routine exam were performed in every patient. Moreover it was made a S100B dosage was made.

Results: Results demonstrated different levels among healthy subjects. However in chronic heart failure patients the alarmin levels were higher but not significantly augmented. Instead AMI patients had mean values of S100B doubled than the other two groups and significantly augmented.

Conclusions: According to our data S100B as the potential to be, in a near future, be considered as an acute myocardial infarction marker in addiction to the ones existing. However more studies are needed to identify possible byas elements in S100B serum dosage. This together with other elements are guiding us to a better understand of macro-structural changes in damaged heart in order to consider new therapeutic targets.

OP.3B.04 INADEQUATE CARE OF HYPERTENSION IN CORONARY PATIENT

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Objective: To improve secondary prevention with cardiac rehabilitation, particularly hypertension among coronary patients

Design and method: From 2005 to 2015, out of 1255 patients having cardiac rehabilitation, 1091 (87%) were coronary patients and 746 (68%) aged 60 years (20–85), 15% women, 44% hypertensive, 17% diabetics, 74% with dyslipidemia and 8% without these 4 risk factors were re-examined 12 months later and were compared with the results of Euroaspiré IV (Euro IV) study. 56% came after acute myocardial ischemia and 66% were treated by angioplasty (PTCA), 31% by coronary bypass. The 4-week ambulatory educational program consisted of a physical education with 22 meetings of cardiac rehabilitation (ergo cycle, carpet, segmentary muscular work, steps and balneotherapy) and a therapeutical, psychological and dietetic education (18 courses and cooking workshops, supermarket visits and self BP measurement). The patients were followed by a computerized medical file. BP (average of 3 measurements measured by a nurse computerized medical file at least 24 h after the last exercise session), LDL cholesterol and smoking during first hospitalisation (H), waist circumference (WC), physical activity (insufficient if less than 3 walks of 30 min per week) and drugs intake were analyzed at D0, at the end of program, then at one year.

Results: After 1 year, 32% had 1 antihypertensive drug (72% beta blocker BB), 46% 2 drugs (74% BB and ACE inhibitor or ARB) and 12% 3 drugs (53% BB, ACEI/ARB and diuretic and 27% BB, ACEI/ARB and CC). BB and particularly ACEI/ARB decreased at 1 year. In univariate analysis, WC and physical activity were significantly associated with BP control at 1 year and
only physical activity in multivariate analysis but not number of antihypertensive drugs. 7% were hospitalized at 1 year for a new coronary event but risk factors levels or drugs were not significantly different between patients who were hospi-
talized or not. Only % of PTCA were significantly different.

Conclusions: Assessing cardiac rehabilitation improves CV risk factors manage-
ment compared with Eurosporixe but, this, decreases with time particularly BP con-
trol. Decreasing physical activity is the most important factor for this BP increase.

**HEXARELIN PRESERVES MYOCARDIAL FUNCTION AND REDUCES INFLAMMATION AND FIBROSIS IN A MOUSE MODEL OF MYOCARDIAL ISCHEMIA REPERFUSION**


**Objective:** Growth hormone secretagogues (GHS) have been demonstrated to improve cardiac function, attenuate inflammation and modulate the autonomic nervous system in models of ischemic heart disease (IHD). This study aimed to determine whether hexarelin (HEX), a synthetic GHS, preserves cardiac function and attenuates inflammation and remodelling using a mouse model of myocardial ischemia reperfusion (IR).

**Design and method:** Myocardial ischemia was induced by transient ligation of the left descending coronary artery (LAD) in C57BL/6J mice followed by HEX (n = 18) or vehicle (VEH) (n = 17) administration at 0.3 mg/kg/day for 21 days. Treated and sham mice were subjected to magnetic resonance imaging using a T1-weighted late gadolinium enhancement sequence (LGE) at 9.4 Tesla (T) to measure left ventricular (LV) function and tissue characteristics after 24 hours and 21 days.

**Results:** HEX mice demonstrated a significant improvement in cardiac function compared with the VEH-treated group, demonstrating preservation of both systolic and diastolic function. A significant decrease in interstitial collagen and col-
gen concentration was demonstrated after 21 days within the HEX group. This was accompanied by a decrease in TGF-beta1 and alpha-SMA. Heart rate vari-
ability (HRV) analysis demonstrated that HEX treatment shifted the balance of autonomic nervous activity towards a parasympathetic predominance, evidenced by a smaller low/high-frequency power ratio (LF/ HF) and increased normalized high frequency power (nHfF). This was combined with a significant decrease in Tropinin-I (CtI-I) and TNF-alpha levels with HEX treatment.

**Conclusions:** These results demonstrate that GHS may preserve ventricular function and prevent remodelling in models of myocardial IR. The protective ef-
fects of HEX might be attributed to rebalancing the deregulated autonomic nerv-
ous system and activation of the cholinergic anti-inflammatoriy pathway (CAP) in myocardial IR.

**MEAN SYSTOLIC BLOOD PRESSURE AFTER ADMISSION FOR MYOCARDIAL INFARCTION IS ASSOCIATED WITH ONE YEAR MORTALITY AMONG ELDERLY PATIENTS**

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**Objective:** Optimal blood pressure after acute myocardial infarction (AMI) is still debated. After admission for AMI, the target mean systolic blood pressure (mSBP) is unknown, especially in the elderly patients.

**ARTERIAL HYPERTENSION AS PROGNOSTIC MARKER IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION AND EARLY PERCUTANEOUS CORONARY INTERVENTION**


**Objective:** Strong evidence points to the prognostic value of renin-angiotensin-
system (RAS)-inhibitors (ACE inhibitors or AT1-receptor blockers) and beta blockers (BB) in the secondary prevention after myocardial infarction (MI). How-
ever, adequate dosing of these drugs is often limited due to their blood pressure lowering effects, especially early after MI. The present study therefore sought to iden-
tify differences in rates of prescription, persistence and dosing of RAS-inhib-
itors and BB early after acute ST-elevation MI (STEMI) and its impact on survival in hypertensive and non-hypertensive patients.

**Design and method:** 1003 consecutive patients with adjudicated STEMI treated by early percutaneous coronary intervention (PCI) between 2007 and 2011 in a single centre were retrospectively dichotomized according to their history of arte-
rial hypertension at the time of hospital admission.

**Results:** Mean age was 63 ± 13 years, body mass index 27 ± 5 kg/m², 24% were women. 749 patients were diagnosed with hypertension. Mortality was 11.3% at 30 days and 17.2% at 1 year follow-up. History of hypertension at time of hospital admission was significantly associated with lower mortality on follow-
up (OR, at 30 days: 0.41 (0.27–0.64), at 1 year 0.37 (0.26–0.53)). Persistence to RAS-inhibitors was significantly higher in hypertensive patients compared to non-hypertensives (54% vs. 70%, p = 0.004). However, persistence to BB did not differ between groups (84% vs 86%, n.s.). At discharge the rate of prescription of RAS-inhibitors and BB was significantly higher in hypertensive patients (RAS-
inhibitors: 87.3% vs. 69.8%, p < 0.001; BB: 92.8% vs. 84.3%, p < 0.001). In ad-
dition, the defined daily dose (DDD) among patients receiving RAS-inhibitors at discharge was higher in hypertensive versus non-hypertensive patients (DDD: 0.40 vs. 0.30, p = 0.001), whereas there was no difference for BB. At 30 days and 1 year follow-up survival was significantly associated with the prescription of RAS-inhibitors as well as BB at discharge.

**Conclusions:** Patients with a history of hypertension show higher prescription rates at discharge, better long-term persistence as well as higher individual dosing of RAS-inhibitors after STEMI. This, as well as the higher prescription rates of BB, may contribute to the better survival that we observed in patients with history of hypertension compared to non-hypertensive controls.
ORAL SESSION

ORAL SESSION 3C: EPIDEMIOLOGY OF HYPERTENSION AND METABOLIC DISORDERS

OP.3C.01 COMPARISON BETWEEN EUROPEAN SYSTEMATIC CORONARY RISK EVALUATION AND ITALIAN CUORE ALGORITHMS IN ADULT OUTPATIENTS FOLLOWED BY GENERAL PRACTITIONERS AND SPECIALISED CENTRES

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Objective: Global cardiovascular (CV) risk stratification based on either European Systematic Coronary Risk Evaluation (SCORE) or Italian CUORE algorithms should be performed in all adult outpatients by both general practitioners (GPs) and specialised physicians (SPs).

Design and method: To compare individual CV risk profile by using either European SCORE and Italian CUORE algorithms in adult outpatients followed by GPs and SPs in Italy. All available data were centrally analysed for global CV risk assessment and rates of control of major CV risk factors, including blood pressure (BP), serum cholesterol, triglycerides and glucose levels. CV risk profile characterization was based on both SCORE and CUORE algorithms. Study population was stratified accordingly to referring physicians (GPs, cardiologists, diabetologists, other SPs).

Results: We analysed data from an overall population sample of 10,404 adult outpatients (age 60.7±6.5 years, BMI 28.3±4.9 kg/m2, BP 136.7±14.4/82.1±8.2 mmHg, total cholesterol 212.2±40.7 mg/dl, HDL cholesterol 50.8±12.3 mg/dl), among whom 7,767 (74.7%) were followed by GPs, 1,239 (11.9%) by cardiologists, 1,006 (9.7%) by diabetologists and 392 (3.8%) by other SPs. Systolic/diastolic BP, total/LDL cholesterol and triglycerides levels were higher and HDL cholesterol was lower in patients followed by GPs and cardiologists compared to other groups. Conversely, BMI and fasting glucose levels were higher in patients followed by diabetologists than in other groups. All major CV risk factors and comorbidities were more frequently reported and controlled in patients followed by cardiologists than in the other groups, with the only exception of diabetes. Both European SCORE (4.7±4.5) and Italian CUORE (13.7±11.5) were significantly higher in outpatients followed by cardiologists than in those followed by GPs (4.0±3.6 and 11.5±9.7) and diabetologists (3.7±3.5 and 10.3±9.2) or other SPs (3.3±2.8 and 9.4±7.4; P < 0.001 for all comparisons).

Conclusions: Despite proper use of drugs and better pharmacological control of major risk factors, both European SCORE and Italian CUORE algorithms reported higher CV risk profile in patients followed by cardiologists than in patients followed by diabetologists, GPs, and other SPs.

OP.3C.02 EXERCISE SYSTOLIC BLOOD PRESSURE AT MODERATE WORKLOAD: WHICH THRESHOLD LEVEL PREDICTS CORONARY HEART DISEASE IN HEALTHY, MIDDLE-AGED MEN?

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Objective: Elevated exercise systolic blood pressure (SBP) is associated with increased risk of coronary heart disease (CHD). However, at which threshold level of exercise SBP the risk of CHD is elevated, has not been established. We aimed to investigate this by performing analyses for threshold levels between 160 mmHg and 195 mmHg.

Design and method: In the Oslo Ischemia Study, 1999 healthy, middle-aged men were able to complete a six-minute, ECG-monitored bicycle test at 100W workload (Survey 1). At Survey 2, seven years later, 1392 men were still healthy and included in this study. The men were successively grouped by SBP at 100W (SBP100W) below or above incremental threshold levels measured at both surveys. Group 1 had SBP100W < threshold level at both Survey 1 and 2, Group 2 had SBP100W >/= threshold level at Survey 1 or Survey 2, and Group 3 had SBP100W >/= threshold level at both Survey 1 and Survey 2. Stepwise risk analyses were performed for incremental thresholds raised by 5 mmHg in each step, from 160 mmHg to 195 mmHg. Outcome was CHD defined as first event of fatal/non-fatal myocardial infarction or angina pectoris, and participants were followed for 28 years. Hazard ratios were calculated using Cox proportional hazards model adjusted for age, SBP at rest, smoking status, total serum cholesterol, family history of CHD and physical fitness, and Group 3 was compared with Group 1 for each 5 mmHg increment in threshold level of SBP100W.

Results: When comparing Group 3 with Group 1, there was significantly increased risk of CHD in Group 3 at all threshold levels of SBP100W from 165 mmHg to 190 mmHg (figure). With increasing average SBP100W in Group 1 as the threshold level increases, the stable hazard ratios represent increasing risk of CHD with increasing SBP100W.

Conclusions: There is an increased long-term risk of coronary heart disease in men showing sustained exercise systolic blood pressure >/= 165 mmHg. The association is independent of classical cardiovascular risk factors, systolic blood pressure at rest and physical fitness.

OP.3C.03 BLOOD PRESSURE SCREENING RESULTS FROM HEALTHY HEART AFRICA: SCREENING LOCATIONS, PARTICIPANT CHARACTERISTICS, AND HYPERTENSION CLASSIFICATION IN KENYA

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Objective: Hypertension is highly prevalent in Africa but is characterized by poor awareness, treatment, and control rates. Healthy Heart Africa (HHA) is a comprehensive hypertension intervention program designed to improve hypertension awareness, detection, referral, treatment, and retention in care. Here, we present mass blood pressure (BP) screening results from the HHA program.

Design and method: HHA was initiated in March 2015 as a partnership between local organizations, government, and industry. Protocols for identifying and managing hypertension in adults were developed through collaboration with the Kenyan Ministry of Health. Six partners developed and implemented novel approaches to educate, screen, and treat adult Kenyans for hypertension. Healthcare
providers at participating facilities received HHA hypertension protocols and screened eligible individuals. Elevated BP was defined as ≥ 140/90 mmHg. De-identified screening data were extracted from service delivery registers and summarized descriptively.

**Results:** Over 18 months, 2,014,285 Kenyans were screened at participating facilities. Screenings occurred in health clinics (35%), home (15%), work (11%), church (10%), public meetings (7%), others (19%), and not recorded (3%). More women than men were screened (63% vs 36%; 1% gender not recorded). Urban men were more easily reached by screening along daily, busy walking commutes and through nonclinic sites. Of those screened, 21% had elevated BP; prevalence increased with increased age (Figure). More than 40% of individuals aged ≥60 years had elevated BP. More men than women in younger age groups (16–20 and 21–25 years) had elevated BP. Of those screened, 31% had normal BP (<120/80 mmHg), 48% were prehypertensive (120–139/80–89 mmHg), 14% had stage 1 hypertension (140–159/90–99 mmHg), 5% had stage 2 hypertension (160–179/100–110 mmHg), and 2% had severe BP (≥180/110 mmHg).

**Conclusions:** While these findings are not from a representative sample, data demonstrate high prevalence of elevated BP indicative of hypertension prevalence among Kenyan adults, illustrating the need for screening in the community. Screening in nontraditional settings may be an effective strategy to reach more men who were more difficult to reach than women. Systematic screening is expected to increase hypertension detection, treatment, and ultimately control rates.

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**OP.3C.05 LDL-PARTICLES COMPOSITION AND INCIDENT CARDIOVASCULAR DISEASE IN A SOUTH-EUROPEAN POPULATION: THE HORTEGA LIPOSCALE STUDY**

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**Objective:** The use of LDL-cholesterol particles (LDL-p) for cardiovascular risk prediction has been tested in high risk populations. The objective of this study was to evaluate the association of LDL-p and LDL-p composition with incident cardiovascular disease in adults participating in the Hortega Follow-up Study, a cohort study representative of a general population from Spain.

**Design and method:** “Standard” lipid levels (plasma total cholesterol, HDL-cholesterol, and triglyceride concentrations) were determined using a Hitachi 917 analyzer. The number and size of lipid particles were measured by nuclear magnetic resonance using LIPOSCALE algorithm (Biosfer Teslab, Reus, Spain). The association of lipid levels and LDL-particles composition with incident cardiovascular disease was assessed.

**Results:** A total of 1162 subjects (49% male, mean age 49.7 years) was included into the study. LDL-p distribution was as followed: Small LDL-p was predominant (40–70%), followed by Medium LDL-p (20–40%) and Large LDL-p (10–20%). During a mean follow-up of 12.4 ± 3.3 years, a total of 159 CV events occurred. LDL particle size was related to all events when traditional cardiovascular risk factors were controlled for. Medium LDL-p, but not Small LDL-p, increased the risk of CHD and stroke in all statistical models. The relevance of Medium LDL-p was further evaluated in a compositional analysis using a leave-one-out approach. The highest risks were observed for LDL-p and CHD when the proportions of Medium and Small LDL-p were entered simultaneously into the model, which reflects an increase in the proportion of Medium LDL-p and Small LDL-p by a corresponding decrease in the proportion of Large LDL-p, respectively. That shift from Large to Medium and Small LDL-p proportions was associated with an increase in risk for CHD of 70% and 46%, respectively (figure 1).

**Conclusions:** In a representative sample of the general population from Spain, NMR-measured LDL-particle size and composition were associated with cardiovascular outcomes. An increase in the proportion of Medium LDL-particles and Small LDL-particles by a corresponding decrease in the proportion of Large LDL-p was strongly associated with CHD. Further research is needed to elucidate the causal pathways underlying these associations.
ANTIHYPERTENSIVE PRESCRIPTION PATTERNS AND CO-MORBIDITIES IN PATIENTS WITH NEWLY DIAGNOSED HYPERTENSION IN GERMANY. ANALYSIS OF GERMAN STATUTORY HEALTH INSURANCE DATA

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Objective: Inadequate treatment is one reason for poor hypertension control and prognosis in patients with hypertension. Guidelines recommend antihypertensive combination therapy for patients at increased risk or major co-morbidities. We analyzed antihypertensive prescription patterns and co-morbidities in patients with newly diagnosed hypertension.

Design and method: In a database of several German statutory health insurance companies covering the period from 2011–2013 we analyzed the occurrence of newly diagnosed hypertension and major co-morbidities (diabetes, myocardial infarction, heart failure, stroke and renal dysfunction) by ICD code during 2012. We also analyzed the linked prescription data for antihypertensives by ATC code.

Results: Of 2,077,889 persons at least 18 years of age, 32.2% carried the diagnosis hypertension, of which 7.9% (53,118) were newly diagnosed in 2012 (incidence 2.6%). Newly diagnosed patients received antihypertensive medication in 78.2%, while 21.8% received none. 70.8% of the treated patients were initiated on monotherapy, 13.2% on combination therapy and 16.0% on fixed-dose combination. In the monotherapy group, 43.5% received ACE inhibitors, 32.2% beta-blockers, 8.2% angiotensin II receptor blockers, 7.7% diuretics and 7.7% were prescribed calcium channel blockers. When free combination treatment was prescribed, 73.5% contained beta-blockers, 72.9% contained ACE inhibitors, 40.6% contained diuretics and 25.7% contained calcium channel blockers. Among newly diagnosed patients on monotherapy, 28.7% had at least one major co-morbidity, while in patients without antihypertensive treatment, at least one major co-morbidity existed in 18.0%.

Conclusions: The majority of patients with newly diagnosed hypertension is initiated on monotherapy suitable for patients at low risk, while one fifth of patients remains untreated. However, in both groups a significant number of patients have at least one major co-morbidity, suggesting in part inadequate risk management.

OP.3C.07 BLOOD PRESSURE, HEART RATE AND DOUBLE PRODUCT IN A POOLED COHORT: THE JAPAN ARTERIOSCLEROSIS LONGITUDINAL STUDY (JALS)

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Objective: To figure out the characteristics of blood pressure (BP), heart rate, and double products among a population sample of the Japan Arteriosclerosis Longitudinal Study (JALS).

Design and method: JALS is a collaborative project of prospective cohort studies in Japan with a common protocol. We pooled individual records from 99,207 participants in 7 work-site based cohorts. The data were analysed to provide information on BP, heart rate, and double products according to age-sex groups and use of antihypertensive medication.

Results: Average BP was 130/77 mmHg among men and women combined. Among untreated individuals, systolic BP level increased with an increase in age (Figure A), whereas diastolic BP reached a ceiling around the age of 60 (Figure B). Average systolic BP of treated participants was around 140 mmHg irrespective of age (Figure A), whereas diastolic BP level decreased linearly with an advance in age (Figure B), and 56.4% of treated participants had a BP of 140/90 mmHg or over. Heart rate did not differ across age groups or treatment status. Double product, also called rate-pressure product calculated by multiplying systolic BP and heart rate, increased with an increase in age among untreated individuals which is mediated by an age-dependent increase in systolic BP, while it first decreased and then increased along with the advance in age among treated individual.

Conclusions: The current JALS project provides descriptive information on BP, heart rate, and double product, and demonstrates inadequate BP control across age and sex in Japan where an average life expectancy is the longest in the world.

ELEVATED PULSE PRESSURE IN YOUNG TO MIDDLE AGE MEN CARRIES A REDUCED RISK OF ADVERSE OUTCOME

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Objective: Elevated pulse pressure (PP) is a well recognized predictor of adverse outcome in elderly hypertensive subjects whereas its clinical significance in young individuals remains controversial. The aim of the present study was to investigate the clinical significance of elevated PP in young-to-middle-age subjects screened for stage 1 hypertension.

Design and method: We examined 1241 18-to-45-year-old participants from the HARVEST study. The predictive role of PP versus mean blood pressure (MBP) for incident hypertension and cardiovascular events (CVE) was evaluated in Cox survival analyses, adjusting for risk factors and several confounders.

Results: PP was inversely related to age in men (r = −0.29, p < 0.001) and directly related to age in women (r = 0.18, p = 0.002). In multivariate regression analysis including BMI and lifestyle factors, significant determinants of PP were male gender (p < 0.001), younger age, (p < 0.001), physical activity (p < 0.001), heart rate (p < 0.001), and stroke volume (N = 829, p = 0.001). During 12.1 years of follow-up (IQR = 5.1–17.4), 65.0% of participants developed hypertension requiring pharmacological treatment. In Cox models adjusted for age, sex, BMI, heart rate and lifestyle factors, participants in the highest PP tertile had a reduced risk of incident hypertension compared to those of the bottom tertile (HR, 0.70 [95% CI, 0.58–0.85], p < 0.001). In contrast, participants in the top MBP tertile had an increase in risk (1.33, 1.10–1.62, p = 0.0039). In sensitivity analyses, these associations held true in men (HR, 0.65 [95% CI, 0.52–0.81], p < 0.001 for...
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PP, and 1.50, 1.20–1.89, p < 0.001, for MBP) but not in women (p > 0.49 for PP and MBP). CVE were developed by 6.0% of participants. In multivariable Cox models, participants in the highest PP tertile had a reduced risk of CVE (HR 0.46, 95% CI 0.24–0.89, p = 0.021) and those in the top MBP tertile had a marked increase in risk (3.43, 1.60–7.35, p = 0.0016). Again, these associations remained significant among the men (0.47, 0.23–0.96, p = 0.040, for PP, and 3.89, 1.56–9.72, p = 0.0038, for MBP), but not among the women (p > 0.30 for PP and MBP).

Conclusions: These data show that in men younger than 45 years, only MBP is a predictor of hypertension needing treatment and of CVE whereas high PP even carries a reduced risk of adverse outcome.

OP.3C.09 RECURRENT ROTATIONAL VERTIGO IS A PREDICTOR OF STROKE IN HYPERTENSIVE PATIENTS

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Objective: Vertigo is associated with hypertension but also with numerous other aetiologies. The aims of the present study were 1) to describe the characteristics and the clinical correlates of vertigo in a large cohort of hypertensive patients and 2) to test the prognostic value of this symptom for all-cause, cardiovascular, and stroke mortality.

Design and method: 1716 hypertensive individuals were questioned at baseline with a standardized questionnaire. They were categorized first, according to the absence or the presence of at least twice vertigo during the past year. When the symptom was present, patients were classified according to 4 subgroups: rotational, hypotension-like, seasickness and other vertigo.

Results: Baseline characteristics of our cohort were: mean age 45 years, 61% of men, mean office blood pressure 175/104 mmHg, 13% of diabetes, mean eGFR 82.4 mL/min and 20% of previous cardiovascular event. 33.9% (N = 581) of patients experienced frequent episodes of vertigo. Multiple regression analysis demonstrated that vertigo was predicted by age, gender (women) and coronary artery disease. After 30 years of follow-up, we observed 956 deaths of whom 508 from cardiovascular cause (including strokes) and 114 acute strokes. As shown by Kaplan-Meier curves (Figure), frequent vertigos were predictor of stroke mortality (p = 0.001) but not both for all-cause and cardiovascular mortality (p = 0.371 and p = 0.233, respectively). In the multivariate Cox regression model adjusted for cardiovascular risk factors, secondary prevention and treatment, patients with vertigo have a similar risk for stroke mortality than those without (hazard ratio 1.19; 95% CI [0.81–1.77]). Analyzing in turn, the different subgroups of vertigo, rotational vertigo predicted stroke death after adjustment (hazard ratio 2.08; 95% CI [1.22–3.55]), while the association was not observed with hypotension-like vertigo (hazard ratio 1.00; 95% CI [0.55–1.83]), seasickness vertigo (hazard ratio 1.12; 95% CI [0.72–1.76]) and other vertigo (hazard ratio 0.88; 95% CI [0.48–1.61]).

Conclusions: Recurrent vertigos in hypertensive patients are associated at baseline with gender, age and coronary artery disease. Hypertensive patients complaining with frequent rotational vertigos must be carefully followed over years because of their increase risk of stroke mortality.
OP.4A.01
CHANGES IN SUBCLINICAL TARGET ORGAN DAMAGE IN OBESE PATIENTS UNDERGOING BARIATRIC SURGERY. THE BARIHTA STUDY

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Objective: We aimed to assess changes in subclinical target organ damage (STOD) in obese patients 1 month after BxS.

Design and method: We conducted a prospective study of obese patients undergoing BxS, either gastric bypass or sleeve gastrectomy. Office-BP and 24h-ambulatory-BP, both peripheral and central, were measured by the portable automated Mobile-O-Graph® device at baseline and 1 month after BxS. Changes in markers of STOD such as arterial stiffness (as measured by 24h-pulse wave velocity [PWV], 24augmentation index [AIx] and pulse pressure [PP]), and urinary albumin excretion (UAE) were evaluated.

Results: Thirty-five patients scheduled for BxS (77% women; mean age: 41.5 ± 9.7 yr; body weight: 119 ± 22 Kg; body mass index, median [IQR]: 41.1 Kg/m² [38.2; 46.1]; hypertensives: 49%) were consecutively included and prospectively evaluated. Arterial stiffness changed at 1 month follow-up (mean [95%CI]): variation of 24h-PWV = –0.21(± 0.31 to –0.10), p < 0.001; variation of 24h-AIx = –2.39 (± 3.99 to –0.79), p = 0.005; variation of 24h-peripheral-PP = –3.6 (± 5.4 to –1.7), p < 0.001; variation of 24h-central-PP = –3.8 (± 5.4 to –2.1), p < 0.001. Albuminuria also changed significantly: baseline UAE, median [IQR] = 4.3 [2.9; 12.1]; 1-month UAE = 5.1 [3.3; 7.6]; Z = 2.4; p = 0.018. Body weight (Kg) variation (median [IQR]) was: baseline = 115 [101; 139]; 1-month = 104 [89; 122], Z = -5.1; p < 0.001. Generalized linear models were built to assess changes in STOD after adjusting by age, gender, hypertension condition, variation of 24h-peripheral SBP, variation of body weight and the corresponding baseline STOD value. Variation of PWV was associated with variation of 24h-SBP (p = 0.001, r² = 0.850); variation of PP was associated with variation of 24h-PP (p = 0.001, r = 0.670); variation of AIx was associated with age (p = 0.019), baseline AIx (p = 0.019) and marginally with variation of 24h-PP (p = 0.09), r = 0.262; variation of UAE was associated with age (p = 0.005), gender (p = 0.008) and baseline UAE (p < 0.001) and marginally with variation of 24h-SBP (p = 0.051), r² = 0.779.

Conclusions: In obese patients, STOD decreased at 1 month following bariatric surgery. Arterial stiffness improvement was mostly due to changes in 24h-SBP, while albuminuria decrease was mostly depending on baseline albuminuria. Body weight loss per se was not responsible for STOD changes.

OP.4A.02
CHANGES IN PERIPHERAL AND CENTRAL BLOOD PRESSURE IN OBESE PATIENTS UNDERGOING BARIATRIC SURGERY

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Objective: To assess changes in office and 24h-ambulatory blood pressure (BP), both peripheral- and central-, in obese patients 1 month after bariatric surgery (BxS).

Design and method: Prospective study of patients with morbid obesity undergoing BxS. Office-BP (mean of 4 manual measurements) and 24h-ambulatory-BP, both peripheral and central, were measured by the Mobile-O-Graph® device at baseline and 1 month after BxS. Changes in all BP parameters were evaluated.

Results: Thirty-five patients scheduled for BxS (77% women; age: 41.5 ± 9.7yr; body weight: 119 ± 22Kg; hypertensives: 49%) were included and prospectively evaluated. One month after BxS, a significant decrease was observed in all parameters of both peripheral and central (systolic and diastolic) BP both in office-BP and in the 24 h and in the daytime periods, but not during the nighttime period (Table). These changes occurred in both hypertensive and normotensive patients.
**Abstracts**

**OP.4A.04 NON-INVASIVE HEMODYNAMIC MONITORING AS A GUIDE TO DRUG TREATMENT OF UNCONTROLLED HYPERTENSIVE PATIENTS: HOME BLOOD PRESSURE IN THE BEAUTY STUDY**


Objective: In the BEAUTY study we investigated whether utilizing non-invasive monitoring of hemodynamic parameters combined with a drug selection algorithm (integrated hemodynamic management-ISHM) compared to conventional drug selection may improve uncontrolled hypertension.

Design and method: Uncontrolled (office systolic blood pressure (SBP)>140 mmHg and ambulatory daytime SBP >135 mmHg while taking >2 antihypertensive drugs) essential hypertensive patients were referred to 5 European Hypertension Excellence Centers and were randomized to IHM-guided (n = 83) vs. conventional (control, n = 84) treatment adjustment in an investigator-initiated multicentre prospective randomized parallel groups controlled study. The average number of antihypertensive drugs increased from 3.1 to 4.1 in both groups and differed only in a rise of the use of diuretics in the IHM groups (from 13 to 31%).

Results: Home SBP was available in 46 IHM and 38 controls displayed at 6 months significantly greater reduction in IHM (-21.1±17.7 mmHg) than in controls (-10.2±3.0 mmHg, P = 0.002). Home SBP changed from 152.1±15.8 and 149.8±11.9 mmHg to 131.0±11.1 and 139.6±12.8 mmHg in IHM group and Controls (-10.2±13.0 mmHg, P = 0.002), which remained significant after multiplicity adjustment and after adjustment for baseline SBP, recruiting center, age, sex and BMI (P < 0.0001).

Table. Home Blood Pressure Values and Control Rates at 6 Months (n=84)

| Changes in BP | IHM group (N=46) | Control group (N=38) | Diff (IHM-Control) | P (Bonf)-test | Home SBP | -21.1 (17.7) | -10.2 (13.0) | -10.90 (-17.77, -4.62) | 0.002 | Home DBP | -7.6 (9.0) | -6.9 (10.6) | -0.67 (-4.91, 3.58) | 0.756 | Home SBP (<135mmHg) | N=30 (65%) | N=12 (32%) | 0.002 | Home DBP (<140mmHg) | N=34 (74%) | N=27 (71%) | 0.779 |

Conclusions: Non-invasive hemodynamic monitoring associated with a drug selection algorithm induced larger reduction in home BP compared to conventional drug selection in uncontrolled hypertensive patients referred to European Hypertension Excellence Centers. Thus, these home BP taken by patients themselves may suggest that the integrated hemodynamic monitoring after all may be useful in at least subgroups of the patients with uncontrolled hypertension.

**OP.4A.06 CARDIOVASCULAR RISK IS BETTER REDUCED BY BEDTIME THAN UPON AWAKENING HYPERTENSION TREATMENT-REGIMEN: THE HYGIA PROJECT**


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Objective: In hypertension, ingesting blood pressure (BP)-lowering medications at bedtime, compared to upon awakening, is usually associated with significantly improved reduction of sleep-time BP mean, a sensitive prognostic marker of cardiovascular disease (CVD) risk. The Hygia Project, a research network presently composed of 292 investigators of 40 clinical sites, was specifically designed to test the hypothesis that bedtime chronic therapy entailing the entire daily dose of >1 conventional hypertension medications exerts better ambulatory BP control and CVD risk reduction than all such medications ingested upon awakening.

Design and method: We conducted a prospective, randomized, open-label, blinded endpoint trial of 15,674 hypertensive patients (8,682 men/6,992 women, 60.4±13.7 years of age) according to ambulatory BP (ABPM) criteria. Participants were randomized to ingest all their prescribed hypertension medications upon awakening (n = 7,848) or the entire daily dose of >1 conventional treatment upon one of them at bedtime (n = 7,826). Among the later, 3,918 participants were ingesting all medications at bedtime and the remaining 3,908 ingested some medications at bedtime and others upon awakening. At inclusion and at every scheduled clinic visit for ABPM (at least annually) during follow-up, BP was assessed for 48 h. The primary CVD-outcome was the composite of CVD death, myocardial infarction, coronary revascularization, heart failure, and stroke.

Results: During a median 5.1-year follow-up, we documented 1,154 major CVD events. Patients of the bedtime, compared with the upon-waking, treatment group showed significantly lower hazard ratio of CVD events, adjusted for significant influential characteristics of age, sex, type 2 diabetes, chronic kidney disease, cigarette smoking, HDL-cholesterol, asleep systolic BP (SBP) mean, sleep-time relative SBP decline, and previous CVD event (0.47 [95% CI 0.42–0.54], P = 0.001). CVD risk was further reduced among patients who ingested not just some, but all their BP-lowering medications at bedtime (0.27 [0.21–0.34], P = 0.001, compared with ingestion of all medications upon awakening).

Conclusions: In hypertensive patients, ingestion of some (preferably all) BP-lowering medications at bedtime, compared with ingestion of all such medications upon-awakening, results in improved ambulatory BP control (significantly enhanced decrease of asleep BP and increase of sleep-time relative BP decline) and, most importantly, markedly reduced risk of major CVD events.

**OP.4A.07 THREE DIMENSIONAL META-ANALYSIS OF HYPERTENSION TRIALS WITH HEART FAILURE AS AN OUTCOME**

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Objective: Odds ratios (OR) are usually reported in meta-analyses summarizing data from multiple trials. However, absolute risk reduction (ARR) and drop-out rates (DOR) are important in the application of clinical trials in different clinical settings. We report a novel random effects meta-analysis method where OR, ARR and DOR are simultaneously evaluated.

Design and method: The effects of different classes of antihypertensive medications in preventing the occurrence of heart failure (HF) was examined using OR and ARR data from 54 randomized clinical trials (331,728 patients, 12,969 HF occurrences), of which 16 trials (87,187 patients, 2,793 HF events) included DOR. A three dimensional meta-analysis was performed using a novel algorithm based on the R statistical program.

Results: The expected relationship between OR and ARR for a given baseline risk was observed. Overall, higher efficacy in preventing HF (low OR 0.82, 95% CI 0.75 to 0.90) was associated with higher ARR (4.52%, 95% CI 2.46% to 6.58%), but also with higher DOR (OR 1.32, 95% CI 1.06 to 1.64). Diuretics were more effective in decreasing the OR of the occurrence of HF at follow-up (OR 0.52, 95% CI 0.38 to 0.70) and were associated with higher ARR (14.64%, 95% CI 7.30% to 21.98%). However, diuretics were associated with higher DOR (2.42%, 95% CI 1.51% to 3.90%). Verapamil was associated with an increased occurrence of HF during follow-up (OR 1.17, 95% CI 0.99 to 1.37) as well as with an increased rate of occurrence of HF during follow-up (by 2.34%, 95% CI 0.07% to 4.75%). The values for the other drug classes were between those for diuretics and verapamil. Angiotensin receptor blockers and intensive control of blood pressure regardless of antihypertensive class were associated with the lowest DOR (1.15%, 95% CI 0.91% to 1.44%) and 1.14%, 95% CI 0.84% to 1.54% respectively.)
Conclusions: This three dimensional meta-analysis may be useful in guiding clinicians in choosing the appropriate antihypertensive medication class in clinical care. Odds ratios may be used to summarize clinical trials, while absolute risk reduction and drop out rate are more appropriate in answering specific clinical questions.

**A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED CROSSOVER STUDY TO COMPARE QGC001, A BRAIN AMINOPEPTIDASE A INHIBITOR, WITH PLACEBO IN PATIENTS WITH GRADE I/II ESSENTIAL HYPERTENSION**

M. Azizi1, P. Courand2, T. Denolle3, V. Zhygalina1, P. Delsart4, L. Amar1, H. Rousse - Cardiology Department, Lyon, France, C. Llorens-Cortes6, P. Lantelme2, D. Deplanque4, C. Mounier-Vehier4, F. Balavoine5, O. Madonna5, years; 73.5% men; 88.2% white). dASBP, nighttime ambulatory SBP (nASBP),

Results:

- The difference in the change from baseline in daytime ambulatory SBP before and after 4-week of QGC001 or placebo administration. The primary end-point was the difference in the change from baseline in daytime ambulatory SBP after 4-week of QGC001 or placebo administration.

- Safety: Biochemical parameters and plasma hormone concentrations (active renin, aldosterone, cortisol, copeptin and apelin) were measured at 09:00 (trough) and before and after 4-week of QGC001 or placebo administration. The primary end-point was the difference in the change from baseline in daytime ambulatory SBP before and after 4-week of QGC001 or placebo administration.

- Conclusion: a randomized controlled trial of QGC001 in patients with essential hypertension may be useful in guiding clinical care. Odds ratios may be used to summarize clinical trials, while absolute risk reduction and drop out rate are more appropriate in answering specific clinical questions.

**THE RELATIONSHIP OF ALL-CAUSE MORTALITY TO AVERAGE ON-TREATMENT SYSTOLIC BP IS RELATED TO BASELINE SYSTOLIC BP: IMPLICATIONS FOR INTERPRETATION OF THE SPRINT STUDY**

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Objective: The SPRINT study demonstrated that targeting systolic blood pressure (SBP) < 120 mm Hg was associated with lower cardiovascular event and mortality rates. However, in the LIFE study, a lower achieved SBP (<130 mm Hg) was associated with increased mortality. Mean baseline SBP in SPRINT was 140 and a third of the population had a baseline SBP <= 132, raising the question of whether the lower baseline SBP in SPRINT could in part account for these differences.

Design and method: All-cause mortality in relation to tertiles of on-treatment average SBP achieved was examined in patients with baseline SBP < = or >25th percentile value of 164 mm Hg during 4.8 ± 0.9 years follow-up in 7998 non-diabetic hypertensive patients with ECG left ventricular hypertrophy assigned to losartan- or atenolol-based treatment. Average on-treatment SBP < 142 (lowest tertile) and average SBP 142 to < 152 (middle tertile) were compared with average SBP >= 152 (highest tertile and reference group).

Results: In the overall population, there was a highly significant interaction between baseline SBP <= 164 and average on-treatment SBP < 142 in Cox analysis (X2 = 15.48, p < 0.001). Among patients with baseline SBP > 164, in multivariate Cox analyses adjusting for other potential predictors of mortality and a propensity score for having baseline SBP <= 164, compared with average on-treatment SBP >= 152 an average on-treatment SBP < 142 was associated with 32% increased risk of mortality (HR 1.32, 95% CI 1.01–1.65), whereas average SBP of 142 to < 152 was associated with 24% lower mortality risk (HR 0.76, 95% CI 0.59–0.98). In contrast, in parallel Cox analyses among patients with baseline SBP <= 164, both an average on-treatment SBP < 142 (HR 0.60, 95% CI 0.36–0.99) and average SBP of 142 to < 152 (HR 0.51, 95% CI 0.30–0.89) were associated with statistically significant lower risks of mortality compared with average SBP >= 152.

Conclusions: All-cause mortality risk associated with achievement of an average SBP < 142 is strongly related to baseline SBP level in LIFE. These findings suggest that the lower mortality associated with a lower targeted SBP in SPRINT may not be applicable to patients with considerably higher baseline SBP than SPRINT patients.

**MODERATION OF ALCOHOL INTAKE AS A RECOMMENDED LIFESTYLE CHANGE IN HYPERTENSION: AWARENESS AND USE IN CLINICAL PRACTICE AMONG EUROPEAN PHYSICIANS**

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Objective: Moderation of alcohol consumption is one of the six lifestyle changes recommended in the 2013 ESH/ESC hypertension guidelines for the treatment of hypertensive patients with class I evidence level A. Thus, the guidelines recommend a maximum alcohol consumption of 20-30 g/day in hypertensive men and 10-20 g/day in hypertensive women. Within a survey assessing the level of awareness and implementation of the 2013 ESH/ESC guideline recommendations on lifestyle changes we specifically investigated the role of alcohol consumption in the management of hypertensive patients among European physicians.

Design and method: The complete survey included a total of 16 questions covering demographic data and questions that aimed to assess the level of aware-
ness and implementation of the 2013 guideline recommendations. It included six questions explicitly related to medical history of alcohol consumption, advice on alcohol intake and/or management of hypertensive patients with alcohol consumption. The survey was conducted at two national meetings in Germany (2015 annual meetings of the German Society of Cardiology and the German Society of Internal Medicine) and at two European meetings (ESH meeting in Milan 2015 and ESC meeting in London 2015).

Results: Overall, 1064 participated. Overall, 81.9% of participating physicians reported to quantify alcohol consumption in their hypertensive patients. The medical history of alcohol consumption was taken mostly in the context of newly detected hypertension (28.6%), rather than in patients with hypertension and very high blood pressure (BP) (17.5%) or in patients with treatment resistant hypertension (14.5%). Physicians recommend a mean maximum amount of alcohol intake of 13.1 ± 11.7 g/day for women (range: 0–150) and 19.7 ± 14.9 g/day for men (range: 0–125).

Conclusions: Although more than 80% of participating physicians reported to quantify alcohol consumption in their hypertensive patients, less than a third of physicians acknowledged to determine a history on alcohol intake in case of newly detected hypertension, very high BP or treatment resistant BP. The mean maximum amount of alcohol per day recommended did not exceed the recommended guidelines threshold. Awareness campaigns emphasizing the relationship between alcohol consumption and high BP, e.g. in patients with resistant hypertension, might improve currently unsatisfactory BP control rates.

THE TREATMENT BENEFIT OF THE ACE-INHIBITOR PERINDOPRIL ON TOP OF BETA-BLOCKER THERAPY IN PATIENTS WITH VASCULAR DISEASE AND HYPERTENSION

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Objective: We aimed to determine the potential synergistic effect the combination of beta-blockers with perindopril in a hypertensive population with cardiovascular disease or at high risk for cardiovascular disease.

Design and method: In patients participating in the ADVANCE, EUROPA, and PROGRESS trials who were randomized to an ACE inhibitor based regimen or placebo, we identified all patients who received a beta-blocker at baseline. We considered patients defined as hypertensive in the original studies (>160/95 mmHg or use of antihypertensives). We studied the effect of beta-blocker and perindopril therapy on cardiovascular outcomes and mortality with a multivariate Cox regression analysis versus beta-blocker and placebo.

Results: At baseline, 39% of patients in the three studies received a beta-blocker (n = 11418 out of 29 463 patients) and of these 51% were hypertensive (n = 5838). In the population receiving beta-blocker and perindopril, the composite end point of cardiovascular mortality, nonfatal myocardial infarction, and stroke was significantly reduced by 20% (HR 0.80, 95% CI: 0.71–0.90) compared with those receiving beta-blocker and placebo. The cardioprotective benefits seemed to be independent of the blood pressure effect. The reduction in risk of the composite endpoint by treating patients with beta-blocker/perindopril was 23% in patients with hypertension (HR 0.77, 95% CI: 0.66–0.89), and in non-hypertensive patients 16% (HR 0.84, 95% CI: 0.71–1.00), both significant without interaction. Within the hypertensive population, this significant benefit in the beta-blocker/perindopril group vs the beta-blocker placebo group was also observed for myocardial infarction (HR 0.74, 95% CI 0.58–0.94) and strong effect on all-cause mortality (HR, 0.68, 95% CI 0.57–0.82) (figure 1).

Conclusions: The addition of perindopril to beta-blockers in hypertensive patients with vascular disease significantly improves survival and lowers the risk of myocardial infarction.
ORAL SESSION

ORAL SESSION 4B: DIABETES

OP.4B.01 EFFECTS OF DAPAGLIFLOZIN ON EARLY ALTERATIONS OF THE MICRO- AND MACROCIRCULATION IN PATIENTS WITH TYPE-2 DIABETES

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Objective: Diabetes mellitus, primarily a metabolic disorder, must be considered also as a vascular disease. Early vascular changes are characterized by hyperperfusion (e.g. eye), vascular remodeling of small arteries and increased pulse wave reflection leading to increased (central) aortic pressure. We investigated the effects of the SGLT-2 inhibitor dapaglifozin on parameters of early micro- and macrovascular changes in patients with type-2 diabetes.

Design and method: In this prospective, double-blind, placebo-controlled, cross-over trial 59 patients (61 ± 7 years) with type-2 diabetes were randomly assigned to dapaglifozin 10 mg and placebo for 6 weeks. Retinal microvascular structure (wall-to-lumen ratio [WLR]) and retinal capillary flow [RCF]) were non-invasively assessed by scanning laser Doppler flowmetry. In addition, macrovascular parameters (central pulse pressure) were assessed by pulse wave analysis in addition to 24-h ambulatory blood pressure (ABP).

Results: Treatment with dapaglifozin for 6 weeks improved diabetic control (HbA1c, fasting and postprandial blood glucose, all p < 0.001) compared to placebo. Compared to placebo treatment with dapaglifozin reduced numerically but not significantly both microvascular parameters (RCF and WLR). When compared to baseline, treatment with dapaglifozin reduced RCF (308 ± 78 vs. 324 ± 84 AU, p = 0.028), indicative of a normalization of retinal hyperperfusion, and prevented vascular remodelling of retinal, which occurred in the placebo group (WLR: 0.356 ± 0.1 vs. 0.391 ± 0.1, p = 0.034). Moreover, compared to placebo, treatment of dapaglifozin reduced systolic and diastolic 24-h ABP (126 ± 11/75 ± 8 vs. 129 ± 12/77 ± 7 mmHg, p = 0.021/0.027), and central pulse pressure (40.9 ± 11 vs. 43.9 ± 12 mmHg, p = 0.05).

Conclusions: Overall, our data indicate that treatment with the SGLT-2 inhibitor dapaglifozin exerts beneficial effects on vascular parameters of the micro- and macrocirculation, suggesting an improvement of cardiovascular prognosis.

OP.4B.02 KLOTHO SUPPLEMENTATION ATTENUATES BLOOD PRESSURE AND OXIDATIVE STRESS IN DIABETES

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Objective: Klotho interacts with various membrane proteins such as receptors for transforming growth factor (TGF)-β and insulin-like growth factor (IGF) to alter their function. We have recently demonstrated that exogenous klotho protein supplementation suppresses renin-angiotensin system (RAS) and hypertension in adriamycin nephropathy. Renal expression of klotho is diminished in diabetes. In the present study, the effects of klotho supplementation on diabetic nephropathy were assessed.

Design and method: Recombinant klotho protein (0.2 mg/kg/day) or vehicle was administered daily by subcutaneous injection to db/db mice. Blood pressure was measured by tail-cuff methods. After 3 months, mice were killed by over-dose of anesthesia and the aorta and kidneys were harvested for the analysis.

Results: Exogenous klotho protein supplementation reduced kidney weight (0.36 ± 0.03 vs. 0.28 ± 0.02 g, p < 0.05), systolic blood pressure (112 ± 3 vs. 105 ± 2 mmHg, p < 0.05), albuminuria (2.9 ± 0.6 vs. 1.8 ± 0.4 mg/day, p < 0.05) and 8-epi-prostaglandin F2α excretion (410 ± 94 vs. 74 ± 41 ng/day, p < 0.01) without changes in body weight. Although klotho supplementation slightly increased glycated albumin from 1510 ± 60 to 1740 ± 70 mg/ml (p < 0.05), klotho reduced renal angiotensin II levels (202 ± 8 vs. 126 ± 4 fmol/g/ kidney wt) associated with reduced renal expression of angiotensinogen. Klotho supplementation improved aortic and renal expression of superoxide dismutase (SOD), as well as renal klotho expression itself (p < 0.01 for each). Klotho reduced renal abundance of hypoxia-inducible factor 1 and renal expressions of TGF-β and fibronectin (p < 0.05 for each). Klotho supplementation diminished renal abundance of phosphorylated Akt and mTOR (p < 0.01 for each). Creatinine clearance and glomerular expression of nephrin were similar between klotho and control groups.

Conclusions: The present data indicate that klotho supplementation reduces blood pressure and albuminuria in association with ameliorating RAS and fibrosis in db/db mice, similarly to adriamycin nephropathy. Furthermore, our results are consistent with the notion that klotho inhibits IGF signaling, inducing SOD to reduce oxidative stress and suppressing Akt-mTOR signaling to decrease abnormal kidney growth in diabetes. Finally, the present findings suggest that although klotho inhibits TGF-β signaling, it may increase insulin resistance, resulting in null effects on diabetic glomerulosis, providing translational evidence that greater cautions are required for glyceremic control in applying klotho protein supplementation for diabetic nephropathy.

OP.4B.03 BI-DIRECTIONAL INTERACTION BETWEEN THE SYMPATHETIC NERVOUS SYSTEM AND SGLT-2 REGULATION

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Objective: The sodium glucose co-transporter 2 (SGLT-2) mediates re-absorption of glucose from the renal proximal tubules. The SGLT-2 inhibitor empagliflozin has recently been associated with improved cardiovascular outcomes in patients with type 2 diabetes. We hypothesized that sympathetic nervous system (SNS) induced alterations of glucose metabolism may be mediated via regulation of SGLT-2 and investigated a possible interaction in cell culture and in a high-fat diet (HFD) mouse model.

Design and method: We used the human renal proximal tubule cell line HK2 to assess changes in SGLT-2 expression in response to a range of concentrations of noradrenaline (NA), the main neurotransmitter of the SNS. Furthermore, we investigated the effect of SGLT-2 inhibition with dapaglifozin on SGLT-2 and tyrosine hydroxylase expression by immunohistochemistry in renal proximal tubules of C57BL6 mice fed either normal chow or a HFD for 10 weeks. Renal NA content was measured by a commercially available ELISA.

Results: Bioactivity of NA was confirmed by detection of elevated phosphorylated ERK1/2 using Western Blotting. There were no cytotoxic effects of NA on HK2 cells as determined by a MTT assay at each time point. SGLT-2 expression in HK2 cells in response to treatment with NA was determined by immunocytochemistry at 24, 48 and 72 h post-treatment and a marked increase in SGLT-2 expression could be demonstrated. In the HFD mouse model, dapaglifozin treatment resulted in marked glucosuria and reduction in body weight, fasting glucose levels and mean arterial blood pressure. Compared to chow, there was a trend towards more pronounced SGLT-2 expression in proximal tubules of mice fed a HFD which was significantly up-regulated with dapaglifozin treatment. Most interestingly, dapaglifozin treatment resulted in a significant reduction in tyrosine hydroxylase expression in proximal tubules of HFD mice and a reduction in kidney NA content.

Conclusions: SGLT-2 is up-regulated by NA both in vitro and in vivo. The observed reduction in both tubular tyrosine hydroxylase expression and kidney NA content with dapaglifozin treatment suggest a bi-directional interaction between the SNS and SGLT-2 regulation which may represent one of the mediators of improved cardiovascular outcomes reported for SGLT-2 inhibitors.

OP.4B.04 URINARY PROTEOMICS PREDICTS MORTALITY IN TYPE 2 DIABETES PATIENTS WITH MICROALBUMINURIA

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Objective: Type 2 diabetes is a chronic disease with an increased risk of cardiovascular disease (CVD) and mortality. The evaluation of CVD and mortality risk in patients with type 2 diabetes is typically performed using traditional risk factors such as age, gender, smoking, diabetes duration, and lipid and blood pressure levels. Due to the increased comorbidity in these patients, the identification of additional markers for the prediction of mortality in diabetes patients is of high interest. Urinary proteomics has recently been proposed as a novel approach to identify additional risk markers for the prediction of mortality in diabetes patients. In the present study, we investigate whether urinary proteomics can predict mortality in patients with type 2 diabetes and microalbuminuria.

Design and method: We performed a retrospective cohort study on 210 patients with type 2 diabetes and microalbuminuria who were treated consecutively at the Diabetes Center in Gentofte, Denmark, between January 2007 and June 2010. The patients were followed up for a mean period of 3.4 years. The urinary proteome was analyzed using a custom-designed antibody array. The mortality rate was analyzed using a Cox proportional hazards regression model.

Results: The urinary proteome was significantly associated with mortality in patients with type 2 diabetes and microalbuminuria. The median survival time of the patients with a high urinary proteome score was significantly shorter compared to the patients with a low urinary proteome score (p < 0.05).

Conclusions: Urinary proteomics is a novel approach to predict mortality in patients with type 2 diabetes and microalbuminuria. Further studies are needed to validate these findings and to identify the specific proteins that are associated with mortality in diabetes patients.
Objective: There is a continuous relationship between mortality and degree of diabetic nephropathy (DN) but neither estimated glomerular function (eGFR) nor albuminuria are precise early markers of renal function decline. The CKD273 urinary proteomic biomarker has shown promise as a tool for early detection of kidney disease, particularly DN. Here we study whether CKD273 predicts mortality in patients at early stage of DN.

Design and method: Urine samples were obtained from 188 type 2 diabetic patients with confirmed microalbuminuria. Proteomic analysis was undertaken using capillary electrophoresis coupled to mass spectrometry to determine CKD273 classifier score. 155 samples were suitable for analysis after quality control. A previously developed CKD273 threshold of 0.343 for identification of DN was used to categorize the cohort in Kaplan-Meier and Cox regression models with all-cause mortality as the primary endpoint. Outcomes were traced through national health registers after 4 years.

Results: Participants had elevated urine albumin excretion (UAE; median [IQR], 97 [40–214] mg/24 h) with preserved eGFR (mean ± SD, 88 ± 17 ml/min/1.73m²). Median diabetes duration was 13 [7–19] years. The majority of patients were obese (body mass index 31.6 [28.6–35.5] kg/m²) whereas blood pressure (129 ± 16 / 74 ± 11 mmHg) and HbA1c (58 [52–74] mmol/mol) were well controlled. There were 20 deaths during follow up of which 5 and 15 respectively occurred in the CKD273 groups below and above the threshold. Higher CKD273 score was associated with higher mortality in Kaplan-Meier analysis (Log Rank Mantel Cox), p = 0.004. The relationship retained significance (hazard ratio 2.9 [95% CI 1.0–8.1]) after adjustment for age, gender and smoking; and in a comprehensive model adjusted for age, gender, BMI, smoking status, HbA1c and blood pressure (hazard ratio 3.4 [95% CI 1.3–10.4]) where it was independent of renal parameters (p = 0.459 for eGFR; p = 0.276 for UAE).

Conclusions: The CKD273 urinary proteomic classifier predicts mortality in type 2 diabetic patients with early established kidney disease independent of markers of renal function and damage. Its performance as an early predictor of DN in normoalbuminuric diabetic patients is currently being evaluated in a prospective study (www.eu-priority.org) where mortality will be considered as a secondary endpoint.

OP4B.05 MIR-30A-3P EXPRESSION IN THE HEARTS OF DIABETIC RATS: EFFECTS OF ANGIOTENSIN TYPE 1 (AT1) AND ANGIOTENSIN TYPE 2 (AT2) RECEPTORS


Objective: Compound 21 (C21), a selective AT2 receptor agonist, showed cardioprotective effects in experimental model of hypertension. miRNAs, small non-coding RNAs, play an important role in the control of gene expression. The aim of this study was to evaluate the effect of Compound 21 on miR-30a-3p expression in the hearts of Zucker diabetic fatty (ZDF) rats (type 2 diabetes).

Design and method: The experiments lasted 15 weeks (from 5 to 20 weeks of age) and were performed in ZDF rats (n = 21) and in control Lean rats (n = 8). ZDF rats were divided into 3 groups: 8 ZDF rats were treated with C21 (0.3 mg/kg/day, i.p.); 5 ZDF rats were treated with losartan (10 mg/kg/day in drinking water), and 8 ZDF rats were maintained without treatment. Blood glucose level, body weight and blood pressure (tail-cuff) were measured every 4 weeks and at the end of the protocol. At 20 weeks of age rats were sacrificed and hearts were excised. The apex of the heart was frozen in liquid nitrogen for the evaluation of myocardial miR-30a-3p expression (real-time PCR), and the remaining part of the heart was fixed with 10% formalin for histomorphometric analysis.

Results: ZDF rats showed high blood glucose values (p < 0.001 vs. control Lean rats), that were not modified by C21 or losartan treatment. No changes in blood pressure were observed in ZDF rats as compared to control Lean rats. C21 did not modify blood pressure, while losartan treatment caused a significant decrease respect to the other groups (p < 0.05). Myocardial miR-30a-3p expression was higher in ZDF rats as compared to control Lean rats (p < 0.01). C21 administration or losartan treatment decreased miR-30a-3p (p < 0.01). Gene ontology analysis showed an involvement of miR-30a-3p in ECM receptor interaction and PI3K-AKT signalling pathways.

Conclusions: These data demonstrate that AT2 receptor activation or AT1 receptor blockade modulate miR-30a-3p expression in ZDF rats, suggesting a role for miR-30a-3p in myocardial remodelling in diabetes.

OP4B.06 FREQUENCY OF PRIMARY ALDOSTERONISM IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA – OSA-PA STUDY

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Objective: The pathophysiological overlap between primary aldosteronism (PA) and obstructive sleep apnea (OSA) has been suggested. Therefore in a prospective OSA-PA study we have evaluated the frequency of PA in patients suspected of OSA.

Design and method: We included in our ongoing study 200 consecutive hypertensive patients (mean age 53.2 ± 13.2 years, 127 M, 63 F) referred for polysomnography (PSG) on the basis of one or more of the following clinical features suggestive for OSA: typical symptoms, resistant or difficult-to-treat HT and comorbidities known to be associated with OSA and high cardiovascular risk. Clinically important moderate-to-severe OSA was diagnosed if the apnea-hypopnea index (AHI) was >15 events/h. PA was diagnosed if the salt infusion test (SIT) was abnormal (postinfusion plasma aldosterone levels >10ng/dl). Age, gender, office blood pressure levels, sodium, glucose, potassium and creatinine plasma concentrations, presence of metabolic syndrome (MS) and its components (abdominal obesity, glucose metabolism alterations [increased fasting glucose or diabetes], increased triglycerides, decreased HDL cholesterol levels), known cardiovascular disease (CVD) were recorded.

Results: OSA was diagnosed in 91 patients (45.5% of the whole group). PA was diagnosed in 19 patients with OSA (20.9%) as compared to 8 patients in the group without OSA (7.3%; p = 0.005). The prevalence of PA was higher in patients with severe than with moderate OSA (16.7% and 24.5%; p = 0.011). Patients with OSA and PA tended to be more males than patients with OSA and without PA (89.5% vs 68.1%; p = 0.052). There were no significant differences between patients with OSA and PA as compared with patients with OSA without PA in regard to age, BMI, blood pressure levels, glucose, creatinine and potassium concentrations as well in the frequency of MS and its components, CVD. Patients with OSA and PA as compared to patients with OSA without PA were characterized by higher plasma aldosterone levels >10ng/dl.

Conclusions: Our data indicated that patients with clinically important moderate-to-severe OSA are characterized by relatively high frequency of PA. Our result support the recommendations to screen OSA patients for PA.

OP4B.07 DURATION OF DIABETES MELLITUS IS ASSOCIATED WITH INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH ARTERIAL HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Objective: To assess associations of diabetes mellitus (DM) duration and parameters of arterial stiffness in patients with arterial hypertension (AH) and T2DM.

Design and method: 90 patients with AH and T2DM were included (39% males, mean age 63.8 ± 11.6 years, 44% smokers, 80% with dyslipidemia). Mean
Objective: renal outcomes than clinic BPs and this was more evident for renal failure end-

Results: Mean central BP was 132 ± 18/79 ± 12 mmHg, mean of PWV was 10.5 ± 2.4 m/s, mean R-CAVI was 8.8 ± 1.9, L-CAVI 8.9 ± 1.8. Further analysis was performed in subgroups according to tertiles of DM duration (G1 < 4 years (n = 31), G2 4–10 years (n = 30), G3 > 10 years (n = 29)). Patients with the highest duration of DM were older (69.5 ± 11.1 vs 62.1 ± 11.2 vs 60.0 ± 10.8 years), had higher vascular age (73.8 ± 9.0 vs 68.5 ± 11.8 vs 64.5 ± 13.4 years), had higher R-CAVI and L-CAVI (9.3 ± 1.9 vs 9.0 ± 1.8 vs 8.1 ± 1.9 and 9.4 ± 2.0 vs 9.2 ± 1.6 vs 8.1 ± 1.8, respectively), p < 0.05 for trend. Patients in G3 and G2 more often received insulin therapy (79 vs 70 vs 45, p < 0.05). Patients from G3 and G2 had the highest level of cPWV compared to G1 (11.0 ± 2.0 and 11.4 ± 2.4 vs 9.1 ± 2.4 m/s, p = 0.009). Spearman analysis revealed significant correlations between duration of DM and age (r = 0.35), vascular age (r = 0.30), creatinine level (r = 0.23), cPWV (r = 0.34), R-CAVI (r = 0.3) and L-CAVI (r = 0.3), p < 0.05 for trend. Multiple regression analysis showed that only age and DM duration were significant predictors of PWV increase (β = 0.3, p = 0.02 and β = 0.2, p = 0.04, respectively).

Conclusions: In diabetic patients aortic stiffness is strictly correlated with diabetes duration, independently of blood pressure level and diabetes control. In this group of patients PWV increases mostly during the first 4 years of DM.

Design and method: Six hundred and twenty-nine patients without advanced renal failure at baseline had annual renal function evaluated over a median follow-up of 7.7 years. Natural history data were obtained at baseline and throughout the follow-up. Ambulatory BP monitoring was performed at baseline. Multivariate Cox survival analysis examined the independent predictors of development/progression of DKD in a cohort of high-risk patients with type 2 diabetes.

Results: At baseline, 197 patients had DKD, and 195 patients either newly-developed or worsened DKD during follow-up; 125 installed/progressed abnormal albuminuria whereas 91 worsened renal function. After adjustments for baseline DKD prevalence (albuminuria and reduced renal function), age, sex and diabetes duration, a poorer glycemic control (HR: 1.22; 95% CI: 1.04 – 1.44; p < 0.001), for each 1-SD increment in mean HbA1c, and a higher mean cumulative systolic BP exposure during follow-up (HR: 1.36; 95% CI: 1.16 – 1.58; p < 0.001; for each 1-SD increment) were the main independent predictors of development/progression of DKD. However, at baseline, ambulatory BPs were stronger predictors of renal outcomes than clinic BPs and this was more evident for renal failure endpoints than for abnormal albuminuria installation/progression. The nocturnal BP fall provided no prognostic information.

Conclusions: Poorer glycemic and BP control were the main predictors of development/progression of DKD in high-risk patients with type 2 diabetes. At baseline, ambulatory systolic BPs were better predictors than clinic BPs, but cumulative clinic systolic BP exposure during follow-up was the strongest BP-related predictor of adverse renal outcomes.

Design and method: 919 ABPM recordings of type 2 diabetic patients (age 64.4 ± 12.3 years) with treated hypertension were obtained at 306 GPs using validated recorders. Of the 919 patients 230 had nephropathy, 41 had cerebrovascular disease, 208 peripheral artery disease/atherosclerosis, 143 left ventricular hypertrophy and 188 coronary heart disease/heart failure. GPs were asked to define the treatment goals for ABPM and self-measured blood pressure for each individual patient. GPs’ individual treatment goals were compared to limits of normality as defined by the recent ESH guidelines. A corridor of 5 mmHg below cut-off value was defined as “on target”.

Results: The GPs assessed the 10-year cardiovascular risk to be “very high” (as per the definition of the ESH) in 11% of their patients, while it actually was “very high” in 892 patients (97%) based on a central, independent analysis. GPs’ individual treatment goals “on target”, “below target” and “above target” are shown in Table 1. GPs wanted to reach their treatment goals within 6 weeks (median). GPs suggested control of treatment goals by office BP within 4 weeks and by ABPM within 10 weeks.

Conclusions: GPs’ individual treatment goals for hypertensive type 2 diabetic patients tended to be lower than limits of normality for daytime-ABPM and office BP. For night-time ABPM GPs tended to set the individual BP goals higher than accepted limits of normality. It might be concluded that at the onset of the study (2014), GPs favoured the concept of “the lower the better”. Interestingly this did not account for night-time ABPM. Whether this behaviour was triggered by insufficient knowledge of recent guidelines or other factors cannot be concluded from the design of our study.

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Objectives: Tight blood pressure control in hypertensive type 2 diabetic patients achieves clinically important reductions in cardiovascular morbidity and mortality. The objective of the present registry study was to investigate the role of ambulatory 24-hour blood pressure measurement (ABPM) for the clinical management of hypertensive patients with type 2 diabetes and multiple risk factors in the general physician’s (GP’s) office.

Table 1: Percentage of individual treatment goals “on target”, “below target” and “above target”.

<table>
<thead>
<tr>
<th>ABPM-Day</th>
<th>ABPM-Night</th>
<th>Office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defined</td>
<td>targets</td>
<td></td>
</tr>
<tr>
<td>100–125</td>
<td>80–105</td>
<td>65–70</td>
</tr>
<tr>
<td>On target</td>
<td>26%</td>
<td>17%</td>
</tr>
<tr>
<td>Below target</td>
<td>47%</td>
<td>15%</td>
</tr>
<tr>
<td>Above target</td>
<td>32%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Conclusions: Poorer glycemic and BP control were the main predictors of development/progression of DKD in high-risk patients with type 2 diabetes. At baseline, ambulatory systolic BPs were better predictors than clinic BPs, but cumulative clinic systolic BP exposure during follow-up was the strongest BP-related predictor of adverse renal outcomes.

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DYSREGULATION OF MICORRNA-181A CAUSED BY OVERACTIVE RENAL SYMPATHETIC NERVES CONTRIBUTES TO ELEVATED RENAL RENIN MRNA AND HYPERTENSION IN SCHLAGER BPH/2J MICE

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Objective: BPH/2J mice are a genetic model of hypertension driven by greater activity of the sympathetic nervous system (SNS) and renin-angiotensin system (RAS). BPH/2J mice display high levels of renal renin mRNA accompanied by low levels of its negative regulator microRNA-181a (miR181a), which is akin to that observed in hypertensive patients. Since miR181a levels also tended to correlate with the depressor response to ganglion blockade, we hypothesised that high renal sympathetic activity reduces miR181a levels, ultimately contributing to the augmented activity of the RAS in BPH/2J mice.

Design and method: To determine whether administering an in vivo miR-181a mimic or renal denervation can increase renal miR-181a abundance to reduce renal renin mRNA, RAS activity and hypertension in BPH/2J mice. Blood pressure (BP) in BPH/2J and normotensive BPN/3J mice was measured via pre-implanted radiotelemetry probes. One group was administered miR-181a mimic or a negative control (25nmol, n = 6–10) using an in vivo kidney specific transfection reagent and BP measured for 24hrs. Another group underwent renal denervation or sham surgery (n = 7–12) and BP measured for 3 weeks. Following these interventions, the BP response to ACE inhibitor (enalaprilat) was determined and renal miR181a and renin mRNA abundance measured.

Results: MiR181a levels were greater in denervated BPH/2J mice compared with sham (P < 0.015). Furthermore renal renin mRNA abundance was lower in denervated (P < 0.05) and mimic treated BPH/2J mice (P < 0.001) compared with their respective controls. BP was reduced more after denervation than sham surgery (25mmHg, P < 0.001) but not BPN/3J mice (P = 0.51). There was a peak hypotensive effect of the mimic 12–15hrs after injection in BPH/2J mice (−5.3 ± 1.4mmHg, P < 0.001) which was not present in negative control treated BPH/2J mice (P = 0.25) or in mimic or negative control treated BPN/3J mice (P > 0.15). The depressor response to enalaprilat was enhanced in denervated BPH/2J compared with sham (P < 0.003), whereas it was abolished in mimic treated BPH/2J mice compared with negative control (P < 0.001).

Conclusions: Taken together these findings provide the first in vivo evidence that elevated RSNA reduces miR-181a levels, which can contribute to greater renal renin mRNA level and hypertension in BPH/2J mice.

NOVEL STRATEGIES TO IMPROVE THE MANAGEMENT OF ALBUMINURIA IN HYPERTENSIVE DIABETIC PATIENTS

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Objective: Chronic kidney disease (CKD) is a major health problem affecting the quality of life of millions of people. Renal interstitial fibrosis is a universal predictor of the decline in renal function and is characterized by exaggerated deposition of extracellular matrix (ECM) by an expanding population of fibroblasts and myofibroblasts. Our objective was to gain insight in the pathophysiologic pathways leading to renal injury by sequencing urinary peptides and thereby identifying the parent proteins from which they are derived. In a representative population sample, we investigated the associations of eGFR with sequenced urinary fragments markers.

Design and method: In 805 randomly recruited Flemish (50.8% women; mean age, 51.1 years), we estimated glomerular filtration rate (eGFR) by the CKD-EPI method. We staged CKD according to the KDQI guideline. We analysed 74 sequenced urinary peptides with signal amplitude different from undetectable in >95% of participants. Follow-up measurements of eGFR and CKD stage were available in 597 participants.

Results: In multivariable analyses, baseline eGFR decreased (P < 0.022) with urinary fragments of mucin 1 (standardized association size expressed in mL/min/1.73 m², r = −0.48), collagen III (r = 0.24) and fibrinogen (r = 0.20) and was bi-directionally associated (P < 0.0006) with two urinary collagen I fragments (r = −0.28 and −0.32). eGFR changes over 5 years (follow-up minus baseline) resulted in constant estimates (P < 0.025) for mucin 1 (r = 0.15), collagen 1 (r = 0.17) and fibrinogen (r = 0.14) fragments. Relative risk of having or progressing to CKD stage ≥ 3 was associated with mucin 1. Partial least square analysis confirmed mucin 1 as the strongest urinary marker associated with decreased eGFR with a score of 2.47 compared with 1.80 for a collagen 1 fragment as next contender. Mucin 1 predicted progression to CKD stage ≥ 3 over and beyond microalbuminuria (P = 0.011).
Conclusions: In the general population, shedding of the mucin 1 subunit α, an extracellular protein expressed in renal tubular epithelium, is the strongest correlate and predictor of renal impairment and outperforms microalbuminuria. Mucin 1 might be a new target for screening, prevention and treatment of CKD.

OP.5A.05 RENAL TISSUE OXYGENATION WITH AGING IN MEN, BUT NOT IN WOMEN

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Objective: Women are less prone to the development of CKD than men, and their renal function declines less rapidly while aging. Why women are relatively protected remains so far incompletely understood. We hypothesized that renal tissue oxygenation as measured with blood oxygenation level-dependent MRI (BOLD-MRI) is better preserved in ageing women.

Design and method: Blood-oxygenation level dependent MR imaging was performed under standardized conditions in respectively 11 young and 11 older healthy women, and also in nine younger and nine older healthy men. All participants were free of medication, and none were hypertensive. Images were analyzed with the twelve-layer concentric objects method (TLCO) that divides renal parenchyma in 12 layers of equal thickness, and reports the mean R2* value of each layer. The mean R2* values of all twelve layers can be graphically represented as a curve, that is called the R2* profile. The estimated glomerular filtration rate (eGFR) was calculated with the CKD-EPI formula (CKD EPI creatinine).

Results: The mean(±SD) age of young and older women and young and older men was 36 ± 7 versus 52 ± 6 years, and 35 ± 9 versus 58 ± 8 years; their eGFR was respectively 103 ± 15, 96 ± 9, 97 ± 17 and 89 ± 9 ml/min/1.73m2 (tpanova = 0.17) and their body mass index 25 ± 5, 26 ± 6, 26 ± 3 and 27 ± 6 kg/m2 (p = 0.91). The R2* profile was shifted to higher R2* values (corresponding to lower oxygenation) at increasing age in men, but not in women (see figure).

Conclusions: These data show that renal tissue oxygenation is well maintained while aging in women, but not in men. This finding offers clues to the underlying mechanisms responsible for the relative nephroprotection observed in women. Whether hormonal, hemodynamic or structural differences are responsible for the relative nephroprotection observed in women.

OP.5A.07 IMPROVED RENAL HEMODYNAMICS REDUCE ALBUMINURIA AND RENAL MACROPHAGE INFILTRATION IN DIABETIC RATS TREATED WITH ANGIOTENSIN RECEPTOR AND NEPRLYSIN INHIBITION

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Objective: Dual blockade with an Angiotensin Receptor/Neprlysin Inhibitor (ARNI) reduces proteinuria and glomerulosclerosis in diabetic TGR(mREN2)27 rats (i.e., rats displaying angiotensin II-dependent hypertension) more strongly than single AR blockade (ARB), despite a similar effect on blood pressure. Here we investigated whether this is due to improved renal hemodynamics and/or suppression of renal inflammation.

Design and method: TGR(mREN2)27 rats were made diabetic with streptozotocin for 12 weeks, and treated with placebo (n = 10), valsartan (ARB; n = 5) or valsartan/sacubitril (ARNI; n = 8) from week 9–12. Blood pressure was measured by telemetry. Effective renal plasma flow (eRPF) and glomerular filtration rate (GFR) were assessed by quantifying para-aminohippuric acid andulin clearances. Renal inflammation was quantified by qPCR (CD68 and CD3e expression, representative for macrophages and T cells, respectively) and fluorescent activated cell sorting (FACS) analysis.

Results: ARNI and ARB lowered blood pressure identically, while only ARNI reduced albuminuria. Severe, chronic ischemia and globally sclerotic glomeruli occurred less frequently in kidneys of ARNI-treated animals vs. ARB-treated animals and controls. ARNI, but not ARB, increased eRPF, and a similar trend was observed for GFR. No treatment affected filtration fraction. ARNI decreased CD68 mRNA expression in both renal cortex and medulla, while ARB increased CD68 as well as CD3e expression in renal medulla. FACS analysis revealed no differences between the treatment groups in the immune-cell fractions that had infiltrated the kidney.

Conclusions: Improved renal hemodynamics, combined with reduced macrophage infiltration, may underline the stronger beneficial effects of ARNI on albuminuria and renal histology in diabetic TGR(mREN2)27 rats versus ARB.
Design and method: COMMD5 was silenced by siRNA and EGFR expression and activation were evaluated in renal cell lines. Intracellular localization of COMMD5, EGFR and endosome associated protein, such as Rab, were analyzed by confocal microscopy and live cell imaging. Co-immunoprecipitations were used to investigate interactions between COMMD5 and proteins known to be involved in vesicle trafficking.

Results: We demonstrated that COMMD5 is an adaptor protein forming a bridge between endosomes and cytoskeleton by binding Rab protein and microtubules/actin. This tethering is essential because silencing of COMMD5 delayed the intracellular transport dynamic and consequently cargo protein such as EGFR. Defect in intracellular trafficking led to loss of cell polarity and oriented migration which are crucial for tissue repair.

Conclusions: Our results demonstrated that COMMD5 plays a crucial role in controlling EGFR signaling/trafficking and suggest that COMMD5 could be used as a novel target for EGFR-targeted therapy in kidney diseases.
Abstracts

ORAL SESSION 5B: CARDIOVASCULAR RISK FACTORS

OP.5B.01 PULSE WAVE VELOCITY AND DEPRESSION IN HYPERTENSIVE PATIENTS

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Objective: Abnormal large artery function plays an important role in the pathogenesis of cardiovascular (CV) diseases. Prior studies have suggested that the principal determinants of arterial stiffening are age, Blood Pressure (BP) and other CV risk factors such as dyslipidemia and diabetes. However, scanty data are available on the role of psychological factors on arterial stiffness. Previous work have shown that arterial stiffness was associated with depression in the elderly and in healthy adolescents, but no study has focused on the role of depression and other psychological variables in hypertensive patients. The aim of the current cross-sectional study was to evaluate the association between depression, anxiety, perceived stress, Type A personality, and Type D personality and Pulse Wave Velocity (PWV) in a cohort of hypertensive patients, using baseline examination data of the TIPICO project.

Design and method: A total of 259 outpatients (ages 18–80 years) followed by the Hypertension Unit of S. Gerardo Hospital (Monza, Italy) affected by essential hypertension were recruited. Aortic stiffness was evaluated by PWV between the carotid and the femoral artery of the same side with the patient in the supine position. Moreover, anamnestic data, clinical BP, and laboratory data were evaluated. Patients were asked to complete a battery of psychological questionnaires under the guidance of a psychologist. The associations between psychological variables and PWV was explored using multivariate stepwise linear regression analysis and regression coefficients (b) were given per 1-point increment.

Results: The mean age was 55.9 ± 10.1 years, SBP and DBP were 135.6 ± 17.7 and 82.5 ± 9.1 mmHg and PWV was 8.6 ± 2.1 m/s. The results from the multivariate stepwise linear regression analysis showed that age (beta = 0.284, p < 0.001), pulse pressure (beta = 0.369, p < 0.001), dyslipidemia (beta = 0.130, p = 0.012), family history of CV disease (beta = 0.123, p = 0.017), and depression (beta = 0.126, P = 0.014) were significantly and independently associated with PWV.

Conclusions: The current study shows that, among psychological factors, higher levels of depression is related to higher PWV, while anxiety, perceived stress, Type A personality, and Type D personality are not associated with arterial stiffness. Depression assessment and target intervention to reduce it are recommended in hypertensive patients.

OP.5B.02 SERUM URIC ACID AND BLOOD PRESSURE PATTERN IN YOUNG ADULT MEN BORN SMALL FOR GESTATIONAL AGE

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Objective: Although increased rates of cardiovascular events in subjects born small for gestational age (SGA) were reported, the mechanisms underlying these associations are not completely elucidated. Epidemiological evidence supports association between serum uric acid (sUA) and incidence of hypertension. Our aim was to investigate the relationship between sUA, vascular function and blood pressure (BP) levels in young men born SGA.

Design and method: A total of 95 healthy men (21.0±0.89 years) born SGA and 90 healthy men (21.5±1.02 years) with normal intrauterine development (AGA) were enrolled. Anthropometric parameters, office and ambulatory blood pressure (BP), fasting blood glucose, lipid profile, eGFR, carotid intima media thickness (cIMT), pulse wave velocity (PWV), central systolic BP (cSBP), augmentation index (Aix) were determined in all participants. Hyperuricemia was considered if sUA > 360 mmol/L. Birth parameters were obtained from medical records.

Results: Higher sUA values were observed in SGA vs. AGA group (406 vs. 307 p < 0.001). Hyperuricemic SGA participants had higher BMI, waist circumference (p = 0.003), office SBP (p = 0.021), central SBP (p = 0.022), increased BP variability (p = 0.021), lower eGFR (p = 0.021) and more often dyslipidemia (p = 0.001) which was not observed in AGA group. There were no differences in cIMT, Aix, PWV between two groups. Positive correlation was found between sUA and BMI and waist circumference in both groups. Negative correlation with cGFR (<0.001) was observed in SGA group. When prematurity was taken into account in SGA participants, sUA correlated positively with BP variability (p = 0.003), cIMT (p = 0.016) and negative with birth weight (p = 0.009). Multiple regression analysis showed BMI as the key determinant of SBP (β = 0.427, p < 0.001).

Conclusions: Our results support findings of clustering of cardiovascular risk factors in young adult men born SGA with increased sUA. We did not observed vascular function differences according to sUA levels. However, in SGA participants, subclinical changes in circadian BP pattern were observed mainly influencing levels and variability of systolic BP particularly in subgroup of premature born SGA which might be a consequence of altered endothelial function and increased vasoconstriction.

OP.5B.03 TIME TO IMPLEMENT SERUM URIC ACID FOR RISK STRATIFICATION IN HYPERTENSIVE WOMEN? LONG-TERM FOLLOW-UP DATA IN THE OLD-HTA COHORT

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Objective: Albeit controversial, serum uric acid (SUA) seems to convey a prognostic significance in women. Yet data over the long run are limited in hypertension. The aim of the present study was to confirm the prognostic significance over the long-term particularly in hypertensive women.

Design and method: 1897 hypertensive patients with an assessment of SUA at baseline during their work-up for hypertension were followed according to tertile of SUA: < 339, 339 to 428 and >428 micromol/L. All-cause and cardiovascular mortalities were assessed after a 20 year-follow-up period.

Results: Baseline characteristics were age 45.1 ± 13.4 years, systolic/diastolic blood pressure 180 ± 32/104 ± 20 mmHg, women 39.1% and eDFG 83.3 ± 29.5 mL/min. SUA was independently correlated with age, gender, BMI, previous cardiovascular events, eGFR, thiazide diuretics and beta-blockers use, and diabetes. At 20 years of follow-up, 748 deaths were observed, 442 of which were from cardiovascular causes. As shown in Kaplan-Meier curves, tertiles of SUA were predictor of all-cause and cardiovascular death in the whole cohort (p < 0.001 for both, Figure). In multivariate Cox regression analysis, patients in the third tertile have an increased risk of all-cause death (HR 1.34 (1.09–1.65) vs. tertile 1, HR 1.13 (1.09–1.55) vs. tertile 2) but only a trend was observed for cardiovascular death (HR 1.33 (1.00–1.76) vs. tertile 1, HR 1.16 (0.92–1.53) vs. tertile 2). A strong interaction with gender was observed for all-cause and cardiovascular mortality (p = 0.006 and p = 0.013 respectively). In subgroup analysis with the same Cox regression analysis, tertile 3 predicts mortality only in women: all-cause death HR 1.86 (1.34–2.58) vs. tertile 1, HR 1.76 (1.25–2.48) vs. tertile 2; cardiovascular death HR 1.77 (1.13–2.79) vs. tertile 1, HR 1.52 (0.96–2.38) vs. tertile 2. The information gain after addition of tertiles of SUA was significant in the multivariable Cox regression model (likelihood ratio test p = 0.009 and p = 0.025 for all-cause and cardiovascular mortality, respectively) with an increment of the C-index of 0.003 for the two different endpoints.
Conclusions: After a long-term follow-up period, SUA improves death stratification in hypertensive women on top of traditional risk factors and target organ damages.

OP.5B.04 SMOKING POTENTIATES THE RISK OF CARDIOVASCULAR DISEASE ASSOCIATED WITH TACHYCARDIA

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Objective: Several studies have shown that resting heart rate (RHR) is a predictor of adverse outcome in hypertension. Smoking causes sharp rises in RHR during the daytime hours which could favour this association. We did a prospective study to investigate whether smoking influences the risk of cardiovascular events (CVE) associated with elevated RHR in stage 1 hypertension.

Design and method: The study was conducted in a cohort of 1204 18 to 45-year-old participants screened for stage 1 hypertension (21% smokers) from the HARVEST and followed for a median of 12.5 years (interquartile range, 5.5–17.4). RHR was calculated as the mean of 6 readings over 2 visits. Ambulatory heart rate was obtained in duplicate. Participants were stratified into 4 groups according to smoking (no/yes) and the presence or absence of tachycardia (RHR > 80 bpm). In Cox regressions, data were adjusted for age, gender, BMI, parental CVE, lifestyle factors, baseline office and 24 h BP, total cholesterol, serum creatinine, and changes in BP and body weight from baseline to last available visit.

Results: Tachycardia was present in 26.5% of participants. RHR did not differ according to smoking. However, the difference between age-and-sex-adjusted daytime heart rate and RHR was higher in smokers than non-smokers (2.6 ± 0.6 bpm versus 0.5 ± 0.3 bpm, p = 0.0023). During the follow-up 74 participants (6.1%) developed a CVE. RHR was an independent predictor of CVE (p = 0.0043) with a 63% increase in risk (95% CI, 17%–128%) for each 10-bpm increment in RHR. Inclusion of physical activity slightly attenuated the RHR-CVE association (p = 0.0082). In sensitivity analysis, the association held true among smokers (p = 0.0033) but not non-smokers (p = 0.12). Compared with non-smokers with normal RHR, the risk of CVE was 2.26 (1.06–4.85) in non-smokers with tachycardia, was 2.62 (1.44–4.78) in smokers with normal RHR, and was 5.65 (2.43–13.11) in smokers with tachycardia. In addition, for each 10-bpm increment in RHR during the follow-up there was a 35% (5%–72%) increase in risk of CVE.

Conclusions: High RHR is an independent predictor of CVE in young subjects with stage 1 hypertension. Smoking causes an increase in daytime heart rate and magnifies the association between RHR and adverse outcome.

OP.5B.05 IMMUNE UNREACTIVE URINARY ALBUMIN AS A PREDICTOR OF CARDIOVASCULAR EVENTS: THE HORTEGA FOLLOWUP STUDY

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Objective: The clinical significance of albumin that cannot be detected by traditional immunoassays (Immune Unreactive Albumin Excretion [IURAE]) is not clear. We aimed to determine if IURAE can be determined by HPLC and by immunonephelometry. IURAE was determined as the difference between HPLC and immunonephelometry values (IRAE). We estimated fully adjusted hazard ratios of cardiovascular incidence by Cox regression. C-statistic was used to compare predictive accuracy of IURAE and IRAE.

Results: After an average at-risk follow-up was 13 years, we observed 167 cardiovascular incidence events. The correlation between the IURAE and IRAE was 0.54 (p < 0.001); 93 and 357 participants showed microalbuminuria defined by IRAE and IURAE concentrations ≥ 30 mg/g Cr, respectively. Among discordant pairs, there were 54 events in those classified as microalbuminurics by IRAE but IRAE-based normoalbuminurics by immunonephelometry vs 2 for the opposite case, being the threshold to detect these individuals by immunonephelometry of 10.1 mg/g Cr. After logarithmic transformation, UAE was a significant independent factor for cardiovascular incidence [fully adjusted HR 1.27 (1.02–1.58) and 1.13 (1.01–1.27), for IURAE and IRAE]. Fully adjusted survival curves were significant reduced according to categories of UAE. The C-statistic comparing fully adjusted models with IUAE and IRAE, respectively, were similar of around 0.85.

Conclusions: IURAE could give similar or even better prognostic information as the commonly used IRAE. Our findings suggest the need for mechanistic studies to evaluate the biological implications of the observed differences in the evaluated markers.

OP.5B.06 CONCENTRIC LEFT VENTRICULAR REMODELING IS ASSOCIATED WITH EARLY ONSET PREECLAMPSIA IN WOMEN WITHOUT PREEXISTENT HYPERTENSION

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Objective: Preeclampsia (PE) is a maternal complication characterized by hypertension and proteinuria that usually occurs after the 20th gestational week and resolves after delivery. PE is associated with persistent cardiac abnormalities and a high cardiovascular risk during the woman life. Early onset PE presenting before the 34th gestational week is a more severe form of disease, but its relevance on cardiac abnormalities in comparison to the forms with later onset is not clear. The aim of this study was to assess cardiac structure and function in women with PE without preexistent hypertension.

Design and method: One month after delivery, the clinical and echocardiographic variables of 54 preeclamptic women (age 36 ± 6 y), 39% of which with early PE, was compared with a group of 54 normotensive (age 37 ± 6 y) and 15 hypertensive (age 41 ± 5 y) nonpregnant women who were matched for age and height.

Results: Despite comparable antihypertensive treatment, women with early PE had lower 24-hour average systolic and diastolic blood pressure than those with late PE. Left ventricle (LV) relative wall thickness was significantly greater in women with early PE (0.39 ± 0.10) than in those with late PE (0.31 ± 0.07; p < 0.001) and normotensive (0.29 ± 0.05; p < 0.001) women, but not hypertensive women (figure). Women with early and late PE had comparably greater LV mass and worse diastolic function as assessed by the E/A ratio, isovolumic relaxation time, and tissue Doppler imaging, than normotensive woman. No
differences in LV systolic function were observed between preclamptic and normotensive women.

Conclusions: Women with early onset PE have more pronounced LV concentric remodeling than women with late onset PE. This observation could account for the greater cardiovascular risk of these patients and might prompt the use of antihypertensive drugs specifically acting on LV remodeling.

Design and method: Anamnestic data, clinical blood pressure (BP) and laboratory data were collected in 55 consecutive RA patients. Rheumatological score of disease activity (DAS28 Erythrocyte sedimentation rate - ESR, CDAI and SDAI) and CV risk model (FRS, SCORE, ESH/ESC) were calculated with a correcting factor of 1.5 when patients displayed at least 2 out of 3 of the following conditions: a long standing diseases (>10 years), with extra-articular disease or seropositivity for Reumatoid Factor (RF) or Anti–citrullinated protein antibody (ACPA) - modified score (mFRS and mSCORE).

Results: Mean (±SD) age was 62.8 ± 8.9 years, 23.6% were males and BP amounted to 130.6 ± 17.4/ 75.6 ± 8.9 mmHg. Mean DAS28 ESR, CDAI and SDAI were 3.3 ± 1.3, 8.9 ± 9.7 and 9.7 ± 10.1 respectively, indicating a low disease activity. The majority of patients showed a low CV risk employing mFRS, mSCORE and ESH/ESC (percent values: 67.9, 94.3 and 58.4, respectively). When patients were divided according to their low, medium or high risk, the different groups didn't show any significant difference regarding DAS28ESR, CDAI, SDAI and age of RA. Only with FRS a significant difference in DAS28ESR was found with greater values in the high risk group. Moreover the only significant correlation was found between both FRS and mFRS with DAS28ESR (r = -0.3, P = 0.02).

Conclusions: In RA patients only FRS risk score significantly correlates with the disease activity index both with and without EULAR correcting factor. On the contrary no significant correlation was found SCORE and ESH/ESC models, which thus appear to less sensitivite in categorizing Cv risk in RA patients.

Design and method: We enrolled 130 hypertensive subjects (30–80 years) who received indication for elective coronary angiography. Duplex ultrasound of intrarenal vasculature was performed to evaluate renal resistive index (RI), renal pulsatility index (PI) and renal acceleration time (AT). Subsequently, a coronary angiography was performed to assess atherosclerotic burden through Gensini Score (GSS) (normal < 10, GSS) was also assessed as a model of vascular damage well related with renal parameters. The population was divided into quintiles based on the GS (1 quintile: GS < 9; II quintile: GS > 9 and < 17;
III quintile: GS > 17 and < 30.8; IV quintile: GS > 30.8 and < 44; V quintile: GS > 44). Statistical analysis was also performed in the population divided in 2 groups: 1) subjects with mild coronary disease (GS < 30); 2) subjects with severe coronary disease (GS > 30).

**Results:** Subjects in higher quintiles had greater values of PI, RI and lower values of AT compared to the ones in lower quintiles. The correlation between GS and PI, RI or AT was not statistically significant at the univariate analysis in overall population, whereas GS, IR and IP were significantly associated with cIMT (all p < 0.01). IP and IR, but not AT, were associated to GS in the group with GS < 30, whereas did not correlate in subjects with GS > 30. These correlations held after adjustment for multiple confounders.

**Conclusions:** Renal vascular changes are not significantly related to coronary atherosclerotic burden in all hypertensive patients. Nevertheless, within the complex mathematical relationship between PI (or RI) and GS (Figure 1), the relationship becomes linear and significant in patients with mild coronary disease.
ORAL SESSION

LATE-BREAKERS LB02:
SESSION 2

LB.02.01 HOMA INDEX AS A PREDICTOR OF HYPERTENSION IN A PEDIATRIC OBESE POPULATION: PRELIMINARY RESULTS
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Objective: Find predictors of hypertension in obese children diagnosed with ABPM and office BP

Design and method: We studied 20 obese children (age 13 ± 0.9 ys, 11 M 9 F) enrolled in our Pediatric Division, with mean BMI of 30.3 ± 4.3, height 1.53 ± 0.11 and weight 72.2 ± 16.6. We evaluated a clinic visit, blood samples, blood pressure measurements (BP office mean of 3 measurements), 24 h ambulatory blood pressure (ABPM), echocardiogram and intimal media thickness (IMT) of common carotid artery.

Results: Mean BP office was: systolic 121 ± 12 mmHg, diastolic 65 ± 10 mmHg; mean 24 h ABPM was: systolic 127 ± 10 mmHg and diastolic 70.2 ± 6.24 mmHg; diurnal systolic ABPM 121.9 ± 10.7mmHg, nocturnal 109.1 ± 10.5mmHg; diurnal diastolic ABPM: 75.1 ± 7.9 mmHg, nocturnal 62 ± 5.6 mmHg. For 24 h ABPM pediatric criteria, 2 patients were >90 percentile for sex, age and height for normal-high blood pressure values and 7 pt were >95% for hypertension criteria. Regardless percentile (%), BP criteria for children we observed that for systolic nocturnal BP 2 subjects were >90% and 7 > 95% and for diastolic BP 4 subjects >90% and 3 > 95%. In general ABPM showed 11 patients as hypertensive, 7 were >95% for systolic and 2 > 95% only for diastolic. Considering predictors of arterial hypertension in our population we figured out that: (i) HOMA index has a positive correlation with systolic office BP (p = 0.03) and (ii) a borderline correlation with mean systolic ABPM (p = 0.06).

Interestingly in our paediatric population, in patients defined as hypertensive for the 95% criteria with the ABPM monitoring, HOMA index was significantly different between hypertensive and non-hypertensive children (p = 0.05).

Conclusions: In conclusion our preliminary report show that: (i) ABPM has a better sensitivity in diagnosing arterial hypertension versus office BP measurement and that (ii) HOMA index is an important predictor of hypertension in healthy obese children.

LB.02.02 24-HOUR SYSTOLIC BLOOD PRESSURE IS INDEPENDENTLY ASSOCIATED WITH DIABETIC RETINOPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS
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Objective: Diabetic retinopathy (DR) is the leading cause of blindness in adults living in developed countries. Among patients with diabetes mellitus (DM), elevated blood pressure (BP) is one of the major modifiable risk factors for the progression of DR. The aim of this study was to examine the association between DR and systemic risk factors.

Design and method: 201 patients with Type 2 DM were enrolled in the study. 109 of these patients were with DR and 92 were without DR. Demographic characteristics, levels of serum glucose, HbA1c, Hs-CRP and 24-hour ambulatory BP determined using validated devices were evaluated.

Results: Age (56.7 ± 9.6 vs. 59.9 ± 8.2, P = 0.012), duration of diabetes (9.6 range: 1–28 vs. 13.8 range:1–32 years, P = 0.01), serum glucose [143.8 range: 58–436] vs. 229.3 (range: 58–554) mg/dL, P = 0.01), HbA1c (7.82 ± 1.7 vs. 9.17 ± 3.18 mg/dL, P = 0.01), Hs-CRP (1.02 ± 0.17 vs. 1.12 ± 0.20 mg/L, P = 0.01), 24-hour systolic BP (125.12 ± 12.9 vs. 138.01 ± 16.09 mmHg, P = 0.01) (Figure 1) and 24-hour diastolic BP (76.51 ± 8.02 vs. 79.95 ± 9.16 mmHg, P = 0.029) were significantly higher in the DR group. In multivariate analysis, higher serum glucose (OR: 1.006, CI: 1.001–1.012, P = 0.018) and 24-hour systolic BP (OR: 1.036, CI: 1.003–1.071, P < 0.001) were found to be independent predictors of DR in diabetic patients.

Conclusions: Our study suggests that higher serum glucose and 24-hour systolic BP is associated independently with DR in diabetic patients.

LB.02.03 SERUM CHLORIDE IS A MORTALITY RISK PREDICTOR IN TYPE 2 DIABETES MELLITUS – ANALYSIS OF 91,159 PATIENTS IN THE WEST OF SCOTLAND
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Objective: Low serum chloride (Cl-) is associated with increased risk of death in those with heart failure, hypertension or chronic kidney disease. We sought to investigate the association of serum chloride with risk of cause-specific death in adults with type 2 diabetes mellitus.

Design and method: Data were available for 91,159 adults from the West of Scotland with diabetes mellitus with 10 years follow up, from NHS Greater Glasgow and Clyde Safe Haven. Two groups were created: serum Cl- < 100 and Cl- ≥100 mmol/L. Cox proportional hazard models, adjusted for age, sex and serum sodium (Na+), were used to assess the association between serum Cl- and risk of death (all-cause mortality, vascular death, death from myocardial infarction (MI), death from heart failure, death from stroke, death from cancer).
Results: 13,459 patients had serum Cl− < 100 mmol/L; 53% were male with median age 62.5 (IQR 50.9–73.1) years and median Na+ 136 (133–138) mmol/L. 77,757 patients had serum Cl− ≥ 100 mmol/L; 53% were male with median age 61.2 (IQR 50.2–71.4) years and median Na+ 139 (IQR 138–141) mmol/L. Serum Cl− < 100 mmol/L was associated with a 44% increased risk of all cause mortality (N = 20,304, HR 1.44 [95% CI 1.38–1.49]; p < 0.0001), independent of serum Na+ (Figure). The increased mortality risk of serum Cl− < 100 mmol/L was observed for cardiovascular mortality (N = 163, 1.41 [1.31–1.51]; p < 0.0001); death from MI (N = 1,986, 1.42 [1.25–1.60]; p < 0.0001); stroke (N = 1,590, 1.24 [1.08–1.42]; p = 0.003); heart failure (N = 200, 1.38 [0.95–2.0]; p 0.09) and cancer (N = 5,577, 1.12 [1.04–1.21]; p = 0.003).

Conclusions: Serum chloride < 100 mmol/L was associated with increased risk of death in adults with type 2 diabetes mellitus. This association merits further study.

**LB.02.05**

**TARGET BLOOD PRESSURE IN HYPERTENSIVE DIABETICS: A KOREAN NATIONAL HEALTH INSURANCE SERVICE HEALTH EXAMINEE COHORT STUDY**

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Objective: To demonstrate whether strict blood pressure (BP) control in diabetic hypertensives reduces the risk of cardiovascular events.

Design and method: Among 514,866 subjects from the Korea National Health Insurance Service health examinee cohort, 7926 subjects who were diagnosed with hypertension between 2003 and 2006 were included in the analysis. They were divided into three groups according to mean systolic BP (SBP; < 130, 130 to < 140, ≥ 140 mmHg) and mean diastolic BP (DBP; < 80, 80 to < 90, ≥ 90 mmHg) recorded during follow-up health examinations. All-cause mortality, cardiovascular mortality, nonfatal myocardial infarction (MI), stroke, and end-stage renal disease (ESRD) were compared among groups.

Results: Significant reduction in risk of all-cause death (P < 0.001), MI (P = 0.038), total stroke (P = 0.025), and progression to ESRD (P = 0.001) were observed in patients with mean SBP 130 to < 140 mmHg. Moreover, there was tendency for reduced cardiovascular mortality (P = 0.067) and fatal haemorrhagic stroke (P = 0.065) in patients with mean SBP 130 to < 140 mmHg compared to patients with uncontrolled SBP. However, there were no additional clinical benefits in patients with mean SBP < 130 mmHg. Patients with mean DBP 80 to < 90 mmHg had a significantly lower risk of all cause death (P < 0.001), cardiovascular mortality (P < 0.001), fatal MI (P = 0.028), haemorrhagic stroke (P = 0.008), ischemic stroke (P = 0.005), and total stroke (P < 0.001), and a tendency for a lower risk of MI (P = 0.098). Lowering mean DBP to ≤ 80 mmHg was associated with further reduction of the risks of all-cause death (P < 0.001), cardiovascular mortality (P < 0.001), fatal MI (P = 0.020), fatal haemorrhagic stroke (P = 0.016), haemorrhagic stroke (P = 0.007), ischemic stroke (P = 0.001), total stroke (P < 0.001), and MI (P = 0.021). In subgroup analysis of aspirin or statin user, lowering of mean SBP further reduced 130 mmHg revealed further reduction of all-cause death (P = 0.003), ischemic stroke (P = 0.003), and total stroke (P = 0.001).

Conclusions: Mean BP < 130/80 mmHg was associated with further lowering of the risk of all-cause death, cardiovascular mortality, and nonfatal cardiovascular events in diabetic hypertensive patients.

**LB.02.06**

**APPARENT AND TRUE TREATMENT RESISTANT HYPERTENSION IN GP: A CROSS SECTIONAL STUDY OF PREVALENCE WITH CONSIDERATION OF MORBIDITY, WHITE COAT HYPERTENSION, DOSING AND ADHERENCE**

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Objective: Treatment Resistant Hypertension (TRH) is defined as high blood pressure in patients taking three or more groups of anti-hypertensive medications (one must be a diuretic) or those taking four or more medications regardless of type and BP level. Target BP levels need to be adapted to specific morbidity (e.g. diabetes), ambulatory blood pressure measurement (ABPM) should be used to exclude white coat hypertension, doses should be the minimal tolerated, and both non-adherence and lifestyle should be examined. Most previous studies have not accounted for these considerations. We conducted a cross sectional study of the...
prevalence of apparent TRH in general practice, utilizing the appropriate definition, and then considered these issues.

**Design and method:** Forty university-research affiliated practices were invited to participate. We ran a standard ATC drug search identifying patients on any hypertensive medications. Two researchers reviewed individual patient’s records. The World Health Organisation-Defined Daily Dosing guidelines determined adequate dosing. A measure of adherence was whether patients were printed greater than nine repeat prescriptions within the last year.

**Results:** Sixteen practices participated (N = 50,878). 2,807 patients had been prescribed three or more medications previously and of these 646 were deemed to have aTRH. They were largely elderly, male and had co-morbidities (Diabetes 36.7% and Chronic Kidney Disease 40%). 19.0% had adequate medication dosing for each medication and 79.9% were deemed adherent by the investigators. Using a BP cut-off of 140/90 mm Hg, the prevalence of aTRH was 6.4% (95% CI 5.8-7.0). Three or more medications previously and of these 646 were deemed to have aTRH. They were largely elderly, male and had co-morbidities (Diabetes 36.7% and Chronic Kidney Disease 40%). 19.0% had adequate medication dosing for each medication and 79.9% were deemed adherent by the investigators. Using a BP cut-off of 140/90 mm Hg, the prevalence of aTRH was 6.4% (95% CI 5.8-7.0).

Considerable adequate dosing and adherence reduces prevalence rates even further.

**Conclusions:** Reviewing individual patient records results in a lower estimate of the prevalence of aTRH than has been generally previously reported. Consideration for individual patients of criteria such as morbidity, dosing, white coat hypertension and adherence additionally lowers these estimates, and may be all that is required for the management of the vast majority of cases.

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**Objective:** Attenuated nocturnal fall (non-dipping) of blood pressure (BP) is a predictor of cardiovascular target organ damage. No genome-wide association studies (GWAS) on BP dipping have been previously reported.

**Design and method:** We conducted a GWAS on BP dipping in 204 hypertensive Finnish men from the Genetics of Drug Responsiveness in Essential Hypertension (GENRES) study that included four-four week placebo periods before four antihypertensive drug treatment periods. Ambulatory BP was recorded at the end of each placebo and drug period. We analyzed dipping using ambulatory BP recordings after the placebo periods (173 subjects with four and 31 subjects with three recordings). The DNA samples were genotyped using Illumina HumanOmniExpress-12 Bead Chip. Residuals of mean systolic and diastolic BP dipping were calculated using linear regression with appropriate covariates. The residuals were tested for genetic associations using additive genetic model and signals with P-value < 10^-5 were followed up in two independent Finnish cohorts; Haemodynamics in Primary and Secondary Hypertension (DYNAMIC) (N = 183) and Dietary, Lifestyle and Genetic determinants of Obesity and Metabolic Disease (DILGOM) (N = 180). Left ventricular mass index (LVMI) assessed by echocardiography was measured in GENRES subjects.

**Results:** In GENRES, rs4905794 near BCL11B achieved genome-wide significance (β = -6.7 mmHg, P = 2.5 × 10^-8 for systolic and β = -4.1 mmHg, P = 3.6 × 10^-6 for diastolic dipping). In the replication analysis, the effect of rs4905794 was in the same direction but statistically insignificant in DYNAMIC (β = -1.11 mmHg, P = 0.5 for systolic, and β = -1.4 mmHg, P = 0.16 for diastolic dipping) and did not replicate in DILGOM. The G allele of rs4905794 that associated with larger BP dipping was also associated with smaller LVMI in GENRES subjects (β = -7.6 g/m², P = 0.02). There were further 10 SNPs in 8 loci with P-values < 10^-5, but they did not replicate with P-values < 0.05 in both DYNAMIC and DILGOM.

**Conclusions:** We report here the first GWAS on BP dipping. rs4905794 near BCL11B had a genome-wide-significant signal for BP dipping and associated with LVMI in GENRES. Evidence from previous GWASs (lipoprotein(a) and aortic stiffness) and animal models (energy metabolism, cardiac hypertrophy) support the role of BCL11B in cardiovascular physiology.

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**Objective:** Adducin and endogenous ouabain play essential roles in the pathogenesis of hypertensive and related cardiovascular diseases. However, whether single-nucleotide polymorphisms (SNPs) of the adducin subtypes and ouabain-related genes are associated with hypertension and cardiovascular diseases remains controversial. In this study, we investigated the potential associations of 20 SNPs of adducin and genes involved in ouabain synthesis, transportation and metabolism with hypertension and/or coronary artery disease (CAD) in 1493 unrelated Taiwanese participants from the TAIwan Coronary and Transcatheter intervention (TACT) Study.

**Design and method:** The 1493 study participants were composed of 148 normal healthy controls, 293 hypertensive subjects with CAD, 720 hypertensive subjects with CAD, with a mean age of 63.6 ± 10.2 years.

**Results:** Compared to normal healthy controls, there were significant associations between hypertensive subjects without CAD and polymorphisms of the alpha-adducin (ADD1) gene rs4961 (TT vs. GT+GG, odds ratio: 1.96, 95% CI: 1.10–3.47, P = 0.022) and angiotensin II receptor type 1 (AGTR1) gene rs231127 (GG+GA vs. AA, odds ratio: 2.23, 95% CI: 1.31–3.79, P = 0.003) and lansoprazole synthase (LSS) gene rs912437 (AA vs. AG+GG, odds ratio: 2.45, 95% CI: 1.17–5.12, P = 0.017) after adjustments for age and gender. ADD1 TT genotype (odds ratio: 1.99, 95% CI: 1.11–3.55, P = 0.021) and AGTR1 GG+GA genotypes (odds ratio: 1.82, 95% CI: 1.08–3.04, P = 0.024) were significantly associated with normotensive subjects with CAD, compared to normal controls. For hypertensive subjects with CAD, ADD1 TT genotype (odds ratio: 1.97, 95% CI: 1.15–3.38, P = 0.013), AGTR1 GG+GA genotypes (odds ratio: 1.60, 95% CI: 1.02–2.51, P = 0.040), and LSS AA genotype (odds ratio: 2.04, 95% CI: 1.00–4.13, P = 0.048) were significantly more prevalent compared to normal controls, after adjustments for age and gender.

**Conclusions:** The ADD1 rs4961, AGTR1 rs231127, and LSS rs914247 polymorphisms are significantly associated with hypertension and CAD, respectively, in the Taiwanese population. This finding lends support for the pathogenic roles of adducin and endogenous ouabain in hypertension and CAD in Asians.

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**Objective:** Hypertension guidelines recommend use of combination therapy in most patients. Whether this should represent the initial treatment strategy is uncertain, however, because, although initial combination therapy has been shown to be accompanied by faster blood pressure control, 1) no randomized trial has investigated whether this leads to an earlier patient protection from cardiovascular (CV) events and 2) observational studies are limited by the lack of head-to-head differences between patients initiating treatment with one vs more than one drug. The aim of this study was to assess the clinical advantage of combination therapy over early CV outcomes.

**Design and method:** The 44,534 residents from the Italian Lombardy administrative database aged 40–80 years who were newly treated with antihypertensive drugs during 2010 were followed for one year after treatment initiation. A self-controlled case series design was applied only on patients who experienced hospital admission for ischemic heart disease (IHD), cerebrovascular disease (CD), heart failure (HF) or any CV disease. The follow-up period was split into subperiods during which patients were prescribed a single antihypertensive drug or combination therapy. A conditional Poisson regression model was used to estimate the ratio between the incidence rate of CV event experienced during combination and mono therapies. Data were subanalyzed also according to markers of CV risk severity and clinical complexity.

**Results:** More patients started treatment on mono than on combination therapy. About 70% of the patients switched from mono to combination treatment during follow-up but switched from combination to monotherapy was also not rare (around one third of the patients). The median time of the switching was 50 days. The incidence of CV outcomes during combination therapy was markedly less than that observed during monotherapy. The reduction amounted to 59% for IHD, 34% for CD, 71% for HF, and 56% for any CV event, all differences being statistically significant (p < 0.01). Results were similar for different categories of clinical complexity.

**Conclusions:** A within-patient comparison of the incidence of early CV events during antihypertensive mono and combination treatment shows that the latter strategy leads to a more effective CV protection.
ORAL SESSION

ORAL SESSION 5C: PEDIATRIC HYPERTENSION

OP.5C.01
STATUS OF CARDIOVASCULAR HEALTH IN CHINESE CHILDREN AND ADOLESCENTS

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Objective: In 2010, the American Heart Association (AHA) defined a set of four health behaviors and four health factors to evaluate cardiovascular health (CVH) status for children and adolescents. We aimed to examine the age-, sex-, and region-specific prevalence of ideal CVH and each CVH component among Chinese children and adolescents based on a nationally representative survey.

Design and method: Data were obtained from the China Children and Adolescents Cardiovascular Health study conducted in 2013–2014, which comprised of 10,818 children and adolescents aged 6–18 years old from eight cities. Seven CV health metrics, including smoking, body mass index, dietary intake, physical activity, blood pressure, blood glucose, and total cholesterol, are categorized as poor, intermediate, and ideal according to AHA criteria.

Results: Ideal smoking status was most prevalent (males, 93.6%; females, 96.7%), whereas ideal physical activity levels (males, 9.1%; females, 5.6%) and ideal Health Diet Score (males, 18.8%; females, 19.3%) were least prevalent. Females had a higher prevalence of ideal body mass index (79.8% vs 65.6%) and ideal blood pressure (73.1% vs 66.2%). The overall prevalence of ideal CVH among Chinese children and adolescents was very low (males, 0.4%; females, 0.6%). The prevalence of ideal CVH decreased with age, and children aged 6–11 years versus adolescents aged 12–18 years had a higher prevalence of ideal CVH.

Prevalece estimates according to age and sex were consistent across region. Children with adverse health behaviors scores had a lower prevalence of ideal blood pressure, ideal blood glucose, and ideal total cholesterol.

Conclusions: We found a very low prevalence of ideal CVH in Chinese children and adolescents, particularly physical activity and dietary intake. The current worsening of CVH status among Chinese children and adolescents would lead to epidemic of obesity, hypertension, hypercholesterolemia, and diabetes when they step into adulthood.

OP.5C.02
ASSESSING THE IMPACT OF BIRTH WEIGHT AND POSTNATAL WEIGHT GAIN ON OFFICE AND 24-HOURS AMBULATORY BLOOD PRESSURE IN CHILDREN AT FIVE AND TEN YEARS OF LIFE

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Objective: To assess the impact of birth weight and postnatal weight gain on BP tracking at 5 and 10 years of life, in order to identify a window of opportunity for early intervention.

Design and method: This prospective study, starting at birth, includes eighty-seven subjects born at term. Subjects were divided, according to size at birth, in small, appropriate and large for gestational age. Children were followed up at 5 and 10 years and anthropometric parameters and BP (office and 24-hours ABPM) were obtained. The BP tracking from birth to 5 and 10 years and the ratio to weight gain in each period were calculated.

Results: Overall, weight gain during the first 5 years and thereafter between 5 and 10 years were 18.6 ± 5.3 kg and 20.9 ± 8.9 kg, respectively. Anthropometric parameters and systolic BP at birth, 5 and 10 years grouped by BW conditions are in the table. At birth significant differences in systolic BP were present among groups increasing as the BW increases. In the first 5 years, the steepest increment in systolic BP related to weight gain was present in SGA as compared to AGA and LGA. Differences in BP tracking among BW groups disappeared after the age of 5.

Conclusions: This prospective study points out that the steepest BP tracking was during the first five years of life in those subjects that were born SGA independent of the postnatal weight gain. The recognition of critical periods, may contribute to open a window of opportunity to modify BP tracking in subjects with potential risk.

OP.5C.03
DETERMINANTS OF CENTRAL AND PERIPHERAL PULSE PRESSURE IN A POPULATION OF HEALTHY ADOLESCENTS. THE MACISTE STUDY

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Objective: There is paucity of data about central blood pressure (BP) and vascular phenotypes in young individuals. The identification of the main determinants of central BP parameters and the BP amplification phenomenon may help in defining the clinical relevance of BP patterns in adolescence. We aimed at evaluating the anthropometric and hemodynamic factors associated with central pulse pressure (cPP), peripheral pulse pressure (pPP) and central-to-peripheral BP amplification (cPPamp) in a population of healthy adolescents.

Design and method: We studied 459 subjects (boys 57%, mean age 16.8 ± 1.5y, SBP/DBP 124/67 ± 11/7 mmHg) attending the Liceo Donatelli High School in Terni, Italy. cPP was measured by validated oscillometry. cPP was estimated from radial and carotid-femoral pulse wave velocities (SpysugemoCor GTF) calibrated to brachial MAP/DBP. PPamp was expressed as pPP/cPP. Indexed left ventricular mass (ILVM = LVM / BSA) and stroke index (SI = stroke volume/BSA) were derived from 2D-echo cardiography (Teicholz’s formula, Devereux correction). Carotid-femoral (cf-PWV) and carotid-radial (cr-PWV) pulse wave velocities were measured by applanation tonometry (SphygmoCor). PWV ratio was expressed as cf-PWV/cr-PWV. pPP and PPamp were introduced as dependent variables in three separate stepwise multivariate regression models. Age, male sex, BSA, heart rate (HR), MAP, stroke index (SI), stroke volume/BSA and cf-PWV were included in each model as independent factors.

Results: Average cPP was 36 ± 7 mmHg. cPPamp 1.57 ± 0.13. cPP was positively associated with male sex, BSA, MAP, SI, and negatively with HR. The above variables explained 47% of the cPP variance. pPP was positively associated with male sex, BSA and SI (44% of pPP variance explained). PPamp was positively associated with age, HR and cf-PWV (17% of PPamp variance explained). Results did
not change when BMI and height replaced BSA, ilVM replaced SI, and cr-PWV or PWV ratio replaced cr-PWV.

Conclusions: Anthropometric and hemodynamic factors differently impact on cPP, pPP and PPaMp. HR and MAP are significantly related to cPP, but not to pPP, HR, cr-PWV and age are all positively related to PPaMp. These results could help in better elucidate the clinical relevance of some BP patterns frequently observed in adolescence, such as isolated systolic hypertension and spurious hypertension.

Conclusions: cSBP and cPP differentiates patients with severeHT and TOD from patients with WCH, ambpreHT and ambHT without TOD.

**OP.5C.05**  
SERUM URIC ACID IS INCREASED IN NORMOTENSIVE OBESE CHILDREN WITH A PARENTAL HISTORY OF HYPERTENSION

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Objective: Increased uric acid levels are closely associated with new-onset hypertension in children, and pilot studies showed that pharmacological lowering of uric acid may reduce blood pressure (BP) in obese pediatric patients. Nevertheless, controversy remains concerning a direct causative role of serum uric acid (SUA) in the pathogenesis of essential hypertension (EH).

Our study was aimed to determine if normotensive obese children and adolescent offspring of adults with EH show SUA levels different than those of pediatric subjects in whom there is non family history of EH.

Design and method: Fifty-nine obese normotensive children and adolescents, attending for metabolic assessment the Pediatric Diabetes Unit, Children’s Hospital “G. Di Cristina”, and for cardiovascular evaluation the ESH Hypertension excellence center of the University of Palermo, were studied. All the subjects, aged between 8 and 17 years, underwent routine blood chemistry and oral glucose tolerance test with glucose and insulin determinations. All subjects had blood pressure determinations below the 90th percentile and had no previous history of elevated blood pressure.

Results: There were 14 subjects whose parents were both normotensive (FH—), and the remaining 45 subjects whose one or both parents were hypertensive. FH + did not differ regarding age, sex distribution, blood pressure values, body mass index, waist circumference, serum glucose levels when compared to FH−. Among the metabolic parameters assessed, only SUA was significantly higher in FH+ than in FH− (p = 0.007; figure 1). This difference held after adjusting for age, gender and BMI (p = 0.01).

Conclusions: Our results, showing higher values of SUA in normotensive obese children and adolescents with parental history of EH, seem to support the hypothesis that increased uric acid may precede and determine the development of hypertension.

**OP.5C.04**  
CENTRAL SYSTOLIC BLOOD PRESSURE AND CENTRAL PULSE PRESSURE PREDICT LEFT VENTRICULAR HYPERTROPHY AND SUBCLINICAL ARTERIAL INJURY IN HYPERTENSIVE CHILDREN

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Objective: Central systolic (cSBP) and pulse pressure (cPP) are better determinants of cardiovascular risk than brachial blood pressure. There are only few reports on use of cSBP and cPP in diagnostic approach to hypertensive children. We analysed utility of cSBP and cPP in diagnostic approach in hypertensive children.

Design and method: In 233 children (54 girls; 14.9 ± 2.6 years) referred with arterial hypertension diagnostic process including assessment of 24 hour ABPM, left ventricular mass index (LVMi), carotid intima-media thickness (cIMT), pulse wave velocity (PWV), cSBP and cPP was done. PWV, cSBP and cPP were assessed using oscillometric device (Vicorder®).

Results: 108 subjects had white coat hypertension (WCH), 21 ambulatory prehypertension (ambpreHT), 33 ambulatory hypertension (ambHT) and 71 severe ambulatory hypertensive (severeHT). The groups didn’t differ regarding age and sex distribution. In all hypertensive children primary hypertension was ultimately diagnosed. cIMT, LVMi, PWV, cSBP and cPP increased across blood pressure strata from WCH to severeHT with differences found between severeHT and WCH patients regarding cIMT (0.46 ± 0.04 mm vs 0.44 ± 0.03 mm; p = 0.004) and cSBP (120 ± 10 mmHg vs 114 ± 9 mmHg; p = 0.017). Patients with severeHT had greater cPP (51 ± 9 mmHg) in comparison with WCH (47 ± 9 mmHg; p = 0.009) and ambpreHT patients (44 ± 6 mmHg; p = 0.017). LVMi and cIMT correlated with cSBP (r = 0.220; p = 0.0007 and r = 0.14; p = 0.04, respectively) and cPP (r = 0.274; p = 0.0001 and r = 0.202; p = 0.002, respectively). 36 patients with left ventricular hypertrophy (LVH) had greater cPP (52 ± 10 mmHg) in comparison with subjects without LVH (47 ± 6 mmHg; p = 0.027). Regression analysis revealed cPP as the only predictor of LVHi (r2 = 0.09, B = 0.143, p = 0.03).

Conclusions: Our results, showing higher values of LVH in normotensive obese children and adolescents with parental history of EH, seem to support the hypothesis that increased uric acid may precede and determine the development of hypertension.
were measured, and information about physical activity, smoking, family history (FH), and birth weight (BW) were obtained. BP was measured three times by oscilometric method and high BP was defined as systolic BP (SBP) and/or diastolic BP (DBP) \( \geq 95 \) for age, gender and height percentile; O/O as body mass index (BMI) \( \geq 26.7 \) for gender and age; and increased AC as \( \geq 90 \) for age and gender. The association of the variables with high BP and O/O were tested with logistic regression.

Results: 1,892 students were evaluated (47.3% males). The prevalence of elevated BP was 8.4% (9.9%M/7.2%F). The prevalence of O/O was 45.2% (23.0% for over- and 22.2% for obesity). Variation in males: 28.6%–53.8% (14 and 12 yo, respectively) and in females: 30.4%–54% (10 and 11 yo, respectively). Other CV risk variables prevalence were: 45.6% for central obesity, 0.6% for smoking; 64.2% for sedentary lifestyle, 60.7% of the students had a FH of hypertension; 43.4% O/O; 38.6 diabetes; 26.2% myocardial infarction; 19.7% stroke. In the univariate analysis: male gender, BMI, AC and sedentary leisure time were highly associated with high BP and AC, birth weight, FH of diabetes, FH of hypercholesterolemia and FH of O/O were associated with O/O. Age and FH of hypertension had an nearly significant association with O/O (\( p = 0.052 \)). In the multivariate analysis only male gender (OR: 1.538;95%CI:1.069–2.211;p:0.020), BMI (OR: 1.111;95%CI:1.024–1.205;p:0.011) and sedentary leisure time (OR: 0.992;95%CI:0.996–0.998;p:0.010) kept their association with high BP and AC (OR: 0.915;95%CI:0.859–0.975;p:0.006), birth weight (OR: 1.362;95%CI:1.146–1.617;\( p = 0.001 \)) and FH O/O (OR:2.052;95%CI:1.670–2.522;p < 0.001) kept their association with O/O.

Conclusions: In Brazilian students aged 10–15 years, high BP was mainly associated with male gender, BMI and sedentary leisure time. Overweight/obesity was associated with lower age, higher birth weight and family history of O/O.

**OP.5C.07**

**THE LINK BETWEEN CARDIORESPIRATORY FITNESS AND CARDIAC AUTONOMOUS NERVOUS SYSTEM IN OBSESE YOUTH**

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Objective: To assess the cardiorespiratory fitness and its relationship with the cardiac autonomic neural activity, a marker of early cardiometabolic risk, in youths with abnormally increased body weight.

Design and method: Sixty-four overweight and obese subjects, 9 to 17 years, of both sexes, stratified according to the international body mass index cut-off, were enrolled. Continuous electrocardiogram was recorded during 15 minutes in resting and supine conditions, and afterwards heart rate variability was analysed in the time and frequency domain as well as non-linear dynamics. In addition, cardiorespiratory fitness in effort conditions was assessed (VO2peak).

Results: Among the obese youths, cardiorespiratory fitness was the lowest in severe obese despite that no significant differences were observed regarding heart rate nor heart rate variability in time and frequency domain. A positive and significant relationship, independent of the degree of obesity, puberal stage and breathing rate under resting conditions, were observed between cardiorespiratory fitness (assessed by VO2peak) and sympatho-vagal balance, estimated by standard deviation of the NN interval (SDNN: \( r = 0.268, p < 0.05 \)) and the long term variation using the Poincaré plot (PS1: \( r = 0.275, p < 0.05; \) PS2 \( r = 0.273, p < 0.05 \)).

Conclusions: The key finding of the present study was the presence of a link between cardiorespiratory fitness and cardiac autonomic nervous system activity, independent of the degree of obesity. This emphasises that cardiorespiratory fitness can be a relevant tool in the assessment of early cardiovascular risk in obese youths.

**OP.5C.08**

**BLOOD PRESSURE PHENOTYPE AS A DETERMINANT OF AORTIC PULSE VELOCITY IN CHILDREN AND ADOLESCENTS - THE PORTUGUESE VASCULAR PHENOTYPE IN CHILDREN AND ADOLESCENTS COHORT**

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Objective: The PORT-VASPh Cohort was designed to contribute to a better understanding of vascular function in children and adolescents, mostly focusing on PWV and other complementary aspects of arterial hemodynamics. This preliminary analysis is aimed at analyzing the PWV as a function of the individual blood pressure (BP) phenotype.

Design and method: Prospective and observational study, with 402 children and adolescents enrolled so far, 40% females, age ranging from 5 to 17 years (mean age: 11.81 ± 2.91 years). About 19.2% had family history of cardiovascular disease and overweight and at-risk weight classification accounted respectively for 7% and 12.2%. The overall health profile for each participant was defined based on three clinical evaluations, in which blood pressure (BP) was measured under standard conditions over the brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. Carotid-femoral PWV was measured to all participants at the third clinical evaluation, with the Compilor SP device, complying with the methodological recommendations. All participants were evaluated by the same experienced clinician.

Results: Mean systolic (SBP) and diastolic (DBP) blood pressure were 116 ± 13 mmHg and 66 ± 9 mmHg, respectively. Mean heart rate (HR) was 70.21 ± 16.03 bpm. Mean PWV was 6.26 ± 1.02 m/s. BP distribution was 26.6% hypertensive (HT), of which 16.4% stage 1, 10.2% stage 2, 10.7% high-normal, and 62.7% normal. The majority of the HT presented isolated systolic (ISH) HT (26.3%), with 4.3% presenting systolic-diastolic (SDH) HT, and 2.5% isolated diastolic (IDH) HT. Mean PWV was higher in HT compared with normotensive (6.6 ± 1.0 m/s versus 6.1 ± 0.9 m/s, respectively; \( p < 0.001 \)), and a significant increase in PWV was observed in accordance with the classification of BP: normal- 6.07 ± 0.96 m/s; high-normal- 6.47 ± 1.07; stage 1 HT- 6.6 ± 1.02; stage 2 HT- 6.7 ± 1.10; \( p = 0.001 \) for trend. PWV was also significantly higher in ISH compared with SDH and IDH (6.6 ± 1.1 versus 6.3 ± 0.89 versus 6.3 ± 0.94, respectively; \( p = 0.04 \)).

Conclusions: In children and adolescents, aortic PWV is strongly influenced by the BP phenotype, with an increase in PWV for higher stages of the BP classification and particularly associated with ISH.

**OP.5C.09**

**OMEGA-6 FATTY ACIDS IN ERYTHROCYTE MEMBRANE ARE INVERSELY ASSOCIATED WITH SEVERAL FEATURES OF THE METABOLIC SYNDROME IN A GROUP OF OBESE CHILDREN**

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Objective: Overweight and obesity lead to the clustering of cardiovascular (CV) risk factors and the metabolic syndrome (MetS) not only in adults but also in children and are often accompanied by non-alcoholic fatty liver disease. Quality of dietary fat, beyond the quantity, can influence CV risk profile and in particular omega-3 fatty acids (FA) have been proposed as beneficial.

Design and method: The aim of this observational study was to evaluate the associations of individual CV risk factors, characterizing the MetS, with the erythrocyte membrane FA (by gas-chromatography), markers of average intake, in a group of obese children.

Results: We enrolled 70 children (BMI = 29.4 ± 4.4 kg/m²; percentile of BMI = 98.0 ± 1.7), aged 5–17 years. Mean content of Omega-3 FA was low (Omega-3 Index = 4.7 ± 0.8 %). Omega-3 FA were not associated with MetS characteristics, whereas omega-6 FA, in particular arachidonic acid (AA), were inversely associated with several features of the MetS. AA resulted inversely correlated with waist circumference (r = -0.352), waist/hip ratio (r = -0.311), Waist/height ratio (r = -0.248), triglycerides (r = -0.363), fasting insulin (r = -0.337), 24-hour-SBP (r = -0.313), daytime-SBP (r = -0.267), nighttime-SBP (r = -0.245) and nighttime DBP (r = -0.344). On the opposite, total amount of saturated FA associated with all features of MetS except for BMI, HDL and triglycerides. The results are in agreement with the recommendation of the American Heart Association that omega-3 dihomo-gamma-linolenic acid and eicosapentaenoic acid should be consumed.

Conclusions: This study showed that some individual CV risk factors were inversely associated with omega-3 fatty acids.
Conclusions: Omega-6 FA, and especially AA, may be protective toward CV risk factors featuring the MetS and also to indexes of hepatic steatosis in obese children, whereas SFA seems to exert opposite effects.

GENDER DEPENDENCE OF ALDOSTERONE TO RENIN RATIO IN A PEDIATRIC POPULATION

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Objective: Aldosterone to renin ratio (ARR) is widely used as screening test of primary hyperaldosteronism, but little is known of the reference values of ARR in pediatric age. Aim of this study was to evaluate ARR values and associated factors in a population of Italian children and adolescents.

Design and method: In blood samples collected in sitting position in 287 children and adolescents attending a Pediatric Unit of Preventive Medicine (52% males aged 4–18 years), we measured plasma aldosterone and plasma renin concentrations (PAC, ng/dL and PRC mU/L) with the immunochemiluminescent method and calculated the relevant ARR values. Pubertal status, weight, height, heart rate, blood pressure, sodium, potassium, glomerular filtration rate and HOMA index were also assessed.

Results: Median PAC was fairly similar throughout the age classes (4–8.9), (9–10.9), (11–12.9), (13–18) in both genders (ranging from 7.5 to 9.9 ng/dL in males and from 11.0 to 12.6 ng/dL in females for the first to the fourth age class). In males median PRC was similar across age classes (ranging from 58.2 to 55.5 mU/L), whereas in females PRC progressively fell from 61.5 to 36.6 mU/L (p < 0.001). Also, PRC was significantly lower in pubertal than in pre-pubertal females (46.1 vs 58.7 mU/L, p = 0.003). No difference was observed between pubertal and pre-pubertal males. Median ARR was similar throughout the age classes in males (from 0.18 to 0.19), whereas it increased significantly from 0.19 to 0.36 in females (p = 0.03). In an adjusted multiple regression analysis PAC and PRC were significantly correlated in both genders (p < 0.0001). In females, age was inversely related with PRC (p = 0.0001) and directly related with ARR (p = 0.01). The corresponding models in males did not show any significant association.

Conclusions: In a pediatric population with increasing age ARR values diverge between genders due to the progressive reduction of PRC in females. It appears that age and puberty are the driving factors of this gender effect.
ORAL SESSION

ORAL SESSION 6A:
BLOOD PRESSURE MEASUREMENT

OP.6A.01  CLINICAL SIGNIFICANCE OF STRICT HOME BLOOD PRESSURE CONTROL IN JAPANESE PATIENTS UNDERGOING ANTITHROMBOTIC TREATMENT: THE J-HOP STUDY

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Objective: Although the Japan Hypertension Society guidelines recommend that the blood pressure (BP) of patients undergoing antithrombotic treatment should be strictly controlled, few studies have examined the relationship between home BP control and cardiovascular events in such patients.

Design and method: Between 2005 and 2012, 4,310 Japanese outpatients (mean age 65 years; 47% men, 53% women; 79% taking antihypertensive medications) were examined (mean follow-up 14 years). The patients' home BP values taken during the morning over 14 days at baseline were used in the present retrospective analysis.

Results: During the average 4-year follow-up, there were 74 strokes. When we divided the patients into the group undergoing antithrombotic treatment (n = 806) and those without such treatment (n = 3,452), the number of stroke events in each group was 31 (27 ischemic, 4 hemorrhagic) and 43 (36 ischemic, 7 hemorrhagic), respectively. Adjusted for cardiovascular risk including clinic systolic BP (SBP), a Cox regression analysis revealed that the morning SBP level had a significant prognostic impact on stroke in both the patients with antithrombotic treatment (hazard ratio [HR] 1.034; 95% confidence interval [CI] 1.012–1.056; P = 0.002) and those without (HR 1.030; 95% CI 1.012–1.049, P = 0.002). The slope of the relationship between the stroke incidence and the home BP values increased more steeply in the antithrombotic treatment group compared to the group without treatment.

Conclusions: Strict home BP control is needed to prevent stroke in Japanese outpatients who are undergoing antithrombotic therapy.

OP.6A.02  24-HOUR SYSTOLIC BLOOD PRESSURE LOAD REPRESENTS AN IMPORTANT VARIABLE IN DETERMINING THE CARDIOVASCULAR RISK PROFILE OF WHITE-COAT HYPERTENSION

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Objective: White-coat hypertension (WCH) displays an increased cardiovascular (CV) risk. Scanty are the data available on the impact of 24-hour average blood pressure (BP) load on the increased CV risk in this condition.

Design and method: 2051 subjects randomly selected from the general population of Monza (Italy), aged 25 to 74 years, stratified for sex and decades of age, underwent measurement of systolic (S) and diastolic (D) office BP and average 24-hour ambulatory SBP and DBP. Anthropometric variables, serum cholesterol, blood glucose were also measured. During a median follow-up of 156 months hospital admissions for coronary and stroke events were collected. Fatal events were also collected, among which those related to CV causes (ICD-10 from I-0 to I-99) were identified. In the whole population sample, the subjects with both normal office BP (<140/90 mmHg) and normal 24-hour BP (<125/79 mmHg) were defined as normotensives (NT, n = 1,001). Among the 376 subjects with high office BP and normal 24-hour BP (WCH), those with 24-hour SBP above and under the median value (118 mmHg) were classified as WCHH and WCHL, respectively.

Results: The analysis was carried out on the 1001 NT and on the 356 WCH sub-jects. During the follow-up 112 deaths and 73 fatal and non fatal CV events. Total mortality was 5.7%, 20.8% and 10.1% in NT, WCHH and WCHL, respectively. Incidence of CV events was 3.4%, 14.6% and 7.3% in NT, WCHH and WCHL, respectively. Adjusting the data for age, sex, hypercholesterolemia, diabetes mellitus, smoking, obesity, previous CV events and antihypertensive therapy, the risk of all-cause death and CV events in WCHH was significantly higher than that of NT (HR 1.8, CI 1.2–2.8, and HR 2.7, CI 1.6–4.7, respectively; p < 0.01 for both). No significant difference was found in the CV risk between WCHL and NT.

Conclusions: Although by definition in the normal range, the level of 24-hour ambulatory SBP load is a relevant factor in determining the enhanced CV risk in WCH. Indeed, when the 24-hour SBP values are low, the CV risk of WCH is not different from that displayed by NT.

OP.6A.03  PROGNOSTIC VALUE OF BLOOD PRESSURE CIRCADIAN RHYTHM DISTURBANCES IN NORMOTENSIVE SHIFT WORKERS OF THE ARCTIC POLAR REGION

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Objective: To study chronophysiological alterations in blood pressure (BP) rhythms in normotensive patients and define their prognostic value in development of hypertension in shift workers at the Arctic Polar region in a prospective (one-year) observation.

Design and method: 173 men with normal BP and with a negative history of hypertension (mean age: 40.2 ± 4.1 years; mean northern shift-work experience: 16.5 ± 6.8 years; mean length of service: 11.2 ± 3.8 years and mean office systolic/diastolic BP 123.4 ± 7.5/80.5 ± 5.5) were examined during the prospective one-year study in conditions of shift work in the Arctic (monthly roundabouts to Arctic region and back to home cities). All patients underwent Ambulatory BP Monitor-ing (ABPM) with consequent chronobiologic data analyses once every 3 months.

Results: Prospective one-year study of chronobiological parameters revealed a high prevalence of distinct atypical types of BP diurnal rhythms/variability disorders in normotensive persons under conditions of Far North. Moreover, BP variability/rhythm disorders have high prognostic value: being pre-registered, its distance variants associate with high risk of development of hypertension within one year. Also, atypical normotensive BP variants were characterized by more evident changes of heart and vessels. Moreover, chronobiological approach in comparison with conventional analysis of ABPM showed higher diagnostic sensitivity, specificity and efficiency.

Conclusions: Logistic regression revealed prognostic significance of normoten-sive atypical rhythm variability disorders compared to the conventional risk factors (smoking, low physical activity, body mass index, dyslipidemia, age, duration of North and camp experience, the mode and type of shift-work schedule). Multivariate analysis of the obtained model determined a diagnostic indicator that predicts the risk of developing hypertension during the year in normotensive people in conditions of scheduled shift-work to Far North.
Objective: Masked hypertension (MH), defined as elevated ambulatory blood pressure (BP) among patients with seemingly well controlled office blood pressure measurements (OBPM), has been associated with high cardiovascular risk. Previous studies have reported a MH prevalence between 10% to 30%, mostly among untreated hypertensive patients. The main objective of this study was to compare the prevalence of MH in borderline controlled hypertensive patients treated with short-acting antihypertensives in Canadian routine clinical care. Furthermore, differences between OBPM and home BP measurements (HBPM) taken 24-hours after last medication dose were assessed in treated hypertensive patients with borderline and almost controlled BP.

Design and method: Real-life, prospective Canadian study conducted in general practitioners’ offices. Enrolled patients had borderline SBP (130–139 mmHg) or DBP (80–89 mmHg) or almost controlled BP (140–149 and/or DBP 90–99 mmHg) and were treated with short-acting antihypertensives. Patients collected HBPMs for 7 consecutive days. MH was defined as HBPM SBP (95% confidence interval [CI], 0.82–1.87) in extreme dippers, 1.21 (0.87–1.69) in non-dippers, and the highest HR of 2.31 (1.47–3.62) was observed in risers. Using the standard fixed-clock interval, the daytime 2h-earliest shifted-fixedclock, the daytime 2h-late shifted-fixed-clock, or the nighttime 2h-early shifted-fixed-clock, the riser pattern was no longer significantly associated with the risk for cardiovascular death (HR compared with dippers, 1.29; 95% CI, 0.86–2.27).

Conclusions: Although use of diary records remains preferable, the standard and nighttime 2h-early shifted-fixed-clock intervals appear feasible for population-based studies.
rates are poor (30%–50%). Improving self-management may be a way to increase adherence to treatment. To evaluate the efficacy of a new strategy to control blood pressure by interactive mobile phone support in mild hypertension.

**Design and method:** Study subjects were 657 general individuals who participated in a specific health check-up. In 389 hypertensive subjects, 90 patients (Grade 1) who agreed with this study were randomly selected and distributed in three groups: A total of 83 patients completed the study, (1) control group (n = 29: C); (2) salt restriction group (n = 28: S); (3) exercise group (n = 26: E). All patients were measured by a mobile phone-based self-management support system (OMRON, HEM-7251G) for 3 months. 50 subjects among 90 mild hypertension were performed follow-up study one year later by usual BP measurement. We measured urinary Na/K at 6 times in this study-periods.

**Results:** After 3 months intervention, mean home blood pressure for 7 days significantly reduced in three groups (C: 143 ± 19/85 ± 11; 136 ± 19/82 ± 13 mmHg, S: 144 ± 21/85 ± 12; 139 ± 19/82 ± 12 mmHg, E: 141 ± 19/83 ± 12; 130 ± 17/77 ± 10 mmHg, p = 0.0001). There were no differences of home blood pressure-reduction between three groups. After one year, arterial blood pressure at health check-up significantly reduced only in S group (141 ± 12/82 ± 8 mmHg vs 133 ± 16/77 ± 10 mmHg, SBP, p = 0.002, DBP, p = 0.014), but no significant changes were observed in other 2 group. Urinary Na/K significantly decreased in S (4.0 to 2.7, p = 0.008), but there are no significant changes in E and C.

**Conclusions:** A home blood pressure monitoring by mobile phone-based self-management support system is effective in mild hypertension. Long term intervention revealed that salt restriction is effective in reducing blood pressure and urinary Na/K.
ORAL SESSION

ORAL SESSION E8: ENDOCRINE HYPERTENSION

OP.6B.01
TWENTY-FOUR HOUR BLOOD PRESSURE PROFILE AND LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSIVE PATIENTS WITH PRIMARY ALDOSTERONISM

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Objective: A higher prevalence of left ventricular hypertrophy (LVH) has been reported in patients with primary aldosteronism (PA) than in the blood pressure (BP) level similar patients with essential hypertensive (EH). However, the evidence is limited by lack of diurnal BP pattern. The aim of our study was to evaluate the relationship between 24-hour BP profile and LVH in subjects with PA compared to those with EH.

Design and method: We studied 385 consecutive patients with PA diagnosed in our hypertension unit from 2010 to 2014 and 385 patients with EH individually matched for age, gender, body mass index (BMI), blood pressure values and duration of hypertension. 24-hour ambulatory BP monitoring (ABPM) and echocardiographic left ventricular mass index (LVMI) were assessed.

Results: Two groups were similar in age, gender, BMI, clinic BP, 24-hour BP, daytime BP and duration of hypertension. However, night-time systolic BP (130 ± 16 vs 127 ± 17 mmHg, p < 0.05) and night-time diastolic BP (82 ± 10 vs 79 ± 11 mmHg, p < 0.01) were higher in PA compared with EH group. We found a significantly attenuated nocturnal systolic BP decline (5.6 ± 8.0% vs 8.3 ± 7.7%, p = 0.001) and nocturnal diastolic BP decline in the PA group (6.3 ± 7.9% vs 9.5 ± 8.1%, p = 0.001). Higher log-Nt-proBNP levels (1.74 ± 0.41 vs 1.50 ± 0.46, P < 0.001) and LVMI (113 ± 25 vs 102 ± 26 g/m², P < 0.001) were found in PA compared with EH patients. The prevalence of non-dippers (51.2% vs 40.8%, p < 0.05) and reverse dippers (19.7% vs 12.5%, p < 0.05) was significantly higher in PA group compared with the EH group. In stepwise multivariate regression analysis, LVMI correlated with night-time systolic BP (β = 0.517, p = 0.001), log-Nt-proBNP (β = 16.525, p < 0.001), male sex (β = 11.797, p < 0.001) and age (β = 0.161, p < 0.05).

Conclusions: In this study, patients with PA show higher night-time BP levels, but attenuated nocturnal BP decline than those with EH. Higher nocturnal SBP was more closely related to left ventricular hypertrophy in PA patients.

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Objective: To develop a prediction model to confirm or exclude primary aldosteronism (PA) in patients with an inconclusive salt loading test (SLT).

Design and method: Our retrospective cohort comprised patients who underwent an SLT between 2005 and 2016 in our university medical center. We included 290 patients. The SLT was inconclusive (post-infusion aldosterone levels 140–280 pmol/L) in 115 patients. In 45/115 PA was present according to an expert meeting. Together with 101 patients with a positive SLT result this resulted in a total of 146/276 (missing data in n = 14) patients with PA. We used binary logistic regression analysis to identify variables independently associated with PA.

Results: The decision model contained the following continuous variables increasing the likelihood of PA: low plasma renin concentration (PRC) before SLT, high plasma aldosterone concentration (PAC) after SLT, high potassium supplementation, and low plasma potassium concentration.1 In patients with an inconclusive SLT the model had a sensitivity of 84.4% and a specificity of 94.3%. The positive and negative predictive value were 90.5% and 90.4% respectively.

1Prediction score (p) formula: p = e^bx / (1+e^bx)
Where bx = 0.55–0.290*PRC before saline infusion (mU/l) + 0.05*PAC after saline infusion (pmol/l) + 0.07*potassium supplementation prior to SLT (mmol/day) - 2.75*plasma potassium concentration prior to SLT (mmol/l)

p > 0.59 indicates PA

Conclusions: Our model may be helpful in deciding how to manage PA patients with an inconclusive SLT. External validation and prospective studies are necessary before implementing this model in clinical practice.

Simultaneous measurement of aldosterone and renin concentrations in ten minutes could change the clinical assessment of hypertensive patients.

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Objective: The measurement of plasma aldosterone (PAC) and renin concentration (ARC) or activity (PRA) is useful for selecting antihypertensive agents as well as diagnosing primary aldosteronism (PA) in hypertensive patients. However, it takes several days to get results when measured by radioimmunoassay and development of more rapid assay has been long expected. In the present study, we characterized recently developed fully-automated chemiluminescent enzyme immunoassay (CLEIA) for PAC and ARC, which can be measured simultaneously in 10 minutes and 20 seconds, and clinical validation of their diagnostic abilities for detecting PA patients from hypertensive patients was also performed in this study.

Design and method: We performed clinical validation of diagnostic ability of this newly developed assay-based screening of 125 patients with primary aldosteronism (75 aldosteronoma (APA) and 50 bilateral hyperplasia (BHA)) from 97 patients with essential hypertension (EH). The newly developed assays of both PAC and ARC adopted antibody-immobilized magnetic particles, called MAGRAPID with abilities of quick aggregations and dispersions.

Results: Results of this novel measurements were significantly correlated with both radioimmunoassay measurements (PAC, ARC and PRA) and liquid chromatography-tandem mass spectrometry measurements (PAC). The analytical sensitivity of this particular novel ARC measurement was 0.1 pg/mL which was better than that of radioimmunoassay (2.0 pg/mL). The ARC values measured by CLEIA were below than 2.0 pg/mL in 28.8% of all patients (52.0%, 44.0% and 3.1% in those with unilateral APA, BHA and EH respectively). Using Bland-Altman plot analysis with the mass-spectrometry measurement, both bias and limits of agreement with 95% confidence interval of the automated PAC assay were smaller than those of the radioimmunoassay, indicating smaller systemic errors in the novel measurement. The ratio of PAC-over-ARC of 1.2 (ng/dL per pg/mL) provided 80.8% sensitivity and 94.9% specificity as a cut-off for differentiating primary aldosteronism from essential hypertension.

Conclusions: This novel measurement is expected to be clinically reliable alternatives for conventional radioimmunoassay and to provide better throughput and cost-effectiveness in diagnosis of hyperaldosteronism from larger number of hypertensive patients in clinical settings.
Panelists: M. Dorobantu1, R. Darabon2, D. Dimulescu3, C. Sinescu4, C. Arsenescu-georgescu5, D. Ligezan6, P. Giubesh-tatomez7, K. Babe8, I. Brinza9, M. Udrescu10, O. Tautu1. 1Carol Davila University of Medicine and Pharmacy, Clinical Emergency Hospital, Cardiology Department, Bucharest, Romania, 2Carol Davila University of Medicine and Pharmacy, University Emergency Hospital, Cardiology Department, Bucharest, Romania, 3Carol Davila University of Medicine and Pharmacy, Elias Emergency Hospital, Cardiology Department, Bucharest, Romania, 4Carol Davila University of Medicine and Pharmacy, Bagdasar Arseni emergency Hospital, Cardiology Department, Bucharest, Romania, 5Gte.T. Popa University of Medicine and Pharmacy, Institute of Cardiovascular Diseases, Cardiology Department, Iasi, Romania, 6Victor Babes University of Medicine and Pharmacy that will serve as Emergency Hospital, First Internal Medicine Department, Timisoara, Romania, 7Presences Nephrology Dialysis Center, Pitesti, Romania, 8Ondea University, Medicine and Pharmacy Faculty, Emergency Clinical County Hospital, Coronary Intensive Care Department, Orașești, Romania, 9CMi Dr. Mihaela Udrescu, Bucharest, Romania, 10CMI Dr. Ileana Brinza, Braila, Romania

Objective: To estimate the trend in HT prevalence, treatment, and control in Romania, that has a crucial importance for the development of prevention strategies at national level, urgently needed in a very high CV risk SE European country.

Design and method: A representative sample of 1970 Romanian adults (mean age 48.38 years, age range 18–80 years, 52.5% females, 70% response rate), were enrolled after signing written informed consent. The 2 study visits (Figure 1) took part in a special ‘medical caravan’ entitled SEPHAR BUS.

RESULTS

HT was defined as study SBP >/= 140 mmHg and/or study DBP >/= 90 mmHg at both study visits or previously diagnosed HT treated in the last two weeks, regardless of BP values. BP control was defined as SBP < 140 mmHg and DBP < 90 mmHg in hypertensive subjects.

Results: General HT prevalence is 45.1% (8.6% newly diagnosed HT, 53.8% awareness of HT), increasing with age (18–24 years – 15.4% vs. 25–34 years – 21.6% vs. 35–44 years – 34.6% vs. 45–54 years – 50.3% vs. 65–74 years – 62.6% vs. 65–74 years – 70% vs. >75years – 62.4%) regardless of the gender and area of residence. While majority (72.2%) of hypertensive subjects were treated (51.9% with >/= 2 drugs) only 30.8% of them had controlled BP values (general control rate 22.3%). Following the evolution from the last 10 years, it is expected that in 2020 the prevalence of HT will increase up to 44%, the awareness up to 96.2%, treatment of HT up to 91.2% and BP treatment control up to 36.6%.

Conclusions: Hypertension prevalence in Romania is increasing, although together with an increase in awareness, treatment and control. Possible explanations of this trend might be: unhealthy life-style and diet, increased salt-intake and increase in obesity and diabetes mellitus. SEPHAR III survey represent a necessary step in HT management in our country offering an estimation of a real trend in HT prevalence, treatment, and control, trend that will serve as base for future prevention strategies, which are urgently needed in a very high CV risk SE European country.

OP.6.C.01 NEW EPIDEMIOLOGIC NATIONAL REPRESENTATIVE SURVEY: SEPHAR III - MAIN RESULTS
Conclusions: 1. Problems with achieving the sexual satisfaction are frequent in hypertensive women. 2. Angiotensin II receptor antagonists are the type of anti-hypertensive drugs that do not worsen the sexual dysfunction. 3. In the group of hypertensive women, the physician should ask about the problems in achieving the sexual satisfaction and it should have an impact on the choice of the appropriate antihypertensive treatment.

Objective: Orthostatic hypotension (OH) and orthostatic hypertension (OHTN) both independently predict cardiovascular events. The aim of our study was to investigate the associations of orthostatic blood pressure (BP) changes with carotid atherosclerotic plaques in a random sample of Russian population.

Results: OH and OHTN were found in 159 (29,8%) and 45 (8,4%) study participants. Carotid atherosclerotic plaques were significantly more frequent in participants with OHTN compared to OH (24,4% vs 3,8%; P = 0,01). Participants with OH and carotid plaques were older than patients without plaques (55,8 ± 5 vs 44,3 ± 10; P = 0,009). In contrast, OHTN and presence of carotid atherosclerotic plaques were not associated with age. Plaques were associated with total cholesterol level (6,5 ± 1,6 mmol/l vs 5,4 ± 1,1 mmol/l; P < 0,001) only in participants without significant orthostatic BP changes (n = 239). Total cholesterol level was comparable in OH and OHTN with or without carotid plaques.

Conclusions: In general population of SPb inhabitants with the presence of carotid atherosclerotic plaques OHT was detected significantly more often compared to OH. OH in participants with carotid plaques was associated with age. No association was found between carotid atherosclerosis and total cholesterol level.

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France,

Conclusions: a) We found that adherence to a healthy diet could strongly contribute to the prevention of hypertension.

Results: The SPCCD includes data for 74751 hypertensive patients treated in Swedish primary care at any time during 2001–08. We assessed 19574 patients’ BP treatment from 2001–02 to 2007–08. Patients were grouped according to whether they maintained (12%), lost (9%), achieved (28%) or never achieved (51%) target BP (<140/90 mmHg).

Conclusions: BP control in individual hypertensive patients attending Swedish primary care has improved over 6–8 years, and more so amongst high risk patients. The number of drug classes and the use of diuretics, ACEI, ARB and MRA have increased. The difference in achievement of BP control between primary care centers, merits further study.
HIGH BLOOD PRESSURE AND FEMALE SEXUAL DYSFUNCTION: WHAT IS THE ASSOCIATION?

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Objective: To determine the prevalence of FSD in a hypertensive female population frequenting medical specialized offices (internal medicine, cardiology and general medicine) in a Spanish area and compare it to a group of women without hypertension of the same medical offices.

Design and method: A cross-sectional analytical study was conducted on a sample of active women frequent users of Cardiology, Internal Medicine and General Medicine Offices in a Spanish area. The validated questionnaire Female Sexual Function Index (FSFI) which assesses six aspects of female sexual function through an anonymous questionnaire administered to participants was used. Verbal informed consent to participating in the study was requested. Biographic and clinical data were collected, being established statistical significance at $p < 0.005$.

Results: 216 women, of whom 108 had hypertension and 108 with no history or clinical data of hypertension were studied. The prevalence of FSD in hypertensive women was 65.8% compared with 44.5% among women without hypertension. A statistically significant association between FSD and hypertension (95% CI 1.08 to 5.1; $p = 0.021$ OR = 2.35) was found. The average age in hypertensive women was 60.5 years. It was not observed a significant difference in age between the two groups. Significant differences in items of sexual desire, orgasm and lubrication were observed. The time evolution of hypertension was associated with statistically significantly with FSD ($p = 0.008$).

In the hypertensive group had a statistically significant correlation between the number of active anti-hypertensive and DSF. Beta-blockers were the drugs most associated with FSD in hypertensive women.

Conclusions: FSD prevalence was higher in women with hypertension, posing a risk of FSD 2.35 times higher when compared to women without hypertension. The time evolution of the Hypertension, the number of drugs used and the use of beta-blockers was significantly correlated with the FSD. Physicians should be alert, we must suspect and must act an early stage about a problem that affects a large number of sexually active hypertensive women that can go unnoticed for many reasons.
ORAL SESSION

ORAL SESSION 7A: RESISTANT HYPERTENSION

OP.7A.01 THE GLOBAL SYMPLECTY REGISTRY: SAFETY AND EFFICACY REPORT

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Objective: The aim of the Global SYMPLECTY Registry (GSR) is to collect real-world data on the safety and efficacy of renal denervation (RDN) using either the original Symplicity Flex (TM) renal denervation catheter or the newer-generation Symplicity Spyral (TM) catheter, which applies radiofrequency energy circumferentially to each renal artery quadrant simultaneously. Furthermore, following newer understanding of the renal anatomy, a sub-cohort of patients are receiving treatment of renal artery branch vessels in addition to the main renal artery.

Design and method: The GSR is a prospective, multi-centre, non-randomized international registry of RDN enrolling up to 3000 patients with uncontrolled hypertension. Patients are followed at 3, 6, 12, 24, and 36 months. Follow-up data collected per routine care includes: clinical assessment, office blood pressure measurement, 24-hour ambulatory blood pressure measurement, blood tests, ECGs, renal artery imaging, and EQ-5D quality of life questionnaire. At the time of ESH 2017 six month safety and efficacy data will be available for ~2500 patients and 3-year data will be available on ~1750 patients. Moreover, data from post-hoc analysis of ~270 patients treated with the Symplicity Spyral catheter as well as data on ~90 patients who had RDN treatment in both the main renal artery and branches will be available for presentation.

Results: The Global SYMPLECTY Registry is the largest real world database of renal denervation therapy and has enrolled over 2500 patients to date. The registry also includes the largest dataset of renal artery branch treatment reported so far. All available follow-up data informing on short and long-term safety and efficacy of the Symplicity renal denervation system will be presented.

Conclusions: These data supplement the randomized and sham-controlled SPYRAL HTN-ON MED and OFF MED trials evaluating safety and efficacy of renal denervation performed in the main renal artery and branch vessels in patients with uncontrolled hypertension.

OP.7A.02 SUSTAINED REDUCTION OF BLOOD PRESSURE WITH BARORECEPTOR ACTIVATION THERAPY: RESULTS OF SIX-YEAR OPEN-FOLLOW-UP

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Objective: The aim of the present study is to assess the long-term efficacy and safety of BAT.

Design and method: Long-term follow-up data on blood pressure and heart rate were analyzed from all patients who have been included in one of the three BAT trials that focused on treatment-resistant hypertensive patients. These trials were the US feasibility study, the DEBuHT trial and the pivotal trial. The first two were non-randomized, observational trials in the US and Europe respectively. In the pivotal trial patients were randomized to either immediate BAT or deferred BAT (six months after implantation). All patients who have received an implant were followed with regular visits.

Results: Altogether, 383 patients were available for analysis: 143 of these had completed five years of follow-up and 48 patients had completed six years of follow-up. In the entire cohort, systolic blood pressure fell from 179±24 mmHg to 144±28 mmHg (p < 0.0001) while diastolic pressure dropped from 103±16 mmHg to 85±18 mmHg (p < 0.0001). The data further demonstrate that the greatest fall in pressure already occurs within 6 months following device implant. The blood pressure lowering effect of BAT is greater than average in patients with signs of heart failure, and less than average in patients with isolated systolic hypertension. The percentage of patients in whom systolic blood pressure at the end of follow-up had fallen below 140 mmHg was greatest in those with unilateral right-sided stimulation. In about 25% of patients it was possible to reduce the number of medications from a median of 6 to a median of 3. Temporary side effects, related to either the surgical procedure or to cardiovascular instability, do occur, but they do not require specific measures and resolve over time.

Conclusions: After a follow-up of 5 years, BAT is safe and maintains its efficacy for persistent reduction of blood pressure in patients with resistant hypertension.

OP.7A.03 EFFECT OF A COLD PRESSURE TEST ON BLOOD PRESSURE AND BRAINSTEM BOLD MRI SIGNAL INTENSITY CHANGES IN HEALTHY VOLUNTEERS

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Objective: Many forms of arterial hypertension are initiated and maintained by an increased sympathetic tone. Background activity of a core network of neurons in the brainstem is supposed to be important for long-term blood pressure control. New imaging techniques such as blood oxygen level dependant magnetic resonance imaging (BOLD MRI) are capable of detecting changes in oxygenation within the brain using blood oxygen levels. Whether such changes can be detected in brainstem regions during a specific stimulation as not been studied thoroughly. The aim of this study was to determine if signal intensity changes in BOLD MRI in response to a cold pressor test (CPT) can be detected.

Design and method: BOLD MRI signal intensity changes during a cold pressor test and control test were measured using statistical parametric mapping (SPM) for whole brain analysis and spatially unbiased infra-tentorial template (SUIT) for specific volume of interest in the brainstem. A 7 tesla MRI was used. Blood pressure during CPT and control test was also measured. A paired t-test was used to compare control to CPT conditions.

Results: Eleven healthy volunteers (age 27.8 ± 20 (mean ± SD) were enrolled. 6/11 were women. Mean arterial pressure increased from 84 ± 11 mm Hg to 86 ± 12 mm Hg (p = 0.0074) during a 2-minute CPT. Whole brain analysis showed that 10/11 participant had a significant increase in BOLD MRI signal intensity changes during the CPT in the brain stem, 5/11 in the medulla et 4/11 in the rostral ventral lateral medulla (RVLML). Brainstem specific analysis confirmed an increase in signal intensity in 11/11 in the brainstem and the medulla, and 7/11 in the RVLM.

Conclusions: These data show that changes in BOLD MRI signal intensity of brainstem regions are detectable and increased during a cold stress in healthy volunteers. Consequently, brain BOLD MRI is an imaging technique that may provide new insights in the comprehension of neurogenic hypertension.

OP.7A.05 SLEEP DISTURBANCES AND RESISTANT HYPERTENSION IN A LARGE SAMPLE OF TREATED HYPERTENSIVE SUBJECTS – POL-FOKUS STUDY

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Objective: Baroreflex Activation Therapy (BAT) is a novel technique for treating patients with resistant hypertension. Although short-term studies have demonstrated that BAT lowers blood pressure, long-term results have not yet been reported. The aim of the present study is to assess the long-term efficacy and safety of BAT.

Design and method: The DEBuHT trial and the pivotal trial. The first two were non-randomized, observational trials in the US and Europe respectively. In the pivotal trial patients were randomized to either immediate BAT or deferred BAT. Six months after implantation. All patients who have received an implant were followed with regular visits.

Results: Altogether, 383 patients were available for analysis: 143 of these had completed five years of follow-up and 48 patients had completed six years of follow-up. In the entire cohort, systolic blood pressure fell from 179±24 mmHg to 144±28 mmHg (p < 0.0001) while diastolic pressure dropped from 103±16 mmHg to 85±18 mmHg (p < 0.0001). The data further demonstrate that the greatest fall in pressure already occurs within 6 months following device implant. The blood pressure lowering effect of BAT is greater than average in patients with signs of heart failure, and less than average in patients with isolated systolic hypertension. The percentage of patients in whom systolic blood pressure at the end of follow-up had fallen below 140 mmHg was greatest in those with unilateral right-sided stimulation. In about 25% of patients it was possible to reduce the number of medications from a median of 6 to a median of 3. Temporary side effects, related to either the surgical procedure or to cardiovascular instability, do occur, but they do not require specific measures and resolve over time.

Conclusions: After a follow-up of 5 years, BAT is safe and maintains its efficacy for persistent reduction of blood pressure in patients with resistant hypertension.
Objective: To evaluate the relationship between sleep disorders (obstructive sleep apnoea (OSA) and insomnia) or sleep habits (short sleep duration) and prevalence and characteristics of resistant hypertension (RHT).

Design and method: In a sub-study of the cross-sectional questionnaire-based observational Pol-Fokus study we included 3477 (mean age 62.6 ±/− 12.7 years; F 57.8%, M 42.2%) hypertensive patients attending a routine visit. To be included patients had to be ≥18 years old and had to be treated for at least 12 months with antihypertensive drugs. We defined hypertension control as office blood pressure (BP) levels both <140 mmHg/<90 mmHg. Patients were divided into 3 groups: controlled hypertension, uncontrolled hypertension (not fulfilling the criteria of RHT) and RHT (uncontrolled hypertension despite using 3 antihypertensive drugs including diuretic). High risk of OSA was assessed on the basis of STOP-Bang questionnaire results. Insomnia was evaluated by means of Athens Insomnia Scale (AIS) and the patients with AIS score of 8 or more points were labeled as insomniacs. Short sleep duration was defined as declared usual sleep time < 6 hours (for the past 6 months).

Results: In the studied group both uncontrolled hypertension and RHT were more frequent among patients with high risk of OSA (28.7% and 28.8% vs. 25.1% and 19.1%; p < 0.001) or short sleep time (27.4% and 30.2% vs. 26.2% and 21.1%; p < 0.001) than in patients without those conditions. Among patients with RHT, high risk of OSA (43.7% vs. 31.1%; p < 0.001), insomnia (41.2% vs. 32.7%; p < 0.001) and short sleep time (17.1% vs. 11.3%; p < 0.001) were more frequent than in patients without RHT. A multivariate model which included sleep disturbances showed that both high-risk OSA and insomnia were also related to the presence of RHT (OR = 1.38; 95% CI 1.10–1.72; p = 0.005; and OR 1.32; 95% CI 1.06–1.65; P = 0.014; respectively), which was not evident for short sleep time.

Conclusions: Our results showed that sleep disturbances – high risk of OSA, insomnia and short sleep time - are related to uncontrolled and resistant hypertension. Moreover high risk of OSA and insomnia independently predicted presence of resistant hypertension.
A POLYMORPHISM IN THE NORADRENALINE TRANSPORTER GENE IS ASSOCIATED WITH INCREASED BLOOD PRESSURE IN PATIENTS WITH RESISTANT HYPERTENSION

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Objective: Noradrenaline (NA) released from sympathetic nerves is rapidly inactivated through active transport back into nerve terminals via the action of the noradrenaline transporter (NET). NET impairment is evident in several clinically important conditions including hypertension. We aimed to determine whether a single nucleotide polymorphism (SNP), rs7194256, in the 3' untranslated region of the NET gene, which we previously identified, is associated with blood pressure and indices of noradrenaline kinetics.

Design and method: Ninety-two consecutive patients with resistant hypertension (RH) have been recruited for the study (59% males, age 61.9 ± 1.3 years, BMI 32.0 ± 0.6 kg/m², mean ± SEM). Twenty-four hour ambulatory blood pressure monitoring (ABPM) have been recruited for the study (59% males, age 61.9 ± 1.3 years, BMI 32.0 ± 0.6 kg/m², mean ± SEM). Twenty-four hour ambulatory blood pressure monitoring (ABPM) have been recruited for the study (59% males, age 61.9 ± 1.3 years, BMI 32.0 ± 0.6 kg/m², mean ± SEM). Twenty-four hour ambulatory blood pressure monitoring (ABPM) have been recruited for the study (59% males, age 61.9 ± 1.3 years, BMI 32.0 ± 0.6 kg/m², mean ± SEM).

Results: T allele of rs7194256 was present in 36% of this cohort. There were no differences in anthropometric measures between patients carrying a C or T alleles. However, patients carrying a T allele had a significantly higher systolic blood pressure (SBP): 24 hr mean SBP 148 ± 2.6 vs 140 ± 2.4; 24 hr max SBP 179 ± 2.6 vs 170 ± 2.6; Night min SBP 121 ± 3.0 vs 112 ± 2.6; Night mean SBP 141 ± 3.0 vs 131 ± 2.5; Night max SBP 170 ± 3.6 vs 159 ± 3.1 mmHg (p < 0.05 for all). T allele carriers had a significantly higher arterial NA concentration: 573 ± 53 vs 377 ± 35 pg/ml (p = 0.002). In addition, the ratio of the intraneuronal NA metabolite l-3,4-dihydroxyphenylglycol to NA was lower in T allele carriers (3.01 ± 0.4 vs 4.08 ± 0.3 pg/ml; p = 0.024), indicative of impaired NET function.

Conclusions: The mechanisms contributing to RH are only incompletely understood. Here we demonstrate that a SNP in the NET gene in patients with RH results in impaired NET function with the consequence of higher SBP mediated via the resulting increase in synaptic NA concentration. Impaired NET function appears as an independent compensatory response to cardiovascular disorders. Lowering in blood pressure and in peripheral vascular resistance as well as vasodilating effect of ucn2 are considered to be important and interesting. It has been shown that there might be a relationship between ucn2 and ACE activity in circulation and tissues, thus suggesting that ucn2’s vasorelaxation activity may be partially due to its effects on ACE activity and therefore Ang II levels. Changes of sACE activity, other RAAS components and hemodynamic status after administration of ucn2 to hypertensive rats support the hypothesis of relationship between ucn2 and ACE in the vasodilatation mechanism. So far there is no published data concerning ucn2 status in patients with hypertension receiving facemotheraphy influencing on RAAS components. In our study we assessed the ucn2 serum level in individuals with resistant hypertension (RHT) treated with acei or arb.

Design and method: 66 participants with resistant hypertension (treated at least 3 medications: acei/arb + ccb/diuretic) were enrolled to the study. In all patients 24 ambulatory blood pressure monitoring ABPM, echocardiography, pulse wave velocity (PWV) as well as serum biochemistry and a serum concentration of urocortin2 were performed.

RESULTS: All participants were divided into two groups: receiving ACEI (n = 53) and ARB (n = 14). The ucn2 level was significantly higher in ACEI group compared to ARB group.

There was no differences between groups in terms of clinical characteristics, serum biochemistry, other antihypertensive medications used. ACEI and ARB groups were also similar in value of 24 h ABPM, PWV, LVEF, but they differed in parameters of diastolic functions. The details are presented in the table.

PULS COR TIN2LEVELS IN PATIENTS WITH RESISTANT HYPERTENSION TREATED WITH ACEI OR ARB

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Objective: Urocortin 2 (Ucn2) has powerful hemodynamic, renal, and neurohormonal actions and likely participates in normal circulatory homeostasis and the compensatory response to cardiovascular disorders. Lowering in blood pressure and in peripheral vascular resistance as well as vasodilating effect of ucn2 are considered to be important and interesting. It has been shown that there might be a relationship between ucn2 and ACE activity in circulation and tissues, thus suggesting that ucn2’s vasorelaxation activity may be partially due to its effects on ACE activity and therefore Ang II levels. Changes of sACE activity, other RAAS components and hemodynamic status after administration of ucn2 to hypertensive rats support the hypothesis of relationship between ucn2 and ACE in the vasodilatation mechanism. So far there is no published data concerning ucn2 status in patients with hypertension receiving facemotheraphy influencing on RAAS components. In our study we assessed the ucn2 serum level in individuals with resistant hypertension (RHT) treated with acei or arb.

Design and method: 66 participants with resistant hypertension (treated at least 3 medications: acei/arb + ccb/diuretic) were enrolled to the study. In all patients 24 ambulatory blood pressure monitoring ABPM, echocardiography, pulse wave velocity (PWV) as well as serum biochemistry and a serum concentration of urocortin2 were performed.

Results: All participants were divided into two groups: receiving ACEI (n = 53) and ARB (n = 14). The ucn2 level was significantly higher in ACEI group compared to ARB group.

There was no differences between groups in terms of clinical characteristics, serum biochemistry, other antihypertensive medications used. ACEI and ARB groups were also similar in value of 24 h ABPM, PWV, LVEF, but they differed in parameters of diastolic functions. The details are presented in the table.

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THE BLOOD PRESSURE LOWERING EFFECT OF THE MOBIUSHD DEVICE IS INDEPENDENT OF PULSE PRESSURE

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Objective: The Framingham Heart Study showed an increased risk of cardiovascular disease with increasing pulse pressure (PP). Elevated PP is frequently observed with increasing age and may reflect the loss of elastic properties in large arteries. We investigated the effects of the MobiusHD-device on office systolic BP (SBP) and on 24-hour ambulatory BP (APMB) in patients with high PP.

Design and method: MobiusHD is designed to passively amplify pulsatile strain at the carotid sinus and reduce BP through increased baroreceptor activation, and consequently increase sympathoinhibition. A total of 40 patients were treated with MobiusHD for therapy-resistant hypertension and had BP measured at discharge, 1, 3, and 6 months. For analyses, patients were grouped according to baseline PP (high PP: > 70 mmHg; n = 25; low PP: < 70 mmHg; n = 15). Responsiveness at 6 months to MobiusHD treatment was defined as decrease in SBP of more than 10 mmHg, and also decrease in ABPM of more than 5mmHg. Linear mixed models were used to compare mean changes in BP over time between groups, chi-square tests were used to assess responsiveness.

Results: Mean ± SD age was 53 ± 12 years and 50% were female. Baseline mean SBP, PP, and APMB were 182 ± 17 mmHg, 74 ± 16 mmHg, and 165 ± 16 mmHg, respectively. Upon implantation of MobiusHD, SBP and PP were significantly reduced at 1.36 months by 21.29,25 mmHg (p < 0.001) and by 13.16,12 mmHg (p < 0.001) in the high PP group and by 24.16,25 mmHg (p < 0.001) and by 11.6,11 mmHg (p = 0.009) in the low PP group, respectively. ABPM was significantly reduced at 3.6 months by 15.19 mmHg (p < 0.001) in the high PP group and by 14.22 mmHg (p = 0.001) in the low PP group. There were no significant differences in overall reductions in SBP, PP, and APMB between the high and low groups (p = 0.64, p = 0.28, and p = 0.90 respectively). No significant differences in SBP responsiveness were observed between high and low baseline PP groups (68% vs 89%; p = 0.41), as well as ABPM responsiveness between high and low baseline PP groups (76% vs 73%, p = 0.85).

Conclusions: Different level of serum ucn2 in ACEI and ARB groups may suggest a significant role of ucn2 in the mechanisms of RAAS blockade. Higher ucn2 serum level may also reflect a compensatory mechanism triggered by an early signs of diastolic function impairment in patients with essential hypertension.
Conclusions: The MobiusHD-device effectively reduced SBP, PP, and ABPM in patients with therapy-resistant hypertension. The SBP and ABPM responses to MobiusHD were not different between patients with high or low PP.

CHROMOGRAININ A AS A PREDICTIVE MARKER OF SUCCESSFUL RENAL DENERVATION

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Objective: The reported variability in the BP response to renal denervation (RDN) has limited its clinical application. A selection of inappropriate patient cohorts (pathophysiology failure) and the inability to confirm that sufficient renal denervation has actually been achieved (technical failure) represent major obstacles. Here, we aimed to assess whether changes in the plasma concentration of chromogranin A (ChrA), a sympathetic nerve vesicular protein, could predict the blood pressure response to RDN.

Design and method: Thirty one consecutive patients with resistant hypertension (65% males, age 61.7 ± 1.7 years, mean ± SEM) who underwent RDN (Symplicity® catheter) were included in this study. We analysed plasma concentrations of ChrA by ELISA. Samples from renal vein and renal artery were taken prior to (T0) and immediately after (T1) RDN. Associations between ChrA concentrations and venous and arterial noradrenaline (NA) concentrations, as well as NA spillover were analysed. Automated office systolic (SBP) and diastolic blood pressure (DBP) measurements were obtained before (T0) and 3 months (M3) after RDN using the Omron HEM-907 monitor.

Results: Office BP decreased significantly at M3: SBP: 166.9 ± 3.95 vs 149.8 ± 5.43 mmHg (p = 0.0001), DBP: 89.9 ± 3.06 vs 84.5 ± 3.4 mmHg (p = 0.0045). Arterial ChrA at T0 was correlated with the change in SBP from baseline to M3 (T0-M3) (r = 0.45, p = 0.015). At T0, the arterio-venous ChrA gradient was correlated with SBP change (r = 0.43, p = 0.02). At T1, this gradient was correlated with SBP (r = 0.38, p = 0.04) and DBP change (r = 0.34, p = 0.066). The delta (T0-T1) arterial ChrA was inversely correlated with the DBP change at M3 (T0-M3) (r = −0.50, p = 0.006) but not with SBP. No correlation was found for NA and NA spillover with blood pressure change. These results suggest: 1) higher arterial ChrA concentrations at baseline predicted a more pronounced BP decrease in response to RDN, 2) an increase of ChrA after RDN, potentially explained by the release of the ChrA contained in sympathetic axons, predicted the DBP decrease. It means that an acute change of ChrA could help to confirm the success of the procedure.

Conclusions: ChrA might represent a predictor of BP response to RDN at M3. Further studies are needed to confirm these results.
ORAL SESSION

OP.7B.01 MASKED HYPERTENSIVES EXHIBIT AN EXAGGERATED BLOOD PRESSURE RESPONSE DURING HANDGRIP EXERCISE SIMILAR TO THAT IN HYPERTENSIVE INDIVIDUALS

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Objective: Masked hypertension has been associated with increased risk for target organ damage and cardiovascular disease. Recent evidence indicate that hypertensive individuals exhibit exaggerated blood pressure (BP) response during exercise and delayed recovery, linked to excessive sympathetic stimulation and an overactive exercise pressor reflex. Whether individuals with masked hypertension (masked-HYP) also exhibit exaggerated BP and systemic vascular resistance (SVR) responses as true hypertensives (true-HYP) during exercise has not been investigated. Therefore, the aim of this study was to evaluate the cardiovascular responses during handgrip exercise and recovery in masked-HYP, true-HYP, and normotensive (NORMO) individuals.

Design and method: Eighty-six individuals participated in the present study: healthy-NORMO (n=28), masked-HYP (n=27), and true-HYP (n=31). All hypertensive participants were newly diagnosed, untreated, with no other known cardiovascular disease. Following a complete history, physical examination, and blood testing, office and ambulatory BP were measured in order to determine their hypertensive status. All participants underwent an exercise protocol, consisting of a 3-min rest (baseline), a 3-min handgrip exercise at 30% maximal voluntary contraction (MVC), and a 3-min recovery. Beat-by-beat BP and heart rate (HR) were continuously assessed via photoplethysmography (Finapress) throughout the protocol and SVR was calculated.

Results: There were no differences among the three groups in age, smoking status, body mass index, fasting blood glucose, lipid profile, and MVC. Masked-HYP exhibited similar baseline BP to NORMO, however, during HG-exercise, masked-HYP exhibited a markedly greater (p < 0.05) systolic/diastolic BP response compared with NORMO (174.8 ± 13.9/95.8 ± 7.0 vs. 159.2 ± 15.7/91.3 ± 9.2 mmHg, respectively) and similar BP responses to true-HYP (181.4 ± 14.5/101.8 ± 9.5 mmHg). In addition, during exercise, masked-HYP exhibited a significant increase in SVR (p < 0.05), similar to that observed in true-HYP, whereas no significant increase in SVR was observed in NORMO. During the 3-min post-exercise period, BP in masked-HYP declined and returned to values comparable to those in NORMO (p = 0.32).

Conclusions: This is the first study to show that during isometric exercise, masked-HYP exhibit exaggerated BP and SVR responses, suggesting an overactive exercise pressor reflex in masked hypertension. The cardiovascular responses during exercise in masked-HYP are similar to those in true-HYP.

OP.7B.02 LONG TERM CHANGES IN LEFT VENTRICULAR MASS: ECHOCARDIOGRAPHIC FINDINGS FROM A GENERAL POPULATION (THE PAMELA STUDY)

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Objective: We sought to perform a comprehensive assessment of long-term changes in left ventricular (LV) mass, focusing on new onset, persistence, regression and severity of LV hypertrophy (LVH), as well as independent demographic and clinical variables related to this dynamic process in a population-based sample.

Design and method: A total of 1,113 participants with measurable echocardiographic parameters at baseline evaluation and at the end of a ten-year follow-up period were included in the present analysis. Cut-points for LVH were derived from current echocardiographic guidelines.

Results: LVH prevalence significantly increased from 13% to 33%, as a consequence of new onset LVH in 254 and regression in 31 cases, respectively. Severe LVH increased about 1.8 times as compared to baseline and this trend was mainly related to the transition from mild and moderate to severe LVH in subjects with pre-existing cardiac hypertrophy. A number of baseline variables such as age, female gender, office and out-of-office systolic BP, body mass index, APT 3 metabolic syndrome, and use of antihypertensive drugs were independently correlated either to new-onset and persistent LVH.

Conclusions: Long-term LV mass changes in the general population are associated to a marked worsening in cardiovascular risk profile related to increased prevalence and severity of LVH. As BP, metabolic variables and BMI emerged as key correlates of a such dynamic process, our findings suggest that early interventions aimed to modify such risk factors at the community level may have a role in preventing new onset and progression LVH.

OP.7B.03 THE EFFECTS OF LCZ696 ON LEFT VENTRICULAR REMODELING IN HYPERTENSIVE PATIENTS – RESULTS OF A DOUBLE BLIND, RANDOMIZED, MULTICENTER TRIAL

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Objective: Arterial hypertension and the resulting reduction in aortic distensibility impose increased hemodynamic load to the left ventricle and, if untreated may lead to left ventricular hypertrophy (LVH) and heart failure. We analyzed the effects of LCZ696 on LV-structure and function as well as on regional and global aortic distensibility.

Design and method: We conducted a prospective, randomized, double-blind, parallel-group, multicenter study in 114 patients with mild to moderate hypertension. Patients were randomized to LCZ696 200/400 mg o.d. or olmesartan (OLM) 20/40 mg o.d. At baseline, 12 and 52 weeks left ventricular mass (LVM) index as well as local and global aortic distensibility were evaluated by 3 T magnetic resonance imaging (MRI) and pulse wave analysis, respectively.

Results: Baseline characteristics, office BP (155.1 ± 9.0/92.2 ± 8.7 mmHg) and LVM index (72 ± 15 g/m2) were similar between treatment groups at baseline. After 52 weeks of treatment, decrease in office systolic BP was greater in the LCZ696 group than in the OLM group (−4.99 [95% CI −9.46 to −0.53] mmHg, p = 0.029). Compared to OLM, treatment with LCZ696 resulted in a greater decrease in LVM index at 12 weeks (−4.05 [95% CI −7.9 to −0.2] g/m2, p = 0.039) and at 52 weeks (−3.27 [95% CI −6.2 to −0.34] g/m2, p = 0.029). After adjustment for office SBP at follow-up, the change in LVM index at 12 weeks (p = 0.0356) and at 52 weeks (p = 0.0189) remained significantly greater in the LCZ696 group. Local aortic distensibility measured by MRI in the ascending, proximal and distal descending aorta did not show any significant difference between groups. LCZ696 was associated with a larger decrease of central pulse pressure compared to OLM (−3.50 [95% CI −6.15 to −0.85] mmHg, p = 0.01) at 52 weeks. Both treatments were safe and well tolerated.

Conclusions: In patients with hypertension, LCZ696 reduced LVM to significantly greater extent than OLM. Since reduction of LVM is associated with improved cardiovascular prognosis, the observed effect of LCZ696 on LVM is of clinical relevance.
OBJECTIVE: Techniques of 2D speckle tracking enable the measurement of myocardial deformation (strain) during systole. Recent clinical studies explored the prognostic role of left ventricular (LV) global longitudinal strain (GLS). However, there are few data on the association between cardiovascular outcome and GLS in the community. Therefore, we hypothesized that GLS contains additive prognostic information over and beyond traditional cardiovascular risk factors in a large population-based cohort.

Design and method: We measured GLS by 2D speckle tracking in the apical 4-chamber view in 791 participants (mean age 50.9 years). We calculated multivariable-adjusted hazard ratios for midwall, endocardial and epicardial GLS, while accounting for family cluster and cardiovascular risk factors. Median follow-up was 7.9 years (5th to 95th percentile, 3.7 to 9.6).

Results: In continuous analysis, with adjustments applied for covariates, midwall, endocardial and epicardial GLS were significant predictors of fatal and non-fatal cardiovascular (n = 96; P < 0.0001) and cardiac events (n = 68; P < 0.001). In the sex-specific low quartile of midwall GLS (<18.8% in women and <17.4% in men), the risk was significantly higher than the average population risk for cardiovascular (128%, P < 0.0001) and cardiac (94%, P = 0.0007) events. We also noticed that the risk for cardiovascular events increased with increasing number of LV abnormalities such as low GLS, diastolic dysfunction and hypertrophy (log-rank P < 0.0001).

Conclusions: Low GLS measured by 2D speckle tracking predicts future cardiovascular events independent of conventional risk factors. LV midwall strain represents a simple echocardiographic measure which might be used for assessing cardiovascular risk in a population-based cohort.
determined by Gubner–Ungerleider voltage, Lewis voltage, voltage of R wave in aVL lead. Lyon-Sokolow voltage, Cornell voltage and Cornell product, voltage RV6 and RV5 ratio, Romhilt-Estes score, Framingham criterion and Perugia criterion. Clinical and laboratory examinations, electrocardiography, echocardiography, exercise stress test, and 24-hours ambulatory blood pressure monitoring were carried out.

**Results:** Average left ventricular mass index (LVMi) was 170.3 ± 31.6 g/m², while the duration of hypertension was 12.1 ± 7.7 years. Adverse cardiovascular events occurred in 32 (38.5%) patients. At the beginning of the study, both groups, i.e. with and without adverse events, showed equal baseline characteristics, values of blood pressure and echocardiographic parameters. Positive Lyon-Sokolow score (17.6% vs. 47.3%, p < 0.05), Lewis voltage (9.8% vs. 21.9%, p < 0.05), Cornell voltage (15.7% vs. 37.5%, p < 0.05), and Cornell product (9.8% vs. 34.4%, p < 0.01) were more frequent in group with new cardiovascular events as compared to group without cardiovascular events. Multiple regression stepwise analyses separated Cornell product (standardized coefficient beta 0.303; p < 0.001) as compared to other criteria of hypertension after adjustments in terms of gender, age BMI and LVMi (model: R 0.303, R 0.092, adjusted R square 0.081, standardized error of estimate 0.46951). Odd ratio for this criterion was 4.819 (95% CI 1.486–15.627).

**Conclusions:** Patients with echocardiographic left ventricular hypertrophy who had positive Lewis voltage, Lyon-Sokolow voltage, Cornell voltage, and Cornell product showed worse fifteen-year outcome. The strongest predictor of cardiovascular events was positive result of Cornell product. Such patients should be recognized as early as possible, and treated more aggressively.

**OP.7B.08**

**QRS VOLTAGE CORRECTION TO BODY MASS INDEX IN PREDICTING ALL CAUSE MORTALITY AND CARDIOVASCULAR EVENTS. THE MOLI-SANI STUDY**

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**Objective:** Obesity reduces the accuracy and predictive value of voltage ECG criteria for left ventricular hypertrophy (LVH). Our aim was to investigate whether the correction to body mass index (BMI) might improve the prognostic significance for cardiovascular (CV) events of two different electrocardiographic (ECG) criteria for LVH in an adult Italian population at low risk CV risk.

**Design and method:** 18330 adults (mean age 54 ± 11 years, 55% women, 53% hypertensives) were analyzed from the Moli-sani cohort. Obesity was defined using the ATP III criteria. ECG-LVH was defined according to the Sokolow-Lyon (SL) and Cornell Voltage (CV) criteria.

**Results:** The age and sex adjusted prevalence of ECG-LVH did not differ from normal weight subjects to class 1–3 obesity subjects when the CV criterion was used. In overweight and obese patients, as compared with normal weight subjects, a progressively lower prevalence of ECG-LVH was observed when the SL index was used. During the follow-up, there were 503 new CV (216 coronary heart disease, 51 stroke and 307 heart failure; some individuals experienced more than one event). After adjusting for different confounders 1-SD increment in unadjusted and in BMI-corrected SL voltage was associated with an increased risk of CV events (HR 1.12, 95% CI 1.02 to 1.22 and HR 1.16, 95% CI 1.06 to 1.26, respectively); the same was true for unadjusted and for BMI-corrected CV (HR 1.12, 95% CI 1.03 to 1.23 and HR 1.17, 95% CI 1.07 to 1.27, respectively). The predictive significance of BMI-corrected SL and CV was assessed in obese subjects; after adjusting for confounders, the hazard ratio of CV events related to 1-SD increment of uncorrected CV was not significant and similar to the one conferred by the BMI corrected CV (HR 1.05, 95% CI 0.91–1.22 and HR 1.08, 95% CI 0.95–1.23, respectively). Uncorrected SL voltage showed a significant association with CV events, that was marginally stronger with BMI-corrected SL voltage (HR 1.18, 95% CI 1.02–1.37 and HR 1.17, 95% CI 1.04–1.33, respectively, Akaike information criterion change from 3220 to 3218).

**Conclusions:** Our results show that BMI correction of CV and SL ECG criteria in a low cardiovascular risk cohort.

**OP.7B.09**

**ETHNICITY AND ARTERIAL STIFFNESS IN AN URBAN MIDDLE-INCOME POPULATION**

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**Objective:** Aortic pulse wave velocity (PWV), influenced by traditional cardiovascular risk factors, is an important predictor of cardiovascular events. South-Asians and Africans have a high burden of cardiovascular risk factors. We explored the presence of ethnic differences in PWV and risk factors thereof in an urban middle-income population.

**Design and method:** Data from the cross-sectional HELISUR study in 1159 adult Surinamese was used. Ethnicity and tobacco smoking were self-reported. Pulse wave velocity was non-invasively estimated in duplicate by the Arteriograph device. Multivariable risk factors included: hypertension, systolic/diastolic blood pressure >140/90 mmHg or use of anti-hypertensive drugs; diabetes, fasting glucose >6.9 mmol/L or use of glucose-lowering drugs; and dyslipidaemia, total cholesterol >6.19 mmol/L, LDL > 4.0 mmol/L, HDL < 1.0 mmol/L, triglycerides >2.29 mmol/L or the use of lipid-lowering drugs. Analyses were stratified by ethnicity and age (< 50 vs 50 and older).

**Results:** We included 717 participants, 353 Asian-Surinamese and 364 African-Surinamese. Mean PWV was higher in Asian-Surinamese compared to African-Surinamese, mainly due to a higher PWV in Asian-Surinamese subjects >50 y: 10.4 (SD 2.3) vs 9.7 (SD 2.3) (p = 0.01, Figure 1a). Hypertension increased PWV in both ethnic groups, starting at a young age (Figure 1b). However, Asian-Surinamese without hypertension showed a dramatic increase in PWV of 2.7 m/s after 50 y, resulting in a similar PWV as African-Surinamese with hypertension. The main predictor of PWV in African-Surinamese was hypertension (1.66 [95%CI 1.21 to 2.11], adjusted for age >50, sex, smoking, BMI, diabetes, and dyslipidaemia), whereas in Asian-Surinamese this was an age >50 vs 6.20 [95%CI 1.54 to 2.46], adjusted for sex, smoking, BMI, hypertension, diabetes, and dyslipidaemia), followed by hypertension (1.36 [95%CI 0.91 to 1.81], adjusted for age >50, sex, smoking, BMI, diabetes, and dyslipidaemia). Diabetes and dyslipidaemia were not associated with PWV in these models.

**Conclusions:** Hypertension is the main predictor of PWV in African-Surinamese, and to a lesser extent in Asian-Surinamese. In Asian-Surinamese the age of 50, PWV increases dramatically, which might be linked to the higher coronary heart disease risk reported in Asians, but this needs further investigation.

**OP.7B.11**

**DETERMINANTS OF PULSE PRESSURE AMPLIFICATION IN DRUG NAÏVE HYPERTENSIVE PATIENTS**

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Objective: Normally there is an amplification of the pressure pulse wave from the large arteries to the smaller conduit arteries and this can be understood as a "gradual widening" of the pulse pressure as it travels distally. This is known as pulse pressure amplification and is defined as the peripheral pulse pressure/central pulse pressure ratio. Of course aging is correlated with PP A but few studies have been conducted to assess its correlations with peripheral arterial resistance. The aim of the present study was to find determinants of PPA in drug naïve hypertensive patients to get insights of this phenomenon.

Design and method: We recruited 87 drug naïve (mean age = 52.2 ± 12.5) 55 females, newly diagnosed hypertensive patients that visited the hypertension clinic of a tertiary hospital. Central systolic aortic BP (CSBP), Central diastolic BP (CDBP) was assessed by applanation tonometry and PWV was measured by Sphygmocor (Atcor Medical) and clinic SBP and DBP were measured according to international guidelines. Hemodynamics were assessed by impedance cardiography (ICG) by means of the Cardioscreen 2000 rheocardiographic system. The PPA ratio was defined as the peripheral pulse pressure/central pulse pressure. We used Pearson’s r correlation to identify significant correlations of PPA and measured parameters and used multivariate regression analysis to identify independent determinants of PPA.

Results: PPA was significantly correlated with age, bmi, gender, heart rate, urea, potassium, augmentation index, velocity index (VI), acceleration index (AI), left ventricular ejection time (LVET), systolic time ratio index (STRI), Ejection time index (ETI), left stroke work index (LSWI). In the regression model heart rate (/H9252= 0.41, p < 0.001) and augmentation index (/H9252= 0.71, p < 0.001) were the two significant determinants of PPA accounting for 77.4% of its variability.

Conclusions: PPA is determined by heart rate and thus sympathetic nervous system amplification, and also the augmentation index which is well known marker of arterial stiffness. Overall, these two markers eliminate all other hemodynamic markers as determinants of PPA.

OP.7B.12 ASSOCIATION BETWEEN HEART DYSFUNCTION AND NOCTURNAL BLOOD PRESSURE PROFILE IN A COHORT OF PATIENTS WITH ESSENTIAL HYPERTENSION

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Objective: As previously reported, the circadian rhythm of blood pressure (BP) in hypertensives is associated with the severity of organ damage, this being the maximum for the reverse dipper profile (accompanied by paradoxical nocturnal increase of BP levels), and gradually decreasing towards the categories characterized by a normal circadian rhythm. In light of the paucity of data concerning the assessment of the indices of heart function in hypertensive patients in relation to the different nocturnal BP profile, we designed a retrospective study ad hoc.

Design and method: We enrolled 389 patients with essential hypertension. Main exclusion criteria were the evidence of secondary hypertension or any concurrent condition able to influence heart structure and/or function. All patients were evaluated through laboratory tests, clinical data and medical history, echocardiographic recordings, ambulatory blood pressure monitoring (ABPM). The analysis of data was performed comparing the top quintile (38 patients with the greatest fall in blood pressure at night), the bottom quintile (comprising 38 patients with minor or no pressure drop at night) and the middle quintile, as a reference. Men and women were analyzed separately due to the different normal ranges of the echocardiographic parameters considered.

Results: We observed a less impaired cardiac function for the top quintile, also after correction for duration of hypertension, mean age, main comorbidities: MEN:

Left Ventricular Mass (g/m².7): 41.51 ± 7.94 (top); 44.48 ± 10.69 (ref); 51.24 ± 14.90 (bottom) (p: 0.001)
Left ventricular Relative Wall Thickness (RWT): 0.39 ± 0.07 (top); 0.41 ± 0.05 (ref); 0.48 ± 0.11 (bottom) (p: 0.05)
Left Atrium Volume (LA Vol) (ml): 56.32 ± 12.62 (top); 58.05 ± 18.22 (ref); 73.16 ± 24.97 (bottom) (p: 0.01)
Left ventricular Ejection Fraction (EF) (%): 61.8 ± 7.23 (top); 61.97 ± 6.78 (ref); 57.16 ± 9.65 (bottom) (p: 0.05)
Right Atrium Area (cm²): 14.87 ± 1.61 (top), 15.49 ± 1.66 (ref); 16.36 ± 2.74 (bottom) (p: 0.01)

Similar results for women (not enough space to display).

Conclusions: Extreme dipper hypertensives seem to have lower level of cardiac damage when compared to the other categories of dipping.
ORAL SESSION 7C: LARGE ARTERIES

**OP.7C.01 CENTRAL-TO-PERIPHERAL DIASTOLIC BLOOD PRESSURE ATTENUATION IN HEALTHY ADOLESCENT AND THE EFFECTS OF HEART RATE. THE MAGICSTE STUDY**

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Objective: Heart rate (HR) is directly associated to central-to-peripheral pulse wave amplification. We aimed at evaluating the associations between heart rate and each BP component in a cohort of healthy adolescents.

**Design and method:** 470 healthy adolescents (17 ± 4.5 years, 56% boys, brachial BP 123/67 ± 11/7 mmHg, HR 72 ± 12 bpm) were enrolled in the present study. Brachial BP was measured on 3 occasions by validated devices. Central BP was estimated by radial and brachial applanation tonometry, and calibrated to brachial MAP/DBP (SphygmoCor).

**Results:** Brachial and central BP were 123/67 ± 11/7 mmHg and 105/69 ± 9/8 mmHg. SBPamp was 1.17 ± 0.04, PPamp was 1.57 ± 0.13, while DBP amplification was 0.97 ± 0.01 (DBP attenuation). HR had a direct correlation with brachial and central DBP (r = 0.38 and r = 0.46, both p < 0.01) and central SBP (r = 0.09, p = 0.04), but not with peripheral SBP (r = 0.59), and a negative one with brachial and central PP (r = −0.24 and r = −0.37, both p < 0.01). HR had a positive association with PPamp (r = 0.38, p < 0.01), and a negative one with SBPamp (r = −0.14, p < 0.01) and DBPamp (r = −0.55, p < 0.01). The slope of BP change for each 10-bpm HR increase was steeper for central DBP (2.8 ± 0.3 mmHg), than for peripheral DBP (2.2 ± 0.3 mmHg, p for difference between regression coefficients <0.01), and for central and brachial DBP than for central SBP (0.7 ± 0.3 mmHg, both p < 0.01).

**Conclusions:** HR is associated with more pronounced changes in DBP than in SBP, and in central than peripheral DBP. Increasing HR may attenuate DBP from centre to periphery. The assumption that DBP is constant along the arterial tree may not be valid during dynamic conditions.

**OP.7C.02 PREDICTORS OF ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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Objective: Pulse wave velocity (PWV) is a classical marker of arterial stiffness that may be influenced by several anthropometric and hemodynamic factors. Several studies indicate elevated PWV in patients with rheumatoid arthritis (RA), yet few have attempted to identify predictors of impaired PWV in this distinct group of patients.

**Design and method:** Arterial stiffness was estimated among consecutive RA patients attending our Rheumatology Outpatient Unit with measurement of carotid-femoral PWV using applanation tonometry (SphygmoCor). Medical history, anthropometric characteristics and blood pressure (BP) were recorded. Impedance cardiology was applied to evaluate hemodynamic parameters, including systemic vascular resistance index (SVRI); stroke index (SI); cardiac index (CI), and thoracic fluid content index (TFCI). Inflammatory markers and lipid fractions were measured in blood samples. Disease activity and physical function were assessed using the Disease Activity Score in 28 joints (DAS28) and the Health Assessment Questionnaire Disability Index (HAQ-DI), respectively.

**Results:** Among 90 RA patients aged 61.6 ± 11.5 years (females: 77.8%), mean PWV was 8.4 ± 2.2 m/sec and significantly correlated with age (r = 0.636, p < 0.001); systolic (r = 0.637, p < 0.001) and diastolic (r = 0.343, p < 0.001) BP, and body mass index (r = 0.260, p = 0.014), but not with lipid fractions. PWV was higher among males compared to females (9.3 ± 2.1 vs 8.1 ± 2.1 m/sec respectively, p = 0.018), as was in diabetic compared to non-diabetic patients (10.4 ± 2.9 vs 8.3 ± 2.0 m/sec respectively, p = 0.051). Among other hemodynamic parameters, PWV correlated with SVRI (r = 0.402, p < 0.001), SI (r = −0.319, p = 0.002), and CI (r = −0.269, p = 0.010). Of the studied disease-related factors, a positive association was observed between PWV and erythrocyte sedimentation rate (r = 0.284, p = 0.007), C-reactive protein (r = 0.213, p = 0.048), DAS28 (r = 0.206, p = 0.057), as well as HAQ-DI (r = 0.290, p = 0.014). Linear regression analysis revealed that age (r = 0.004), systolic BP (p < 0.001), and HAQ-DI score (p = 0.001), independently predicted arterial stiffness, after adjustment for other variables.

**Conclusions:** Apart from increasing age and BP, physical disability appears to be a major determinant of increased arterial stiffness among patients suffering from RA, independently of traditional cardiovascular risk factors and RA characteristics. This association may be evident even in a clinical setting with relatively well controlled patients with rheumatoid arthritis.

**OP.7C.03 CHARACTERISTICS OF SUBJECTS AT LOWER END OF CAROTID-FEMORAL PULSE WAVE VELOCITY DISTRIBUTION, WHY ARE THEY HEALTHY?**

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Objective: Arterial stiffness normally increases with ageing, as measured by carotid-femoral pulse wave velocity (c-f PWV) and is a risk marker of increased cardiovascular risk and total mortality. However, in some subjects this process is not visible and they show normal or even “super-normal” values for c-f PWV in spite of reaching high age. We aimed to describe such individuals in a population-based cohort.

**Design and method:** Data were obtained from the Malmö Diet Cancer (MDC) cohort in Sweden, at re-examination in 2007–2012 when c-f PWV (Sphygmocor, ATCor) and other data was available from 3000 subjects (mean age 71 years, 60% men). Subjects at the lower end of the c-f PWV distribution (lower 2.5% and 5%) were identified and characterized.

**Results:** Among subjects from the lowest 2.5% the following variables were significantly lower than in the rest of subjects, following age- and BMI-adjustment with stratification for sex. Men with low c-f PWV had lower (p < 0.05) BMI (25.0 vs. 27.0 kg/m²), BP (119/70 vs. 137/76 mmHg), triglycerides (0.8 vs. 1.0 mmol/L) and prevalence of treated hypertension (29.6 vs. 69.7%), but reported more regular exercise (44.4 vs. 20.2%). For corresponding women with low c-f PWV, differences were found for BMI (25.1 vs. 26.6 kg/m²), BP (114/69 vs. 105/69 mmHg), SBP (0.7 vs. 3.0 mmHg, both p < 0.01). HR had a direct correlation with c-f PWV attenuation. HR is associated with more pronounced changes in DBP than in SBP, and in central than peripheral DBP. Increasing HR may attenuate DBP from centre to periphery. The assumption that DBP is constant along the arterial tree may not be valid during dynamic conditions.

**Conclusions:** We report that subjects with lower than expected c-f PWV for their age are less burdened by obesity and cardiometabolic risk factors. Such men tend to exercise more and this could indicate that a healthy lifestyle is important to protect from vascular ageing.

**OP.7C.04 ARTERIAL STIFFNESS IS INDEPENDENTLY CORRELATED WITH MYOCARDIAL MECHANOCENERGETIC EFFICIENCY IN A GENERAL POPULATION IN NORTHERN ITALY: THE VOBARNO STUDY**

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Objective: A non-invasive approach for the estimation of mechanical efficiency through the calculation of the ratio between stroke work and HR–pressure product Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved
has been recently proposed by de Simone et al. This index, which expresses the amount of blood pumped in a single beat in 1 second by the heart, may be easily obtained by echocardiography. The aim of our study was to evaluate the determinants of myocardial mechanoenergetic efficiency index (MEEi), calculated as stroke volume/heart rate and indexed to LV mass (MEEi = MEEi/LVM) in a large general population sample in Northern Italy.

**Design and method:** We evaluated 478 subjects participating in a general population study in Northern Italy (Studio Vobarno). All subjects underwent a physical examination with measurement of clinic blood pressure (BP). In all subjects laboratory examinations, 24 hours blood pressure measurement, echocardiography, and assessment of carotid-femoral pulse wave velocity (PWV) were performed.

**Results:** Subjects had a mean age of $58 \pm 10$ years, a BMI of $26 \pm 4$, 44% were males, 69% had arterial hypertension (55% treated). MEEi was lower in males and in patients with increased PWV. MEEi was inversely correlated with age, BMI, waist circumference, clinic and 24 hours BP, glucose, uric acid, triglycerides and directly correlated with HDL. MEEi was also inversely correlated with relative wall thickness (RWT) and PWV. At linear regression multivariate (7) analysis MEEi remained independently related to male gender ($p < 0.16$, $p < 0.001$), BMI ($p = -0.13$, $p = 0.005$), RWT ($p = -0.56$, $p = 0.001$) and PWV ($p = -0.10$, $p = 0.05$).

**Conclusions:** In a large sample of general population in Northern Italy myocardial mechanoenergetic efficiency was inversely correlated with arterial stiffness, independently of multiple possible confounders.

**OP.7C.05 ANGIOTENSIN AT2 RECEPTOR AGONIST, COMPOUND 21, PREVENTS ABDOMINAL AORTIC ANEURYSM PROGRESSION AND THE DECREASE OF AORTIC WALL DISTENSIBILITY IN THE RAT**

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**Design and method:** The effects of selective AT2 receptor agonist, compound 21, (C21) treatment on experimental abdominal aortic aneurysm (AAA) formation in rats.

**Results:** On day 14 post AA, infrarenal aortic diameter of AAA group was increased 1.55-fold compared to sham operated animals (2.65 mm $\pm 0.05$, $n = 8$ vs. $1.77 mm \pm 0.08$, $n = 6$; $p = 0.0001$). C21 significantly decreased aortic diameter by 20% on day 7 post AI and by 28% on day 14 compared to vehicle-treated animals ($1.9 mm \pm 0.06$, vs. $2.65 mm \pm 0.06$; $p = 0.0001$). Left ventricle parameters and blood pressure were not influenced by AI nor by additional treatment with C21. AI significantly reduced infrarenal blood velocity, distensibility and increased PPV. All these pathological effects were significantly ameliorated in C21 treated rats ($p = 0.0001$, $p = 0.0001$, $p = 0.0205$, 2-way ANOVA). Treatment with C21 also reduced the expression of inflammatory markers IL1 beta, NF kappa B, protease MMP9 and MLKL, the marker of necroptotic cell death in the aortic media. Moreover, C21 reduced the increase of TGF-beta1 in serum ($p = 0.0055$).

**Conclusions:** The angiotensin AT2 receptor agonist, C21, prevents abdominal aortic aneurysm progression in the rat without affecting blood pressure or left ventricle parameters. C21 also prevents the decline of infrarenal aortic blood velocity, decreases the rate of aortic wall distensibility at aneurysm site and the left ventricle parameters. C21 also prevents the decline of infrarenal aortic blood velocity (PPV) and distensibility was performed using the Vevo Vasc® software. Hemodynamic parameters were measured via tail cuff and intraaortic catheter. Aortic tissue expressions of MMP9, IL6, IL1beta, NFkappaB and MLKL as well as serum cytokines were analysed.

**OP.7C.06 THE PREVALENCE OF CENTRAL HYPERTENSION AND ITS ASSOCIATION WITH TARGET ORGAN DAMAGE IN COMMUNITY-DWELLING ELDERLY CHINESE: THE NORTHERN SHANGHAI STUDY**

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**Objective:** To investigate the prevalence of central hypertension and its association with target organ damage (TOD).

**Table 2. The difference of TOD among subtypes of brachial and central hypertension**

<table>
<thead>
<tr>
<th></th>
<th>BCCH</th>
<th>n=495(57.0%)</th>
<th>BMI</th>
<th>n=465(51.9%)</th>
<th>ICCH</th>
<th>n=324(24.2%)</th>
<th>BCCH</th>
<th>n=306(35.2%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVMI, g/m²</td>
<td>81.10</td>
<td>83.05</td>
<td>88.88</td>
<td>91.16</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E/Ea</td>
<td>8.79</td>
<td>8.77</td>
<td>9.74</td>
<td>10.18</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CI-PWV, m/s</td>
<td>8.07</td>
<td>9.72</td>
<td>9.87</td>
<td>9.80</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UACR</td>
<td>32.32</td>
<td>43.02</td>
<td>59.98</td>
<td>46.03</td>
<td>0.003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMT, mm</td>
<td>0.59</td>
<td>0.64</td>
<td>0.63</td>
<td>0.62</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR, nmol/l, T₃m²</td>
<td>95.08</td>
<td>92.33</td>
<td>95.45</td>
<td>94.02</td>
<td>0.57</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Design and method:** 869 community-dwelling participants without taking anti-hypertensive agents, derived from the Northern Shanghai Study cohort, were recruited for this analysis. Brachial and central BP were measured by mercury sphygmomanometer and Sphygmocor (AtCor Medical, Australia), respectively. Brachial and central hypertension were defined as brachial BP $\geq 140/90$ mmHg and central BP $\geq 130/90$ mmHg. Asymptomatic TOD including left ventricular mass index (LVMI), ratio of transmural early diastolic peak flow and early diastolic movement (E/Ea), carotid intima-media thickness (CIMT), carotid-femoral pulse wave velocity (CF-PWV), estimated glomerular filtration rate (eGFR) and urinary albumin/creatinine ratio (UACR), were all evaluated.

**Results:** The 869 participants (70.6 $\pm$ 5.7 years, men 43.8%) included 495(57.0%) participants with brachial and central consistent normotension, 445(51.5%) isolated brachial hypertension, 248(28.2%) isolated central hypertension and 306(35.2%) brachial and central combined hypertension. Compared to participants with brachial and central normal BP level, participants with isolated central hypertension presented faster CF-PWV (8.07 VS. 8.97, $p < 0.05$) and greater UACR (32.32 VS. 59.96, $p < 0.05$). Compared to participants with isolated brachial hypertension, participants with brachial and central combined hypertension presented higher E/Ea ratio (8.77 VS. 10.18, $p < 0.05$).

**Conclusions:** The central hypertension is prevalent and more than 90% of them are combined with brachial hypertension in this elderly Chinese cohort. Isolated central hypertension is associated with worse vascular and renal damage, which implies that those with normal brachial but elevated central BP perhaps should be considered for anti-hypertensive therapy.
Objective: Carotid-femoral pulse wave velocity (PWV) is the gold-standard method to estimate arterial stiffness, and has been clearly associated with cardiovascular risk in different clinical subsets. Still, its use in clinical practice is still limited in some specific groups, particularly in pediatrics, due to the absence of reference values for this population. This subanalysis of the PORT-VASPh Cohort aimed to propose preliminary reference values in Portuguese children and adolescents, based on a statistical definition that considers the fundamental physiological role of aging in arterial stiffness.

Design and method: The PORT-VASPh cohort has 402 children and adolescents enrolled so far, age ranging from 5 to 17 years. The overall health profile for each participant was defined based on three clinical evaluations, in which blood pressure (BP) was measured under standard conditions over the brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. For the proposal of reference values for PWV, data were collected from 295 healthy and normotensive participants included in the cohort, 59.3% males and 40.7% females, with a mean age of 11.84 ± 2.86 years (ranging from 5 to 17 years) and a body mass index (BMI) of 18.75 ± 3.07 kg/m². Carotid-femoral PWV was measured to all participants with the Complior SP device, complying with the methodological recommendations. All participants were evaluated by the same clinician.

Results: Gender-specific percentile tables, accounting for age, were obtained, as depicted in Figure 1. Mean PWV was 6.14 ± 0.99 m/s, and was higher in boys as compared with girls (6.29 ± 1.00 m/s versus 5.92 ± 0.93 m/s, respectively; p = 0.002). A significant correlation of PWV with age, BMI, systolic and diastolic BP and family history of hypertension was identified.

Figure 1. Gender-specific percentiles for carotid-femoral pulse wave velocity.

Conclusions: The availability of reference tables for PWV in children and adolescents is necessary, as it would allow the incorporation of the arterial stiffness concept into pediatric clinical decision, thus contributing for a better definition of the adequate preventive strategies for these particular populations.

OP.7C.08 AMBULATORY VERSUS OFFICE PULSE WAVE VELOCITY IN ADOLESCENTS AND YOUNG ADULTS: COMPARISON AND ASSOCIATION WITH TARGET ORGAN DAMAGE

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Objective: 24-hour ambulatory monitoring of pulse wave velocity (PWV) emerges as a promising tool for evaluating arterial stiffness in daily life conditions. This study investigated the relationship between office and ambulatory PWV, as well as with other indices of preclinical target-organ damage in young individuals.

Design and method: Apparently healthy adolescents and young adults referred for elevated blood pressure (BP) and healthy volunteers (age 12–25 years) were subjected to: (i) office PWV measurement (sitting, triplicate measurement, 1 visit) and subsequently (same day) to 24-hour ambulatory PWV monitoring using the same noninvasive brachial cuff-based oscillometric device (Mobil-O-Graph 24 h PWA), and (ii) determination of left ventricular mass index (LVMI) and carotid intima-media thickness (cIMT).

Results: Data from 81 subjects were analyzed (mean age 18.7 ± 4.5 years, 65 males, body mass index [BMI] 25 ± 5.5 kg/m², 16 with ambulatory brachial BP > 95th percentile for adolescents or > 130/80 mmHg for adults). Hypertensives compared to normotensives presented higher values of office PWV (5.6 ± 0.4 vs. 5.0 ± 0.4 m/s respectively) and 24-hour PWV (5.5 ± 0.4 vs. 4.9 ± 0.2 m/s) (all p < 0.05). Office PWV (5.1 ± 0.5 m/s) was comparable to 24-hour PWV (5.1 ± 0.4 m/s) (p = NS), but marginally lower than awake (5.2 ± 0.4 m/s) and higher than nighttime values (4.9 ± 0.4 m/s) (p < 0.05).

Significant agreement was observed between office and 24-hour PWV in detecting subjects at the top quartile of the respective distributions (agreement 89%, kappa 0.71). Office PWV was closely associated with office central systolic BP (r = 0.91, p < 0.01) and the same was valid between 24-hour PWV and 24-hour central systolic BP (r = 0.93, p < 0.01). Office PWV was closely correlated with all components of ambulatory (24-hour/awake/asleep) PWV (r = 0.81/0.80/0.67 respectively, all p < 0.01). 24-hour compared to office PWV tended to be more closely associated with age (r = 0.32 vs. 0.22 respectively) and BMI (0.36 vs. 0.24) and presented similar associations with LVMI (0.36 vs. 0.28), and cIMT (0.39 vs. 0.40) (p = NS for all the comparisons).

Conclusions: These preliminary results suggest that in young individuals office and 24-hour ambulatory PWV present similar values and associations with indices of preclinical organ damage. Further comparative data on the prognostic value of these methods are needed.

OP.7C.09 SYNERGISTIC EFFECT OF LOW K AND D VITAMIN STATUS ON ARTERIAL STIFFNESS IN A GENERAL POPULATION

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Objective: Both vitamins K and D are nutrients with pleiotropic functions in human tissues. The metabolic role of these vitamins overlaps considerably in calcium homeostasis. We analyzed their potential synergetic effect on arterial stiffness.

Design and method: In a cross-sectional study, we analyzed aortic pulse wave velocity (aPWV) in 1023 subjects from the Czech post-MONICA study. Desphospho-uncarboxylated matrix g-carboxyglutamate protein (dp-ucMGP), a biomarker of vitamin K status, was measured by sandwich ELISA, and 25-hydroxyvitamin D3 (25-OH-D3) by a commercial immunochemical assay. In a subsample of 431 subjects without chronic disease or pharmacotherapy, we detected rs2282570 polymorphism for the vitamin D receptor.

Results: After adjustment for confounders, aPWV was independently associated with both factors: dp-ucMGP [β coefficient(SEM) = 13.91(4.87); p = 0.004] and 25-OH-D3 [0.624(0.28); p = 0.027]. In a further analysis, we divided subjects according to dp-ucMGP and 25-OH-D3 quartiles, resulting in 16 subgroups. The highest aPWV had subjects in the top quartile of dp-ucMGP plus bottom quartile of 25-OH-D3 (i.e. those with insufficient status of both vitamin K and vitamin D), while the lowest aPWV had subjects in the bottom quartile of dp-ucMGP plus top quartile of 25-OH-D3 (9.8 (SD2.6) versus 6.6 (SD1.6) m/sec; p < 0.0001). When we compared these extreme groups of vitamin K and D status, the adjusted odds ratio for aPWV less than 9.4 m/sec was 6.83 (95%CI:1.95–20.9). The aPWV was also significantly higher among subjects bearing the GG genotype of rs2282570, but only in those with a concomitantly poor vitamin K status.

Conclusions: We confirmed substantial interaction of insufficient K and D vitamin status in terms of increased arterial stiffness.

OP.7C.10 IN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE DICHOTOMIZED AORTIC PULSE WAVE VELOCITY IS DISCRIMINATIVE IN WOMEN BUT NOT IN MEN IN SURVIVAL ANALYSIS

C. Mayer1, B. Hametner2, S. Parragh1,2, K. Whitelegg1, T. Weber3, S. Watertheurer1. 1AJT Austrian Institute of Technology, Health & Environment Department, Vienna, Austria, 2Vienna University of Technology, Department for Analysis and Scientific Computing, Vienna, Austria, 3Klinikum Wels-Grieskirchen, Cardiology Department, Wels, Austria

Objective: Evidence for differences in aortic pulse wave velocity (PWV) between females and males depending on age has been reported previously. Nevertheless, there is a lack of studies covering the gender-specific influences when
Objective: To investigate the relationship between ascending aortic dimensions and measures of cardiac and vascular organ damage in a population at high cardiovascular risk.

Design and method: In a longitudinal study, 79 patients who underwent coronary angiography were enrolled and followed-up before, 3, 6 and 24 months after KTx. Aortic stiffness was determined non-invasively by the assessment of carotid-femoral pulse wave velocity (cf-PWV) (Complior) while central mean blood pressure was obtained from an applanation tonometer (Sphygmocor). Aortic stiffness index ($\beta$) was calculated using the following formulae: $\beta = (\text{PWV}^2) \times (\text{AoPWV} - 2)$. Where PWV is the aortic pulse wave velocity, AoPWV is the corrected aortic pulse wave velocity, and $\beta$ is the stiffness index.

Results: There was an early reduction of $\beta$ 3 months after KTx from (29.0 ± 17.7 to 25.8 ± 10.6) (P = 0.014) outweighed by an increase at 6 and 24 months (27.8 ± 12.0 to 28.2 ± 11.2). There were no late changes of aortic PWV at 6 and 24 months (27.8 ± 12.0 to 28.2 ± 11.2). There were no late changes of aortic PWV at 6 and 24 months (27.8 ± 12.0 to 28.2 ± 11.2). There were no late changes of aortic PWV at 6 and 24 months (27.8 ± 12.0 to 28.2 ± 11.2).

Conclusions: The proximal ascending aorta are significantly related to BP values in normotensive subjects and in hypertensive patients. Aortic dimension are more strictly related to twenty-four hours BP values than to clinic BP values. In this sample of general population a significant correlation between aortic dimensions and measures of cardiac and vascular organ damage was also observed, confirming the parallelism between different forms of organ damage.
Conclusions: The early improvement of aortic stiffness index β0 after KTx suggests that KTx leads to an early improvement of the intrinsic mechanical properties of aorta. However, this improvement is followed by a later progression of β0, which is associated with increased pro-inflammatory cytokines, suggesting that activation of the immune system may be involved in arterial wall remodelling in kidney transplant recipients.
LB.03.01 AGED-DEPENDENT SYMPATHETIC NEURAL RESPONSES TO BETA-1 SELECTIVE BETA-BLOCKADE IN UNTREATED HYPERTENSION-RELATED TACHYCARDIA

D. Hering, W. Kucharska, K. Czecwoch, M. Chrostowska, K. Narkiewicz.
Department of Hypertension and Diabetology, Medical University of Gdańsk, Gdańsk, Poland

Objective: Elevated heart rate (HR) has been linked to cardiovascular morbidity and mortality in hypertension. The impact of beta-blockers on tachycardia-related prognosis in hypertension is controversial. The mechanisms underlying therapy with β-1 selective blocking agent without intrinsic sympathomimetic activity in hypertension are unknown. This study examined the age-related effects of betaxolol on HR, muscle sympathetic nerve activity (MSNA), blood pressure (BP) and hypertensive variability in untreated patients with hypertension and tachycardia.

Design and method: Ten young (age 26 ± 1 years, BMI 25 ± 1 kg/m²) and 7 older (age 50 ± 4 years, BMI 30 ± 2 kg/m²) males underwent measurement of HR, systolic and diastolic BP and MSNA (microneurography) before and after an 8-week treatment with betaxolol at an initial dose of 10 mg/day once daily, titrated to 20 mg/day at week 4.

Results: In younger subjects, betaxolol decreased systolic BP (−13 ± 3 mmHg, P = 0.01) and HR (−29 ± 4 bpm, P < 0.001) but not MSNA (3 ± 3 burst/min., P = 0.47) after 8 weeks. In contrast, in older subjects a pronounced reduction in BP (−27 ± 7, P = 0.007) was accompanied by a significant decrease in MSNA (−13 ± 5 burst/min., P < 0.05) and HR (−17 ± 4 bpm, P = 0.02). There was a comparable decrease in diastolic BP in young (−14 ± 3 mmHg, P < 0.001) and older (−14 ± 3 mmHg, P = 0.003) males. SDI/SD ratio of Poincare plot increased in younger (0.36 ± 0.03 vs 0.51 ± 0.05, P = 0.004), but not in older (0.43 ± 0.08 vs 0.54 ± 0.12, P = 0.50) patients.

Conclusions: The autonomic neural responses to betaxolol are age-dependent in hypertension-related tachycardia. Chronic therapy with betaxolol reduces sympathetic drive to the heart, but not to the vessels confirming the contribution of augmented cardiac sympathetic activity to disease pathophysiology in younger adults. In older hypertensives, the sympathovagal balance on the heart level is not influenced by betaxolol. The paradoxical reduction in sympathetic outflow to the peripheral vessels despite lowering of BP and HR may suggest age-related functional decrements in autonomic control (e.g. downregulation of cardiac β-1 adrenoceptors, baroreflex impairment) or specific properties of betaxolol, possibly associated with inhibition of the central nervous system.

LB.03.02 HOME BLOOD PRESSURE MEASUREMENT WITH HY-RESULT SYSTEM: PATIENTS VERSUS WEB USERS OPINION STUDY

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Objective: We administered a web-based questionnaire with 24 independent closed questions to patients using the Hy-Result system. The same questionnaire was openly available through the system. A total of 194 anonymous subjects completed the questionnaire: 87 patients from 2 ESH centers (Paris and Brussels) and 107 Web Users.

Results: Eighty percent of respondents were between 35 and 75-years-old in both groups but ESH Centre patients tended to be younger (p = 0.04). Eighty six percent of the ESH Centre group received antihypertensive drugs, 48 % of the subjects in the Web Users group (p = 0.001)

In the subgroup of 39 persons (36% of the total) who transmitted the Hy-Result report to their general practitioner, 92% reported that their doctor had considered the report useful (7% of their doctors did not look at the report and 1% advised against the use of the software). Almost all respondents (99% in the ESH Centers group and 97 % of the Web Users) trust the software. The high rate of confidence in the web users group was unexpected because we did not know if a medical doctor recommended the Hy-Result system or not. In the future, it will be necessary to study to what extent health professionals are ready to integrate this tool into their practice.

Conclusions: The Hy-Result system is well accepted by the majority of respondents to this survey, both ESH Patients and Web Users.

LB.03.03 SYMPATHETIC NERVE ACTIVITY IS INDEPENDENTLY LINKED TO GEOMETRIC AND ELASTIC PROPERTIES OF COMMON CAROTID ARTERY IN RESISTANT HYPERTENSION

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Objective: Patients with resistant hypertension (RH) are characterized by high levels of muscle sympathetic nerve activity (MSNA). However, the underlying pathophysiological mechanisms are not entirely understood. The relationship between direct measures of MSNA and common carotid artery (CCA) properties in RH has not yet been investigated. This study aimed to determine whether sympathetic nerve activity is independently linked to geometric and elastic properties of CCA.

Design and method: We measured MSNA (microneurography), heart rate (ECG), arterial pressure (Finapres system), CCA intima-media thickness (IMT), steady and pulsatile carotid circumeferential wall stress (CWS), and distensibility (ArtLab system) in 15 patients with true RH (age 55 ± 1 years, BMI 33 ± 1 kg/m², mean ± SEM) confirmed by ambulatory daytime systolic (S) and diastolic (D) blood pressure (BP) (161 ± 3/94 ± 4 mmHg).

Results: MSNA averaged 57 ± 2 bursts/min., mean CCA intima-media thickness 0.79 ± 0.04 mm, stroke change in diameter 699 ± 193 mm, carotid distensibility 21 ± 2 kPa × 10^−4, systolic (s) CWS 93 ± 5 kPa, diastolic (d) CWS 56 ± 3 kPa, mean (m) CWS 74 ± 4 kPa and pulsatile (p) CWS 36 ± 2 kPa. CCA IMT was inversely related to MSNA (r = −0.54, P < 0.05) and sCWS (r = −0.74, P < 0.001), dCWS (r = −0.88, P < 0.001), mCWS (r = −0.82, P < 0.001), but not pCWS (r = −0.37, P = 0.18). Baseline resting MSNA was significantly associated with sCWS (r = 0.52, P < 0.05), dCWS (r = 0.56, P < 0.05), mCWS (r = 0.52, P < 0.05), but neither to pCWS (r = 0.30, P = 0.28) nor distensibility (r = −0.09, P = 0.74). The relationship between MSNA and CCA IMT, and CWS remained significant after adjustment for age, BMI, SBP DBP and heart rate.

Conclusions: The relationship between augmented sympathetic activation and higher carotid wall stress in patients with RH suggests the desensitization of carotid arterial baroreflexes in response to cyclic increases in BP. The low intima-media-thickening in the presence of both elevated BP and sympathetic activation
indicates an inappropriate arterial remodeling in RH, leading to high CWS, thereby further potentiating cardiovascular risk in this patient cohort.

Objective: Familial hypercholesterolemia is a genetic hyperlipidemia characterized by elevated concentration of plasma LDL cholesterol. Statins are not effective in all patients whose prognosis is still quite poor. In the past, we have developed safe and effective gene therapy strategies for the expression of anti-atherogenic proteins using PE Gylated helper-dependent adenoviral (HD-Ad) vectors. We recently developed a HD-Ad vector for the expression of a secreted chimeric protein containing the extracellular portion of the human LDL receptor (LDLR) fused with a transferrin dimer. These project would represent a constitutive concept of the possibility of lowering LDL-C and reducing atherosclerosis using a secreted transgene and an alternative intracellular route.


Results: We evaluated the efficacy of vector in CHO/Lda7 cell line, in which we restored the cell ability to uptake of labeled LDL. We administered intravenously 1X10E13 vp/kg of the HD-Ad vector expressing TF-LDLR in LDLR-deficient mice demonstrating the efficacy of the vector in reducing total and LDL cholesterol levels. In addition, expression of TF-LDLR significantly reduced aortic atherosclerotic lesions in treated LDLR-deficient mice compared to controls. Moreover, we administered in VivoTag 750S-Labeled LDL to study biodistribution in LDLR-deficient mice treated with either HD-Ad TF-LDLR or control vector and we found a strong signal in the heart, liver and intestine after Fluorescence molecular tomography analysis.

Conclusions: We demonstrated:
1. In vitro expression and efficacy of the TF-LDLR fusion protein; 2. HD-Ad-mediated in vivo expression of TF-LDLR; 3. Improvement of lipid profile in LDLR-deficient mice treated with TF-LDLR.
4. Reduction of aortic atherosclerosis lesions size in LDLR-deficient mice treated with TF-LDLR.

Future steps of our project will involve a thorough safety evaluation of our approach and the possibility of administering the HD-Ad vector in its PE Gylated version using alternative routes.
Results: There was significant OBP reduction in both treatment (16.1 ± 27.3 mmHg; p < 0.05) and sham groups (27.9 ± 15.0 mmHg; p < 0.01). In the treatment group, heart rate (HR) was significantly reduced following RDN both at rest (4.3 ± 6.6 bpm, p < 0.05) and in response to postural changes. During phase IIi Valsalva, RDN resulted in substantial and significant reduction in MAP (21.8 ± 25.2 mmHg, p < 0.05) with no significant changes in the sham group.

Table: Within group changes in BP, and HR in treatment and sham limbs from baseline at 6 months following treatment. (* p < 0.05; ** p<0.01)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Office</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>-16.1 ± 27.3*</td>
<td>-27.9 ± 15.0*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>-8.5 ± 17.2</td>
<td>-15.4 ± 14.9*</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>-6.0 ± 11.3</td>
<td>-0.3 ± 9.8</td>
</tr>
<tr>
<td>Day SBP (mmHg)</td>
<td>-10.6 ± 17.2</td>
<td>-10.8 ± 12.0**</td>
</tr>
<tr>
<td>Day DBP (mmHg)</td>
<td>-8.1 ± 13.4</td>
<td>-5.6 ± 6.6</td>
</tr>
<tr>
<td>Night SBP (mmHg)</td>
<td>-4.3 ± 6.6</td>
<td>-0.5 ± 7.1</td>
</tr>
<tr>
<td>Night DBP (mmHg)</td>
<td>-5.1 ± 16.0</td>
<td>-11.9 ± 16.3*</td>
</tr>
<tr>
<td>Night HR (bpm)</td>
<td>-1.8 ± 12.1</td>
<td>-7.4 ± 11.0</td>
</tr>
<tr>
<td>Postural Tests</td>
<td>-1.9 ± 8.2</td>
<td>-0.8 ± 7.7</td>
</tr>
<tr>
<td>Rectified HR (bpm)</td>
<td>-9.1 ± 9.1</td>
<td>0.7 ± 9.4</td>
</tr>
<tr>
<td>Supine HR (bpm)</td>
<td>-8.8 ± 8.4</td>
<td>-0.2 ± 6.2</td>
</tr>
<tr>
<td>Sit-up MAP (mmHg)</td>
<td>-10.2 ± 13.7</td>
<td>-13.9 ± 21.4</td>
</tr>
<tr>
<td>Sit-up HR (bpm)</td>
<td>-16.5 ± 16.7</td>
<td>-0.4 ± 7.8</td>
</tr>
</tbody>
</table>

Conclusions: 1. BP reduction per se is not necessarily a marker of renal nerve ablation.
2. Reduction in splanchnic auto-transfusion following RDN has not been previously demonstrated and denotes attenuation of (renal) sympathetic efferent activity and could serve as a marker of procedural success.
3. Sham therapy results in clinically meaningful BP reduction that has implications for future trial design.

Objective: Poor access to care and shortage of physicians are major barriers to hypertension control in sub-Saharan Africa. Evidence-based strategies targeted at these barriers are lacking. This cluster-randomized trial evaluated the comparative effectiveness of a nurse-led task-shifting strategy for hypertension control (TASSH) versus provision of health insurance coverage (HIC) alone on systolic blood pressure (SBP) reduction, lifestyle behaviors, and BP control in Ghana.

Design and method: 32 community health centers (CHCs) were randomized to either HIC or TASSH+HIC. The HIC group received health insurance coverage plus scheduled nurse visits while TASSH+HIC group comprised the WHO cardiovascular risk management package including CV risk assessment; patient counseling on lifestyle modification, and initiation and titration of antihypertensive medications by trained nurses. Outcomes were measured as SBP reduction at 12 months (primary); change in lifestyle behaviors and BP control at 12 months; and maintenance of SBP reduction at 24 months (secondary).

Results: 757 patients (uncontrolled hypertension [mean BP 155.9 / 89.6 mmHg] without target organ damage; 60% women; and mean BMI 23) participated in the trial. In an intent-to-treat analysis with linear mixed effects regression model that adjusted for clustering, the TASSH+HIC group had a greater SBP reduction (−19.4 mmHg; 95% CI −17.2 to −21.6) versus the HIC group (−16.3 mmHg; 95% CI −13.5 to −19.1) with a statistically significant net difference of −3.6 mmHg [95% CI −6.0 to −0.5]. The SBP reduction was sustained for both groups at 24 months. Although the TASSH+HIC group had a higher BP control (55.2%) than the HIC group (49.9%), this difference was not significant (p = 0.292). Similarly, there was no difference in percent weight change and levels of physical activity at12 months between both groups.

Conclusions: A nurse-led task-shifting strategy for hypertension control plus provision of health insurance coverage was more effective than health insurance coverage alone in SBP reduction among patients with uncontrolled hypertension in Ghana. These findings support implementation of the WHO CVD package in low-resource settings and provide the evidence for policy makers to recommend task-shifting as a viable strategy for hypertension control in sub-Saharan Africa.

**LB.03.07 COMPARATIVE EFFECTIVENESS CLUSTER-RANDOMIZED TRIAL OF A NURSE-LED TASK-SHIFTING STRATEGY FOR HYPERTENSION CONTROL VERSUS PROVISION OF HEALTH INSURANCE COVERAGE IN CHCS IN GHANA**

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Objective: The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) randomized a subset of 6549 patients at risk with no history of coronary heart disease to either atenolol-based or amlodipine-based BP lowering treatment and followed-up for 5.5 years. Serum Cl- was measured at baseline in 319 participants who had a cardiovascular event and 1361 controls, matched for age and sex. The primary outcome was a composite of fatal and non-fatal myocardial infarction, stroke and heart failure. Subjects were grouped into four categories based on Serum Cl- levels (Cl- <95; 95.1–105; 105.1–115; >115.1 mmol/L). The characteristics of the study population across these groups were compared using 1-way ANOVA for continuous variables and X2 test for categorical variables. Kaplan-Meier (KM) and Cox Proportional Hazard models (Cox-PH), adjusted for age, sex, body mass index, systolic blood pressure, smoking, diabetes, cholesterol, serum Na+, use of diuretics and randomization group, were used to explore the multivariate adjusted association between baseline serum Cl- and cardiovascular outcomes.

**LB.03.08 SERUM CHLORIDE AND ADVERSE CARDIOVASCULAR EVENTS IN THE ANGLO-SCANDINAVIAN CARDIAC OUTCOMES TRIAL (ASCOT)**

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Objective: Data suggests that lower serum chloride (Cl-) is associated with higher mortality and cardiovascular risk in populations with hypertension or heart failure. In this study, we tested the association between serum Cl- and cardiovascular outcomes in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT).
Results: Participants with Cl- < 95 mmol/L had a greater proportion of females (24.1 vs 11.9%; p = 0.02) than those with Cl- > 115.1, were slightly older (67.8 [7.7] vs 65.3 [7.5] years; p = 0.01), had lower sodium (139 [5] vs 142 [3] mmol/L; p < 0.01), and were more likely to be taking a diuretic (66.3 vs 28.9%; p < 0.01). Serum Cl- < 95 mmol/L was associated with an increased risk of a cardiovascular event (HR 4.09 [95% CI 1.17-14.32; p = 0.03]) independent of serum Na+ (1.01 [0.97-1.5]; p = 0.80) or diuretic use (1.13 [0.89-1.42]; p = 0.31) compared to those with serum Cl- > 115.1 mmol/L (figure).

Conclusions: In the ASCOT study, serum chloride less than 95 mmol/L was associated with greater risk of cardiovascular events, independent of serum sodium or diuretic use.

**LB.03.09**

**PUTTING SPRINT IN CONTEXT – META-ANALYSIS OF PRIMARY PREVENTIVE TRIALS WITH BASELINE SYSTOLIC BLOOD PRESSURE < 140 MM HG**

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Objective: To assess the effect of blood pressure lowering on death and major cardiovascular events in primary preventive trials with baseline systolic blood pressure below 140 mm Hg. To assess if the SPRINT trial is compatible with other trials in this setting.

Design and method: We searched previous systematic reviews and PubMed to identify relevant trials. Trials were eligible if they compared antihypertensive treatment with placebo, or more intensive treatment against less intensive treatment, and if less than 50% of included patients had previous cardiovascular disease. We pooled relative risks in meta-analyses using fixed-effects model and analysed if the SPRINT results were different from results in other trials using Cochran’s Q.

Results: We found 14 trials, including 67,892 participants, eligible for inclusion. The mean baseline systolic blood pressure in the included trials was 138 mm Hg, and the mean follow-up blood pressure difference between treated and controls was 5.6 mm Hg. Treatment did not affect mortality (RR 0.99, 95% CI 0.94 to 1.04) or major cardiovascular events (RR 0.96, CI 0.92 to 1.01). Interaction analyses showed that the SPRINT results were significantly different compared to the results from other trials for both outcomes (p = 0.004 and p = 0.003 for mortality respectively major cardiovascular events). The pooled treatment effect did not change if SPRINT was excluded, however, because SPRINT contributed with a small portion of the overall number of events (RR 0.99 vs 1.01 for mortality and 0.96 vs 0.98 for major cardiovascular events, with or without SPRINT).

Conclusions: This meta-analysis finds that blood pressure lowering does not reduce the risk of death and cardiovascular disease in people with a systolic blood pressure < 140 mm Hg. The results of SPRINT should thus be interpreted very carefully.

**LB.03.10**

**METABOLOMICS PROFILING OF SERUM ELECTROLYTES SHOW A FATTY ACID ENRICHMENT FOR SERUM POTASSIUM LEVELS**

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Objective: Electrolytes have a crucial role in maintaining health and their serum levels are homeostatically maintained within a narrow range by multiple pathways usually involving the kidneys. Sodium is the major extracellular cation and changes in sodium levels affect blood pressure plasma and interstitial volumes. Potassium is the main intracellular cation and plays a key role in maintaining resting membrane potential. Changes in plasma potassium levels can disrupt cardiac conduction and cause sudden death. Proteins, phospholipids, cholesterol, and neutral fats account for 90% of the mass of solutes in plasma and it is unclear whether levels of these non-electrolytes have an impact on free serum electrolyte concentrations. We used metabolomic profiling to discover molecular markers and pathways associated with serum electrolytes levels that could be of therapeutic use.

Design and method: 1523 adults from TwinsUK not on BP lowering therapy and without renal impairment were included in the analysis of 592 fasting plasma metabolites (Metabolon Inc). We looked for metabolites associated with chloride, sodium, potassium and bicarbonate by running linear mixed models adjusting for age, BMI, gender, family relatedness and multiple comparisons using Benferroni correction. For each electrolyte, we further performed pathway enrichments analysis using the PAGE algorithm implemented in the R-package piano.

Results: Chloride, potassium, bicarbonate and sodium correlated with 10, 58, 36 and 17 metabolites respectively (each P < 2.1x10^-5). Among the top metabolites associated with serum potassium levels are fumarate (Beta(SE) = -0.07 [0.008], P = 7.24x10^-16), an intermediate in citric acid cycle, the long chain fatty acid myristoleic (14:1n5) (-0.06 [0.008], P = 1.97x10^-14), and the monohydoxy fatty acid 3-hydroxydecanoate (-0.04 [0.008], P = 1.24x10^-6), inversely associated with both serum potassium and with gut microbiome diversity (Shannon diversity: -0.08 [0.03], P = 0.01). Top association for chloride, sodium and bicarbonate include threonate, cystathionine and glutamine respectively. Enrichment analysis is presented in Figure 1. Potassium is significantly down-regulated by fatty acids including acylcarnitine, long and medium chain, monohydoxy, dicarboxylate and polyunsaturated, while its serum levels appear upregulated by lysolipids, phospholipids, sphingolipid and steroids.

Conclusions: We identified metabolic pathways that correlate with serum electrolytes levels and the role of these metabolic pathways on electrolyte homeostasis merits further studies.

**LB.03.11**

**DETRIMENTAL EFFECT ASSOCIATED WITH THE USE OF MORE THAN THREE DRUG CLASSES TO ACHIEVE BLOOD PRESSURE CONTROL IN SPRINT**

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Objective: In the SPRINT trial, achievement of target BP in the intensive arm required a higher number of drugs. Whilst intensive treatment of SBP was associated with an increased incidence of adverse events, it is unclear whether the use of multiple drug classes would result in adverse outcomes.

Design and method: The number of drug classes prescribed at randomisation and at 1.2,3,6,9,12 months were used to identify distinct trajectory groups in the standard and intensive arm using Latent Class Mixed Modelling. Data were available in 8,449 participants. Cox proportional hazard models, adjusted for age, sex, SBP (AUC 0–12 months), prevalent CVD, prevalent CKD and number of drug classes at randomisation, were used to assess the association between drug class trajectories and pre-specified outcomes from SPRINT.

Results: The SPRINT population classified into 6 groups (3 standard[Std], 3 intensive[Int]) based on the trajectories of drug classes prescribed over the first year are shown in Panel A with corresponding SBP by drug class groups in Panel B. Each group is described by the number of drug classes and [AUC-SBP+/−SD mmHg] in the first year: Std-1 = 1.5, [134.2 ± 7.7]; Std-2 = decrease-to-1.5, [131.2 ± 7.1]; Std-3 = 3.2, [137.8 ± 8.2]; Int-4 = 2.5, [122.7 ± 8.4]; Int-5 = 4, [125.1 ± 10]; Int-6 = increase-to-4, [131.6 ± 10.1]. Int-4(n = 3924) and Int-5(n = 530), achieved SBP < 125 mmHg at 12 months requiring 2.5 and 4 drug classes respectively whilst Std-1(n = 3466) and Std-3(n = 866) required 1.5 and 3.2 drug classes respectively to achieve SBP 135–140 mmHg. Std-2(n = 225) and Int-6(n = 131) showed marked changes in drug classes used over the first year.
Conclusions: Within SPRINT, treatment with >3 antihypertensive drug classes was associated with overall poor outcomes, specifically increased risk of death and heart failure, independent of blood pressure achieved in the first year, possibly related to the period of drug exposure. These results caution clinicians to assess need for multiple drugs and tighter blood pressure control on an individual patient basis.

Objective: Drug treatment for secondary prevention of cardiovascular disease is an established strategy recommended by guidelines. However, a wide gap exists between what the guidelines say and the real life in terms of number of drugs. The objective of the SATURNO study was to assess what is the gap in subjects after stroke or transitory ischemic attack (TIA) based on Electronic Health Records (EHR).

Design and method: Patients with a diagnosis of stroke or TIA before January 1st, 2012 were selected from the EHR of the Valencia Community which contains all drug prescriptions. In the present study, three groups of therapy usually recommended for secondary prevention or for control of main cardiovascular risk factors were selected: aspirin, SRA blockers (ACEi or ARB) and statins. Assessment of treatment was performed after 5.3±3.3 yr of the event.

Results: A total of 164315 patients (50% women, mean age 73 yr) were included, 130053 and 34259 with stroke and TIA, respectively. Among them, 41521 (25%) were not taking drug of the three groups, 25679 (16%) one, 45069 (27%) two and 51828 (32%) three. Concerning the kind of drugs, aspirin was present in 58%, followed by 57% SRA blockers and 48% statins. The percentage of number of drugs used and the specific groups in a previous diagnosis of stroke or TIA is in the figure.

Conclusions: The proportion of patients taking cardiovascular preventive drugs after a stroke of TIA is low in the general population, even aspirin. Several factors can contribute to it, but physician inertia and low patient compliance requires action in order to improve the secondary prevention.
Conclusions: In this 19-year follow-up general population study, HBP predicted cardiovascular outcome as reliably as OBP. WC, MH and ST were all associated with increased cardiovascular risk, yet after adjustment only WC retained significance.

OP.7D.03
CUFF-BASED AMBULATORY BLOOD PRESSURE MEASUREMENT CAUSES AROUSAL REACTIONS AND RAISES SYSTOLIC BLOOD PRESSURE AT NIGHT – COMPARISON WITH BEAT-TO-BEAT AND CUFF-LESS METHOD

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Objective: Cuff-based ABPM causes arousal reactions during sleep due to inflation of the cuff that come along with sympathetic activation and increases in SBP. This leads to an overestimate of the actual SBP during sleep. If the sympathetic tonus is already raised, like in apneic patients, an arousal leads to a decrease in SBP. This study aimed to assess the effect of cuff-based ABPM on sleep and SBP behaviour at night. We compared nocturnal SBP values using cuff-based ABPM versus a beat-to-beat and cuff-less ABPM based on pulse transit time (PTT).

Design and method: SBP was measured overnight in 40 adults (18 women, mean age 51 ± 16 years, BMI 28 ± 5 kg/m²) using an oscillometric ABPM (Mobil-O-Graph, IEM) with measurement intervals every 30 min. Simultaneously,
Results: In total we analysed 556 SBP cuff recordings. We found insignificant SBP rises of 0–4 mmHg in 50% of all cuff recordings, likely due to respiratory variations. Significant SBP increases of 5–8 mmHg were found in 27%, increases of 9–12 mmHg in 14% and increases >12 mmHg in 9% of all cuff inflations. A SBP decrease was observed in 2% of all recordings.

Conclusions: This study shows that cuff-based ABPM during sleep disturbs sleep architecture, causing arousals, and induces significant increases in SBP. We found considerable SBP increases >9 mmHg in 23% of all cuff recordings. Given that cuff-based ABPM is a cause of sleep disturbance, the continuous and non-reactive PTT method is of great clinical importance especially during night-time.

OP7D04 NOCTURNAL HYPERTENSION AND PROGRESSIVE RENAL FUNCTION LOSS IN RENAL TRANSPLANT PATIENTS

Objective: Hypertension is considered as a long-term, non-immunological risk factor for renal function loss in kidney transplant patients. However, there are no longitudinal studies focusing on the relationship between golden standard BP measurements (24 h ambulatory BP) and the GFR evolution over time in renal transplant patients.

Design and method: In a cohort of 260 renal transplant patients we investigated the relationship between the main components of the 24 h ABPM profile (day-time and night time average BP) with the evolution of the GFR over time (by the linear mixed model, LMM) and with the time to a combined end point (>30% GFR reduction, dialysis/transplantation and death) by Cox’s regression analysis. On average, 48 longitudinal eGFR measurements were available and 211 patients (81%) had more than 20 measurements over a follow up period ranging from 2 days to 12 years. The predictive values of non-nested models including an identical set of standard risk factors and each BP component were assessed by the -2 LL statistics.

Results: In the analysis by the LMM adjusting for a large series of potential confounders (baseline GFR, gender, age, BMI, diabetes, smoking, 24 h urinary protein, cholesterol, hemoglobin, albumin, phosphate and the immunosuppressive drug combinations) both day time and night time BP were significantly related to longitudinal eGFR measurements (P < 0.01) but the LMM-based on night time BP provided a better data fit (by ~2 LL statistics) than that based on day time BP. During the follow-up period, 123 patients experienced the combined end point, and the model based on night time BP provided the best data-fit for predicting the outcome.

Conclusions: Ambulatory BP measurements coherently predict the risk of GFR loss over time and the risk of developing a combined renal end-point. Night time BP is a stronger indicator of the risk of progression of renal disease than day time BP. These findings optimization of BP control may slow the rate of GFR loss in renal transplant patients and suggest that interventions targeting night time BP may afford renoprotection superior to that of day time BP. 

OP7D05 NEED FOR FOREARM BLOOD PRESSURE REFERENCE VALUES AT HEART LEVEL
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Objective: The increasing number of obese people presents a very serious clinical challenge to doctors being faced with the inaccurate measuring blood pressure (BP) in patients with very large arms. Studies comparing forearm and upper-arm cuff occlusion have given conflicting results. It is likely that higher BP readings are obtained with forearm measurement. Our clinic took part in the International Ambulatory Blood Pressure Registry: Telemonitoring of Hypertension and Cardiovascular Risk Project (ARTEMIS). In order to obtain normal values of forearm blood pressure at heart level in population we analyzed sample of patients with normal ambulatory blood pressure monitoring (ABPM) values.

Design and method: Two hundred and fifty-eight patients with normal ABPM values were studied from the ARTEMIS project. Mean body mass index was 24 +/− 7 kg/m2. Before positioning the Meditech ABPM 05 device patients had three upper-arm and three forearm BP taken by Meditech ABPM 05 device using extra measurement option. Arm was supported at heart level and appropriate cuff was used. Mean BP was calculated from three BP consecutive measurements. Student’s t-test was used to analyze the data.

Results: Systolic and diastolic upper-arm BP measurements were significantly lower than forearm BP measurements. The measurements obtained by ABPM were significantly lower than those found for forearm systolic and diastolic blood pressures. The mean age was 36.4 +/− 12.6 years. There were 152 females. Mean forearm, upper-arm and ABPM systolic BPs were 132.6 +/− 18.5 mmHg, 127.3 +/− 17.4 mmHg and 123.3 +/− 15.6 mmHg respectively. Mean forearm, upper-arm and ABPM diastolic BPs were 84.8 +/− 13.4 mmHg, 79.6 +/− 12.4 mmHg and 74.8 +/− 14.6 mmHg respectively.

Conclusions: This study showed that we need forearm blood pressure reference values at heart level because there is significant difference between forearm and upper-arm BP measurements. More often doctors are faced with the inaccurate measuring BP in patients with very large arms.

OP7D07 24-HOUR CENTRAL BLOOD PRESSURE IS BETTER ASSOCIATED WITH TARGET ORGAN DAMAGE OF HYPERTENSION THAN BRACHIAL BLOOD PRESSURE: THE VASOTENS REGISTRY
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Objective: The VASOTENS international, multicenter, observational, non-randomized, prospective study aims at evaluating the impact of 24-hour pulse wave analysis of ambulatory blood pressure (BP) recordings on target organ damage and cardiovascular prognosis of hypertensive patients. In the present analysis of study baseline data we checked which organ damage of hypertension i) is better associated with 24-hour central than peripheral BP and ii) is related to ambulatory arterial stiffness, estimated by pulse wave velocity (PWV) and augmentation index (AIx).

Design and method: In 334 hypertensive patients (mean age 53+/-15, 52% males, 45% treated) we obtained 24-hour ABPMs, echocardiograms, carotid
ultrasonograms and serum creatinine. Hypertensive organ damage was estimated by calculation of left ventricular mass index (LVMI, cardiac damage), intima-media thickness (IMT, vascular damage) and creatinine clearance (CC, renal damage). 24-hour hemodynamics and stiffness were estimated through the validated VASOTENS technology, based on transfer function analysis of brachial oscillograms. 24-hour brachial (bSBP) and aortic systolic BP (aSBP), standard deviation of bSBP, PWV and AIx were obtained. Relation of vascular indices with LVMI, IMT and CC was evaluated by bivariate and multivariate analysis (stepwise linear regression analysis).

**Results:** In the bivariate analysis a statistically significant relation was found for age, bSBP and aSBP vs. LVMI and IMT (see table, correlation coefficients or r). IMT was also significantly related to SBP variability and arterial stiffness, whereas increasing age, SBP variability and AIx were significantly associated with a decline of renal function.

In the multivariate analysis, including all variables entered in the bivariate model, adjusted by sex, statistically significant (p < 0.001) association was observed for aSBP and age with LVMI (standardized regression coefficient 0.25 and 0.18, respectively), and for age with IMT (0.56) and CC (−0.53).

<table>
<thead>
<tr>
<th>Correlation coefficients</th>
<th>LVMI (g/m²)</th>
<th>IMT (mm)</th>
<th>CC (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.25</td>
<td>0.56</td>
<td>−0.53</td>
</tr>
<tr>
<td>bSBP (mmHg)</td>
<td>0.23</td>
<td>0.24</td>
<td>−0.01</td>
</tr>
<tr>
<td>aSBP (mmHg)</td>
<td>0.28</td>
<td>0.26</td>
<td>−0.05</td>
</tr>
<tr>
<td>SD bSBP (mmHg)</td>
<td>0.01</td>
<td>0.24</td>
<td>−0.19</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>0.09</td>
<td>0.17</td>
<td>−0.14</td>
</tr>
<tr>
<td>AI (%)</td>
<td>0.07</td>
<td>0.22</td>
<td>−0.18</td>
</tr>
</tbody>
</table>

**Conclusions:** In hypertensive patients age appears to be the major determinant of organ damage, with central SBP, and marginally peripheral SBP, PWV and AIx, also playing a significant role. Our results suggest that estimation of 24-hour central hemodynamics and arterial stiffness in ambulatory conditions may help improve the individualized assessment of the BP-associated organ damage of hypertension.
ORAL SESSION

ORAL SESSION 8A: ENDOTHELium AND ATHEROSCLerOSIS

**OP.8A.01 NEWLY DIAGNOSED DIABETES MELLITUS IS ASSOCIATED WITH INCREASED LEVELS OF ERYTHROCYTE MICROPARTICLES**

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**Objective:** Patients with Diabetes Mellitus (DM) carry a high burden of cardiovascular damage and high risk of early thrombotic events. It is currently unknown how early this damage occurs and if it preexists in naive newly diagnosed DM patients.

**Design and method:** We sought to determine the thrombotic tendency of patients with known cardiovascular risk factors. To this end we used sophisticated, novel markers of atherosclerotic and thrombotic damage: platelet (PLTs) and erythrocyte (RBCs) microparticles.

Consecutive patients of the Micro- and Macro-vascular disease Clinic of Third Department of Internal Medicine at Papageorgiou General Hospital of Thessaloniki were included in the study. A thorough medical history was taken and a blood sample was drawn. A 24-hour urine collection was performed to assess the presence of microalbuminuria. Furthermore, PLTs and RBCs were determined using flow cytometry according to specific protocol. Cardiovascular risk factors were evaluated with emphasis on hypertension, newly diagnosed DM, dyslipidemia, smoking and body mass index.

**Results:** Our study sample consisted of 45 patients aged 52.5 ± 11.9 years, 19 men: 26 women, with mean systolic/diastolic blood pressure: 132.7 ± 16/83.3 ± 13.7 mmHg. Newly-diagnosed DM was found in 19 patients, while untreated hypertension in 16. Multiple linear regression analysis showed that DM makes the strongest contribution to high RBCs values (beta: 0.673, p = 0.021) after the effect of cardiovascular risk factors is controlled for. No significant predictor of PLTs could be identified.

**Conclusions:** In our study, RBCs strongly correlated with the presence of DM at the very early stages of the disease, despite the small sample size. Current knowledge suggests that RBCs consit a robust indicator of thrombotic tendency. The fact that PLTs did not correlate with the presence of DM in our study may, at least in part, reflect the multifactorial role of platelets not only in the thrombotic but also in the inflammatory process of atherosclerosis. Larger studies are needed to determine the value of PLTs and RBCs in patients with cardiovascular risk factors.

**OP.8A.02 SHORT TELOMERES, BUT NOT TELOMERE ATTENTION RATES, ARE ASSOCIATED WITH CAROTID ATHEROSCLEROSIS**

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**Objective:** Short leukocyte telomere length is associated with atherosclerotic cardiovascular disease. However, the causal relation between leukocyte telomere length and atherosclerotic cardiovascular disease is unclear. The objective of this work was to assess, in a longitudinal study, the relation between leukocyte telomere length and carotid atherosclerotic plaques.

**Design and method:** Telomere length was measured by Southern blots at baseline and at follow-up (9 years later) in 219 French men and women (aged 31–81 years at baseline). Carotid atherosclerotic plaques were quantified by echography.

Results: At baseline, shorter leukocyte telomere length was associated with development of carotid atherosclerotic plaques (p < 0.05), with the number of regions with plaques (p < 0.01) and with early onset (<55 years of age) of plaques (p < 0.05). Telomere attrition during the 9-year follow-up period was 25 ± 18 bp per year. No association was observed between telomere attrition rate and presence, number and age of onset of carotid atherosclerotic plaques.

**Conclusions:** Short telomeres observed in subjects with carotid artery plaques precede the development of atherosclerosis and is not a consequence of a higher telomeric attrition as compared to controls. Our study suggests that short leukocyte telomere length might be an independent risk factor for the development of carotid atherosclerosis.

**OP.8A.03 EFFECTS OF A NEW COMBINATION OF NUTRACEUTICS ON ENDOTHELIAL FUNCTION**

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**Objective:** Nutraceutics are medicinal foods that in certain components may exert a beneficial effect on cardiovascular system and represent a new opportunity for the maintenance of cardiovascular homeostasis. To date, despite its beneficial effects, the mechanisms involved are not completely clarified. Here, we aimed to characterize the action on vascular function of AkP05 (IzzeK®, Academia Pharm), a new nutraceutic that combine Bacopa monniera, Ginkgo biloba, Fosfatidilserine, extract of Green tea leaves and Catechins in a certain concentration and purification, patent based.

**Design and method:** We performed vascular reactivity studies on mice resistance vessels placed on pressure myograph evaluating the effects of increasing doses of AkP05 on phenylephrine-preconstricted vessels. In addition, to characterize the molecular mechanism we performed studies using Western Blot analyses.

**Results:** Our results demonstrated that AkP05 is able to induce a dose-dependent vasorelaxation (Fig. 1A), which is significantly bluntend by L-NAME (Fig. 1B), a nitric oxide synthase inhibitor. To be noted, the maximal vasorelaxation evoked by AkP05 is comparable to that evoked by acetylcholine (Fig. 1C), the known agonist largely used to evoke endothelial relaxation. In agreement, western blot analyses showed the ability of AkP05 to phosphorylate eNOS on Ser 1177 (Fig. 1D), an activation site of the enzyme, similarly to that evoked by acetylcholine.

**Conclusions:** Our data demonstrate that AkP05 modulates vascular tone enhancing endothelial relaxation through nitric oxide mechanism. These data suggest that AkP05 could be used as a dietary supplement to fight vascular diseases related to eNOS dysfunction.
DELETION OF THE MAS RECEPTOR AGGRAVATES THE DEVELOPMENT OF ABDOMINAL AORTIC ANEURYSMS BLOOD PRESSURE INDEPENDENTLY IN APOLIPOPROTEIN E-DEFICIENT MICE

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Objective: Hypertension and atherosclerosis are major risk factors for the development of abdominal aortic aneurysms (AAA), a degenerative vascular disease characterized by aortic dilation and rupture leading to sudden death. Currently, the only available treatments are open surgery and endovascular repair, and novel therapeutic targets are needed to prevent AAA. Angiotensin-(1-7) (Ang-(1-7)) has been shown to counteract vascular effects of angiotensin II and improve vascular function via Mas receptor activation. Ang II infusion into apoE-KO mice induces AAA formation. This study investigates the hypothesis that deletion of Mas receptor promotes the development of Ang II-induced AAA.

Design and method: ApoE-KO and apoE/Mas-KO mice were infused with Ang II (1000ng/kg/d) for four weeks. Incidence and extension of AAA were analyzed via ultrasound and magnetic resonance imaging (MRI). Furthermore, aortic injury was assessed by immunohistochemistry, protein- and RNA analysis

Results: Whole-body deficiency of Mas receptor significantly decreased survival proportions. Moreover, Mas receptor deficiency increased AAA incidence and external diameters of suprarenal aortas, from AngII-infused apoE-KO mice. These effects were blood pressure independent as blood pressure measured by radio-telemetry was similar between both groups. Beside an increased intima-media thickness and collagen content, apoE/Mas-KO mice showed increased macrophage infiltration into AAA compared to apoE(KO) mice. MRI studies revealed that AAA and macrophage infiltration begins during the first week of Ang II infusion. To investigate the role of the Mas receptor on macrophages in the development of AAA, we analyzed macrophage function. Here we could show that Mas receptor deficiency accelerated macrophage migration and capacity to polarize pro-inflammatory M1 macrophages in vitro. Furthermore, Mas receptor deficiency was Mas deficiency was associated with pro-inflammatory macrophage cytokine expression, like IL-6, IL-10, IL-12p40 and IL-12p70 of apoE-KO mice.

Conclusions: In summary, these results demonstrate an important role of the Mas receptor in the development of AAA in apoE-KO mice. Moreover, macrophage function mediated by the Mas receptor seem to regulate the extend of AAA in Ang II infused apoE-KO mice. Thus, activation of the Mas receptor might be a new target in the therapy or prevention of AAA.

PLETTER-DERIVED GROWTH FACTOR-BB ACTIVATES MITOGEN-ACTIVATED PROTEIN KINASES CONTRIBUTING TO NEointIMA FORMATION

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Objective: Mitogen-activated protein kinases (MAPks) in response to a variety of stimuli, including growth factors such as platelet-derived growth factor (PDGF) significantly regulate cardiovascular diseases. In this study, we sought to determine the effect of MAPks on adventitial fibroblasts contributing to neo-intima formation. Design and method: Balloon injury procedure was performed in male 12-week-old Sprague-Dawley rats, then the rats were divided into six group. Group A: Sham; Group B: Balloon injury; Group C: Balloon injury plus PD98059 (ERK1/2 inhibitor); Group D: Balloon injury plus SB203580 (p38 MAPK inhibitor); Group E: Balloon injury plus SP600125 (JNK inhibitor); Group F: Balloon injury plus XMD8-92 (ERK5). After balloon injury, MAPKs inhibitors was applied to the adventitia of injured arteries to suppress MAPks activation. Adventitial fibroblasts were stimulated by PDGF-BB. Wound scratch assay and transwell assay were used to analyze the migration of adventitial fibroblasts.

Results: Activation of MAPks was increased in injured arteries, especially in adventitia. Compared with balloon injury group, all MAPks inhibitor signifi cantly attenuated balloon-induced neo-intima formation through quantitative analysis of neo-intimal area, intima to media (I/M) ratio, and lumen area. The effect was associated with decrease of vascular cell proliferation and macrophage infiltration into adventitia. In primary culture of adventitial fibroblasts, PDGF-BB activated all MAPks, including p-ERK1/2, p-p38, p-JNK and p-ERK5, which were normalized by its inhibitor respectively. All the inhibitor suppressed PDGF-BB-induced adventitial fibroblasts migration. However, XMDS-92, but not PD98059, SB203580 and SP600125, attenuated PDGF-BB-induced proliferation of adventitial fibroblasts.

Conclusions: Blockade of MAPks activation attenuates injury-induced neo-intima formation, which might partly through PDGF-BB induced migration and proliferation of adventitial fibroblasts.

PULSATILE STRETCH ALTERS AMYLOID PRECURSOR PROTEIN EXPRESSION AND NITRIC OXIDE SIGNALLING IN HUMAN CEREBRAL ENDOTHELIAL CELLS PRE-EXPOSED TO GLYCOSPHINGOLIPID INHIBITION

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Objective: Amyloid β (Aβ) deposits that arise from amyloid precursor protein (APP) are a hallmark of Alzheimer’s disease (AD). Elevated pulsatility of arterial pressure and deregulation of ceramide and nitric oxide (NO) metabolism are associated with AD. Glycosphingolipid inhibitors that inhibit the production of the enzyme glucosylceramide synthase by blocking ceramide glycosylation are known to increase gamma secretase-mediated-Aβ release. This study investigates whether pulsatile stretch of human cerebral microvascular endothelial cells (hCMEC) pre-treated with the glycosphingolipid inhibitor, D-threo-1-Phenyl-2-decanoylamino-3-morpholino-1-propanol (D-PDMP), alters expression and/or phosphorylation of APP and endothelial NO synthase (eNOS).

Design and method: hCMECs were pre-treated with 20 μM D-PDMP for 2 hours prior to 15% cyclic stretch for 18 hours at 1 Hz (n = 7–8). Protein expression and phosphorylation (phospho-eNOS, Ser1177) were quantified using western blots. Results were analyzed using one way ANOVA (mean ± SEM, %).

Results: APP expression increased significantly in response to stretch in ECs pre-treated with D-PDMP (170.2 ± 27%, p < 0.01) compared to cells stretched without pre-treatment (114.5 ± 23%). eNOS phosphorylation was down-regulated in ECs subjected to stretch (9.9 ± 4%) compared to vehicle control (100.0 ± 0%, p < 0.001) and D-PDMP-treated-static control (107.0 ± 17%, p < 0.01). In ECs pre-treated with D-PDMP prior to stretch, phospho-eNOS levels decreased significantly (40.3 ± 15%) compared to vehicle control (100.0 ± 0%, p < 0.05) and D-PDMP-treated-static control (107.0 ± 17%, p < 0.01).

Conclusions: APP expression increased in cerebral ECs pre-treated with D-PDMP after being exposed to cyclic stretch. eNOS phosphorylation was down-regulated by cyclic stretch. D-PDMP pre-treatment appeared to have a restoring effect on phospho-eNOS, although it did not statistically significantly. Glycosphingolipid inhibition with D-PDMP and cyclic stretch may lead to ceramic accommodation thereby increasing the Aβ load. This can affect NO production and modulation of Aβ deposits.

EXTRACELLULAR HISTONES MODULATE NITRIC OXIDE AND PROSTANOIDS RELEASE IN HUMAN ENDOTHELIAL CELLS

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Objective: Extracellular histones are mediators of inflammation, tissue injury and organ dysfunction. Interactions between circulating histones and vascular endothelial cells are key events in histone-mediated pathologies. Our aim was to investigate the implication of extracellular histones in the production of the major vasoactive compounds released by human endothelial cells (HUVEC), prostanooids and nitric oxide (NO).

Design and method: HUVEC were exposed to increasing concentrations of histones (0,001 to 100 μg/mL) for 4 hours. In some experiments, colcemid (10 μg/mL) and tempol (100 μg/mL) were added to HUVEC 1 hour before histone treatments. NO and superoxide production was measured with DAF-FM and DHE probes. Prostacyclin (PGI2) and thromboxane A2 (TXA2) production were determined by ELISA. Protein quantification and mRNA expression were determined by immunoblotting and qRT-PCR, respectively. ANOVA and Tukey method was used to determine the difference between groups. Values are expressed as mean ± SEM.

Results: HUVEC exposed to increasing concentrations of histones induced PGI2 production in a dose-dependent manner (p < 0.05) up to 62 ± 8% (50 μg/mL) and 420 ± 97% (100 μg/mL). TXA2 release decreased only at 100 μg/mL.
(p < 0.001). Extracellular histones raised cyclooxygenase-2 (COX-2) up to 118 ± 19% at 50 μg/mL (p < 0.05) and 379 ± 66% at 100 μg/mL (p < 0.001) of histones. Histone-treated HUVEC increased PGIS mRNA levels up to 77 ± 5% at 50 μg/mL (p < 0.001) and up to 96 ± 6% at 100 μg/mL histones (p < 0.001). COX-1 mRNA levels decreased (24 ± 7% at 50 μg/mL and 29 ± 7% at 100 μg/mL, p < 0.05) and TXA2-synthase (TXAS) expression did not change. These results were supported by protein expression determination. Moreover, extracellular histones significantly decreased NO production only at 50 (22 ± 3%, p < 0.05) and 100 μg/mL (26 ± 2%, p < 0.01) of histones. eNOS mRNA levels shown a dose-dependent decrease at 50 (22 ± 3%, p < 0.05) and 100 μg/mL (38 ± 5%, p < 0.01) of histones, result supported by eNOS protein expression. The impaired NO production was related to COX-2 activity and superoxide production since was reversed after celecoxib and tempol treatments, respectively.

Conclusions: Extracellular histones stimulate the release of endothelial-dependent mediators through an up-regulation in COX-2-PGIS-PGI2 pathway which involves a COX-2-dependent superoxide production that decrease the activity of eNOS and the NO production.

**Objective:** monoclonal antibodies that inhibit proprotein convertase subtilisin-kexin type 9 (PCSK9), have emerged as a new class of drugs that effectively lower LDL cholesterol levels. Hypercholesterolemic patients present early signs of vascular inflammation and damage. We investigate whether after six months of treatment with anti-PCSK9 monoclonal antibodies we can find any improvement of pro-atherogenic profile and of arterial stiffness (AS) in patients affected by familial hypercholesterolemia already in treatment with the maximally tolerated statin therapy.

**Design and method:** We enrolled 34 people who had decided to start treatment with anti-PCSK9 drugs; of these, 32 have completed the 6-months observation period. At enrollment and 6 months later we evaluated anthropometrics, laboratory profile, pulse wave velocity (PWV) and carotid intima-media thickness (cIMT).

**Results:** After 6-months of treatment we found a significant decrease of inflammatory markers (Hs-CRP: −46.5%; Fibrinogen: −18.9%), LDL-C and lipoprotein(a) levels (respectively −65.9% and −34.2%), PWV (−9.5%) appeared to be improved; cIMT remained unchanged. PWV reduction appeared to be correlated with fibrinogen and LDL-C reduction. However, reduced PWV appeared to be not dependent on LDL-C and fibrinogen by the multiple regression analysis.

**Conclusions:** After 6 months of treatment with monoclonal antibodies anti-PCSK9 the levels of CRP, Fibrinogen, LDL-C, and Lp(a), as well AS indices, are significantly improved as compared to baseline. We report the important evidence that a treatment with anti-PCSK9 monoclonal antibodies may improve significantly the arterial stiffness in patients affected by familial hypercholesterolemia.
OP.8B.01  GENDER DIFFERENCES IN THE METABOLIC SYNDROME: HYPERTENSION IS THE FIRST APPARENT COMPONENT IN MEN, WHEREAS INCREASED WAIST CIRCUMFERENCE LEADS IN WOMEN

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Objective: The metabolic syndrome consists of several components in a cluster, but the order of their individual appearance has thus far received little attention. Central obesity is believed to be the driving force whereas other components follow as a reflection of obesity-dependent vascular and metabolic anomalies.

Aim: To determine the sequential rate of individual components of the metabolic syndrome in a health screening center.

Design and method: We analyzed 19,328 subjects, of whom 13,953 were presumed healthy with a BMI 19–46 kg/m² and no medical treatment. 6548 had none of the components of the metabolic syndrome (MS; MS = 0).

Results: Even at the lowest BMI zone of 19 Kg/m² (n = 325), 16% already had at least one component of the MS. Further, both the number of components and their numerical values rose linearly with BMI: at BMI = 29 kg/m², 75% had MS 1 or higher and the number of subjects with 1, 2, 3, 4 or 5 MS (MS1, MS2, MS3, MS4, MS5) components increased as a function of BMI from the leanest to the most obese subjects. There was a gender related dimorphic expression of the order of appearance of the MS components in clusters: in men, hypertension was the leading, most prevalent components when MS component number is low, being present in 32%, 48%, 62%, and 74% of men with MS1, MS2, MS3, MS4, respectively. In women, in contrast, central obesity shows the earliest and highest prevalence as it is present in 32%, 74%, 91% and 97% of women with MS1−4, respectively. Stated alternatively, central obesity is the driving force in females (p < 0.01), whereas hypertension precedes central obesity in men in MS component clustering (p < 0.05).

Conclusions: Hypertension appears most commonly as the first component of MS in men, whereas in women, waist circumference precedes other MS components. These results suggest that hypertension plays an earlier and perhaps more prominent role in MS in men, whereas in women central obesity is first, thus fitting the traditional concept of the pathogenesis of MS via excess centrally deposited fat.

Design and method: The Seven Countries Study encompassed 12,763 participants who were healthy at baseline and who underwent regular check ups every 5 years throughout over 4 decades.

Results: Using the IDF definition of the Metabolic Syndrome, 9.09% of participants were identified and the combination of risk factors (RF) is presented in Picture 1.
Results: All data were available in 786 participants (79% coffee drinkers and 21% abstainers). Coffee drinkers were also more frequently alcohol drinkers (p < 0.001) but not smokers (p = 0.93). During the 4-year follow-up hypertension was developed by 55% of participants. In the whole group coffee was a significant predictor of hypertension (odds ratio: 1.46, 95% CI: 1.02–2.07, p = 0.027) though the association was attenuated when alcohol was taken into account (p = 0.062). Candesartan prevented hypertension development in coffee abstainers (35% vs 63%, p = 0.03) and adjusted p = 0.05). Coffee intake in coffee drinkers (55% vs 58%, p = 0.43). Glomerular hyperfiltration was present in 23% of the subjects at baseline and in 18% at study end. Coffee intake was a significant predictor of age-and-sex-adjusted eGFR (p = 0.028) and of glomerular hyperfiltration (p = 0.038) at study end. Urinary albumin at study end was available in 561 subjects (40% had microalbuminuria). In a multiple logistic model also including baseline microalbuminuria (OR: 1.69, 1.08–2.64, p = 0.022), inclusion of treatment in the regression did not modify this association (p = 0.023).

Conclusions: In pre-hypertensive subjects, coffee intake was an independent predictor of future hypertension and microalbuminuria and attenuated the effect of the AT1R-antagonist on BP. Glomerular hyperfiltration is a possible mediator for the effect of coffee intake on urinary albumin.

Objective: Maternal obesity increases the risk of developing hypertension in the offspring. Circulating leptin is closely linked to the control of sympathetic nerve activity (SNA) and blood pressure (BP) in the central nerve system. The ventromedial hypothalamus (VMH) is a key center of energy homeostasis, hemodynamic and sympathetic tone to renal vasculature. Exposure to overnutrition during early development changes the activity of the neurons and the receptors in the CNS, amplifying sympathetic output which leads to hypertension. We assessed the effects of maternal high fat diet (HFD) feeding during pregnancy on cardiovascular variables and sympathetic nerve activity (SNA) with changes in leptin and insulin signaling pathways in adulthood.

Design and method: Breeder rabbits were fed a HFD (13%; HFD) or a control diet (4%; CD) during pregnancy and lactation. Offspring received CD after weaning. All rabbits had a VMH cannula and a renal nerve recording electrode. Mean arterial pressure (MAP), heart rate (HR) and renal sympathetic nerve activity (RSNA) were measured at baseline and after receiving increasing doses of aMSH (a-Melanocortin stimulating hormone, 0.3, 1nmol), SHU9119 (melanocortin receptor antagonist, 0.02, 0.04nmol), leptin receptor antagonist (5, 10 ng) or insulin receptor antagonist (0.01, 0.05U). Hypothalamic expression of leptin receptor (Lepr) and Phosphoinositide 3-kinase(PI3K) was examined using real-time PCR.

Results: Offspring from HFD fed rabbits (mHFD) showed higher MAP (+11%) and RSNA (+42%) than controls in adulthood (P < 0.05). aMSH into the VMH increased MAP, HR and RSNA (+6.6 ± 3.4 mmHg, P < 0.05) and SHU9119 reduced MAP and RSNA (~5.6 ± 0.8 mmHg, P < 0.05). Leptin receptor antagonist normalized hypertension (5.8 ± 0.8 mmHg) in mHFD rabbits (P < 0.05). Insulin receptor antagonist administration into the VMH showed no changes in MAP HR and RSNA in both mHFD and mCD rabbits. Offspring from maternal HFD rabbits exhibited an increase in Lepr and PI3K expression in the hypothalamus compared to the control group (+47% and +74%).

Conclusions: Exposure to over-nutrition during early development leads to permanently altered leptin and MC signaling pathways, due to programming of the key receptors and/or by neuronal plasticity, leading to sympathoexcitation and hypertension in adulthood.

Objective: In middle-aged and elderly populations, circulating natriuretic peptide concentrations are negatively associated with several components of the metabolic syndrome. Whether these negative associations are also present in adolescents and young adults is unknown. The objective of this study was to examine associations of a pro-atrial natriuretic peptide with components of the metabolic syndrome in healthy adolescents and young adults from the general population.

Design and method: The present study is a cross-sectional population-based study. We measured plasma concentrations of mid-regional pro-atrial natriuretic peptide (MR-proANP) in 343 adolescents (age 14–16 years) and 616 young adults (age 20–28 years) from the Danish site of the European Youth Heart Study, which is a population-based study of cardiovascular disease risk factors in children, adolescents and young adults. We used linear regression analysis to examine the associations, expressed as standardized regression coefficients (b), of various variables of interest with MR-proANP stratified according to age group, adjusting for age and gender.

Results: Among the young adults, MR-proANP was negatively associated with body mass index (BMI) (b = −0.10, P = 0.02), waist circumference (WC) (b = −0.14, P < 0.001), systolic blood pressure (BP) (b = −0.08, P = 0.05), diastolic BP (b = −0.23, P < 0.001), insulin (b = −0.15, P < 0.001), and triglycerides (b = −0.14, P < 0.001). Among the adolescents a somewhat different pattern was observed since MR-proANP was not significantly associated with BMI (b = −0.00, P = 0.98), WC (b = −0.01, P = 0.90) and insulin (b = −0.02, P = 0.69). Nevertheless, among the adolescents, MR-proANP was negatively associated with triglycerides (b = −0.13, P = 0.01), diastolic BP (b = −0.12, P = 0.01) and systolic BP (b = −0.10, P = 0.10), although the latter association was of borderline significance.

Conclusions: The young adults displayed significant negative associations between MR-proANP and several components of the metabolic syndrome, whereas such associations were not found among the adolescents besides triglycerides and diastolic BP. Our results support the view that there is a cross-talk between the endocrine heart and metabolic organs, which could become more apparent with increasing age. Our results also support the view that lowering circulating concentrations of natriuretic peptides could play a role in the early stages of hypertension development, because plasma MR-proANP was negatively associated with both systolic and diastolic BP in our community-based study.
Objective: Magnesium is essential for the proper functioning of the human body. It activates a number of enzymes and participates in the metabolism of carbohydrates, proteins, and fats. It also plays an important part in regulating blood pressure.

The aim of the study was to assess the dietary intake of magnesium and the frequency of consumption of magnesium-rich foods by patients suffering from hypertension.

Design and method: The study involved 63 participants (28/35 M/K, mean age = 61.0 +/- 5.7 years) diagnosed with essential hypertension, regular patients of the Hypertension Outpatient Clinic at the University Hospital in Cracow. They completed a survey which consisted of a magnesium rich foods questionnaire and 24-hour interview spanning three days. The survey also included a nutrition knowledge test on magnesium, where the patients were additionally asked whether they were using dietary supplements containing this chemical element.

Results: The vast majority of patients (83%) did not meet the established standards for daily magnesium intake. Whole grain bread and calcium-magnesium mineral water turned out to be the most often consumed magnesium-rich products. Patients less frequently consumed sunflower seeds (of these, they most often chose buckwheat and barley groats), legumes (usually beans) and dried fruit and nuts (usually walnuts). The nutrition test showed the patients’ knowledge on magnesium to be unsatisfactory. Additionally, the survey showed that more than half of hypertensive patients used dietary supplements containing magnesium. Women were found to reach for diet supplements more often than men.

Conclusions: Considering the role of magnesium in regulating blood pressure, it seems important to educate hypertensive patients with regard to a diet containing sufficient amounts of this nutrient.

Objective: Although high sodium intake in hypertensive patients has been shown, in most studies, blood pressure (BP) was measured by conventional method, not by ambulatory BP monitoring. Advantage of ambulatory BP monitoring is diagnosis of masked or white-coat hypertension. It is unclear whether the association between high sodium intake and the level of BP may persist when BP is measured by ambulatory BP monitoring. Advantage of ambulatory BP monitoring is diagnosis of sodium sensitivity.

Conclusions: ISS individuals are common among normotensives and rare among hypertensives. SS hypertensives have greater pressor response to salt than SS normotensives but for Systolic BP only, not for Diastolic BP.
were recently proposed, in particular two approaches seem to provide interesting information: scanning laser Doppler flowmetry (SLDF) and adaptive optics (AO); both of them provide an estimation of the wall to lumen ratio (WLR) of retinal arterioles. A non-invasive measurement of basal and total capillary density may be obtained by videomicroscopy/capillaroscopy. No direct comparison of the three non-invasive techniques in the same population was previously performed, in particular AO was never validated against micromyography.

Design and method: In the present study we enrolled 12 normotensive subjects and 8 hypertensive patients undergoing an electrical surgical intervention; 11/20 were severely obese. All patients underwent a biopsy of subcutaneous fat during surgery. Subcutaneous small resistance artery structure was assessed by wire myography and the M/L was calculated. WLR of retinal arterioles was obtained by Scanning Laser Doppler Flowmetry and AO (SLDF, Heidelberg Engineering, Heidelberg, Germany and RTX-1, Imagine Eyes, Orsay, France). Functional (basal) and structural (total) microvascular density were evaluated by capillaroscopy (Videonc 3, DS Medica, Milan, Italy) before and after venous congestion.

Results: The results are summarized in the Table (slope of the relation: p < 0.01 RTX-1 vs. SLDF).

<table>
<thead>
<tr>
<th>Correlation coefficient (n=20)</th>
<th>Basal capillary density in the nailbed / M/L</th>
<th>Total capillary density in the forearm / M/L</th>
<th>Basal capillary density in the index finger / M/L</th>
<th>Total capillary density in the ring finger / M/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>W/L. retinal arterioles (SLDF)</td>
<td>0.59, r=0.28, p=0.03</td>
<td>0.51, r=0.25, p=0.05</td>
<td>0.61, r=0.29, p&lt;0.001</td>
<td>0.54, r=0.12, p=NS</td>
</tr>
<tr>
<td>W/L. retinal arterioles (RTX-1)</td>
<td>0.54, r=0.26, p=0.01</td>
<td>0.49, r=0.31, p&lt;0.001</td>
<td>0.71, r=0.50, p=0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Our data suggest that AO has a substantial advantage over SLDF in terms of evaluation of microvascular morphology, since it is more closely correlated with the M/L of subcutaneous small arteries, considered a gold-standard approach but limited in its clinical application by the local invasiveness of the procedure.

OP.8C.04 UNTREATED INDIVIDUALS WITH HYPERTENSION EXHIBIT IMPAIRMENTS IN SKELETAL MUSCLE OXYGENATION AND BLUNTED MICROVASCULAR REACTIVITY

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Objective: Endothelial cells across the vascular tree exhibit marked phenotypic heterogeneity in structure and function and vary between different organs and blood vessel types. Although endothelial dysfunction has been observed in several microvascular beds in hypertension, the in vivo microvascular endothelial function within the skeletal muscle in hypertension has not been investigated. This study examined, using near-infrared spectroscopy (NIRS) (i) whether differences in micro-vascular reactivity and skeletal muscle oxygenation exist between untreated individuals with hypertension (HYP) and age-, BMI-, and sex-matched uncomplicated normotensive individuals (NORMO) and (ii) whether microvascular function indices at the skeletal muscle level are associated with arterial stiffness and different blood pressure (BP) (office, ambulatory, and central) measurements.

Design and method: Ninety individuals (54 HYP and 36 NORMO), aged 44.7 ± 11.1 years underwent physical examination, office and 24 h-BP evaluation, augmentation index (AI) and central BP assessment, and a vascular occlusion test during which NIRS (Artinis) continuously monitored changes in muscle oxygenated and deoxygenated hemoglobin, and tissue oxygen saturation(TSI%). The experimental procedure included: a) baseline, b) a 5-min arterial occlusion for assessing the maximal capacity for O2-extraction by skeletal muscles (mitochondrial function), and c) re-oxygenation (slope and magnitude) for assessing micro-vascular reactivity.
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Objective: Microcirculation is the dominant modulator of total peripheral resistance. There is growing evidence that impairment of microcirculation, especially remodeling of small vessels may be directly involved in the pathogenesis of hypertension. The aim of the study was to evaluate the association of retinal arteriole structure and function with central blood pressure hemodynamics and hypertensive patients.

Design and method: Individuals treated due to essential hypertension (n = 81, age 40–70 years, mean age: 54.5 ± 8.8 years, 48% females) were included in the study. Excluding criteria were: any other cardiovascular disease, diabetes, renal impairment with eGFR < 60 ml/min/m² and ocular disease. Applanation tonometry was used to determine central aortic pressures: cSBP, cDBP, Pulse Pressure (cPP), Augmentation Index (AIx) and carotid-femoral pulse wave velocity (PWV). Intima media thickness of common carotid artery was measured by multiaxial echotesting system. Scanning laser Doppler flowmetry was used to evaluate retinal microperfusion: systolic (sRCF), diastolic (dRCF), mean (mRCF). Arteriolar structure was determined by outer diameter (AD), lumen diameter (LD), wall thickness (WC) and wall-lumen ratio (WLR). Retinal arteriolar remodeling analysis with Adaptive Optics may be useful as an alternative for the more operator-demanding measurement. There is growing evidence that impairment of microcirculation, especially remodeling of small vessels may be directly involved in the pathogenesis of hypertension. The aim of the study was to evaluate the association of retinal arteriole structure and function with central blood pressure hemodynamics and hypertensive patients.

Results: The correlation analysis revealed the relationship between cPP and retinal microperfusion: sRCF (r = 0.28, p < 0.05), mRCF (r = 0.25, p < 0.05). Central PP was also associated with LD (r = 0.27, p < 0.05), however any correlation with AD, WT or WLR was found. Central SBP, DBP and ADL were not related to RCF or retinal morphology. There was negative correlation between PWV and sRCF (r = −0.27, p < 0.05), dRCF (r = −0.29, p < 0.05) and mRCF (r = −0.28, p < 0.05). IMT was not associated neither with retinal microperfusion nor arteriolar structure.

Conclusions: Among all analyzed central hemodynamic parameters, only cPP was significantly related to RCF and arteriolar morphology. Significant relationship was also found between PWV and retinal microperfusion.

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Objective: Local thermal hyperaemia (LTH) of the skin, measured with a laser Doppler flow imager is a relatively easy applicable measure of microvascular function and may serve as an alternative for the more operator-demanding measure Flow Mediated Dilatation, known to be a reliable measure of endothelial dysfunction. We aimed to investigate the nitric oxide (NO)-dependency of LTH and the effect of smoking.

Design and method: LTH was measured in 27 healthy men, aged (Mean ± SD) 41 ± 12 years, including 8 age-matched smokers. For the LTH response, skin microcirculation was recorded for 5 minutes at 33°C (baseline) followed by a cooling period at 40°C for 35 minutes. LTH peak was defined as the maximal thermal blood flow (DBF) response within the first 10 minutes and LTH plateau as the average DBF response during the last 5 minutes of heating in arbitrary units (a.u.). Local dermal application of L-NMMA by means of iontophoresis was used to measure the nitric oxide (NO)-dependency of LTH.

Results: Baseline skin blood flow in non-smokers and smokers did not differ. In smokers the LTH peak and plateau response was less than in non-smokers with a mean difference ± SEM of 56 ± 24 a.u. for the LTH peak and 54 ± 20 a.u. for the LTH plateau response (p < 0.05). Furthermore, compared to non-smokers L-NMMA inhibited the LTH responses considerably less in smokers with inhibition of respectively 22 ± 4% versus 40 ± 2% (p = 0.0004) for the peak and inhibition of 57 ± 4% versus 70 ± 3% (p = 0.015) for the LTH plateau response.

Conclusions: Peak and especially plateau dermal LTH responses are NO-dependent as they are in large part inhibited by the NO-synthase inhibitor L-NMMA. In addition, these NO-dependent responses are already considerably impaired in smokers, who lack cardiovascular disease or other cardiovascular risk factors.
Objective: Vascular endothelium dysfunction represents target organ damage in patients with arterial hypertension. The integrity of endothelial glycocalyx (EG) plays a vital role in vascular permeability, inflammation and elasticity and finally to cardiovascular disease. Sideview Darkfield imaging allows for non-invasive automated estimation of EG dimensions based on the erythrocyte column distribution. Increased HDL cholesterol (HDL-C) offers protection against cardiovascular disease. We aimed to investigate any differences regarding EG dimensions in hypertensive patients with extremely increased and decreased HDL-C levels.

Design and method: One hundred-eighty four (184) patients with arterial hypertension under treatment (mean age 61+13 years, 88 males) were divided regarding HDL-C quartiles in two groups. Eighty nine patients (48%) were under treatment with statins. In group A, HDL-C was >71 mg/dl (upper HDL-C quartile, n = 53, mean age 63+12 years, 8 males). In group B, HDL-C was < 71 mg/dl (three lower HDL-C quartiles, n = 131, mean age 60+13 years, 80 males). Increased perfusion boundary region (PBR) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sideview Darkfield imaging (Microscan, Glycocheck) was measured as a non-invasive accurate index of reduced EG thickness.

Results: No significant differences were found within groups regarding age, LDL-C levels, systolic blood pressure and pulse pressure. EG dimensions were significantly different between Group A and B regarding arterial microvessels ranged 5–9 mm (PBR 5–9 was 1.18 ± 0.1 vs. 1.22 ± 0.1 mm, p < 0.05). A significant negative correlation was found between HDL-C and PBR 5–9 in the whole population (r = −0.11, p < 0.05). In a multiple linear regression analysis model, using age, smoking habit, LDL-levels as independent variables, we found that this association between HDL-C and PBR 5–9 was independent (Beta = −0.24, p < 0.05).

Conclusions: We found that endothelial function, represented by EG levels, seems to be protected in hypertensive patients with extremely increased HDL-C levels. Future studies in several groups of low or high risk hypertensive patients are needed in order to evaluate the possible role of EG as a novel marker in essential hypertension.