

POSTER SESSION

POSTERS' SESSION PS01:

EPIDEMIOLOGY AND RISK FACTORS

CARDIOVASCULAR RISK PREDICTION- A SYSTEMS MEDICINE APPROACH

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Objective: During the last decade, more attention has been paid on the development of risk scores in primary prevention, while patients with established cardiovascular disease are usually categorized into a clinically high risk population without further stratification. Even those high risk patients show heterogeneity in their individual risk. Therefore further risk stratification might identify those with would benefit from specific risk reduction strategies the most. We have developed the first long-term risk prediction model of cardiovascular mortality in patients with established coronary heart disease and in patients with an experienced myocardial infarction based on newly available machine learning techniques.

Design and method: 2879 patients from the LURIC study who have presented in hospital were included in this analysis. Over a medium follow-up of 9.9 years, 540 patients had died of cardiovascular causes. 184 biomarkers and 21 clinical data were ranked according to the prediction accuracy using three different ranking methods (correlation, information gain and information gain ratio). Seven different predictors (random forest, random tree, naïve bayes predictor, rule based predictor, linear regression, polynomial and radial bases function support vector machine) were used to generate risk models.

Results: The main predictive biomarker was NT-proBNP, CT-proAVP followed by TnT and estimated GFR. Using more than five biomarkers lead to a comparatively high increase in cost and effort without further improving the accuracy of the generated models. Comparing all biomarkers over all prediction algorithms with respect to the area under the curve, we found that the random forest approach yielded the best results followed by the rules based approach, logistic regression and the radial basis function support vector machine. Adding clinical variables further improved the models. Generally the machine learning risk models predicted five- and ten-year cardiovascular mortality better than the conventional statistical approaches.

Conclusions: We have developed the first CV mortality prediction model based on machine learning techniques, (1) on an extensive database of clinical, routinely and non-routinely measured laboratory data, (2) created a fully automatic and self-validated framework, (3) which is easily to apply on all spectra of population, events and time frames.

INCIDENTAL RISK OF HYPERTENSION ACCORDING TO THE CHANGE OF BODY WEIGHT IN KOREAN MEN

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Objective: Despite accumulated evidence of strong relationship between obesity and hypertension, risk for hypertension according to the change of body weight (BW) is not clearly identified. Therefore, this study was to evaluate the incidental risk of hypertension according to the change of BW.

Design and method: 26,483 normotensive Korean men had been followed up from 2005 to 2010. Based on baseline BW in 2005, the changes of BW [(BW at censoring time – BW at baseline)/follow-up period (person-years)] were categorized into 5 groups according to their change levels from the lowest to the highest quintile (1st – 5thquintile). On the base of 3rd quintile, 1st and 2nd quintile had negative changes of BW, and 4th and 5th quintile had positive changes of BW. Cox proportional hazard models and spline-smoothing method were used to evaluate the effect of BW change on the incidental risk of hypertension.

Results: During follow-up, 4,445 (16.8 %) cases of hypertension newly developed (quintile 1: 19.0%, quintile 2: 12.9%, quintile 3: 12.4%, quintile 4: 14.8%, quintile 5: 24.8%). When quintile 3 was set as a reference in adjusted model, the hazard ratios (HRs) for incidental hypertension exhibited a J-shaped relationship with the BW changes (quintile 1: 1.66 [95% confidence interval (CI): 1.41–1.95], quintile 2: 0.96 [95% CI: 0.80–1.14], quintile 3: 1.00 [reference], quintile 4: 1.30 [95% CI: 1.10–1.54], and quintile 5: 3.39 [95% CI: 2.91–3.96], respectively).

Conclusions: The incidental risk of hypertension increased in weight loss as well as weight gain, which demonstrated J-shaped relationship. This finding warrants further studies to investigate the incidental relationship between BW changes and hypertension.

URIC ACID PREDICTS CORONARY ARTERY DISEASE BUT NOT STROKE IN ESSENTIAL HYPERTENSION: DATA FROM A GREEK 8-YEAR-FOLLOW-UP STUDY

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Objective: The aim of the present study was to assess the predictive role of uric acid for the incidence of coronary artery disease (CAD) as well as stroke in essential hypertensive patients.

Design and method: We followed up 2415 essential hypertensives (mean age 58.4 years, 1208 males, office blood pressure (BP) = 143/88 mmHg) for a mean period of 8 years. All subjects had at least one annual visit and at baseline underwent echocardiographic study and blood sampling. Moreover, CAD was defined as the history of myocardial infarction or significant coronary artery stenosis and stroke was defined as rapid onset of a new neurological deficit persisting at least 24 hours unless death supervened confirmed by imaging findings.

Results: The incidence of CAD and stroke was 2.2% and 1% respectively. Hypertensives who developed CAD (n = 53) compared to those without CAD at follow-up (n = 2362) had at baseline higher baseline uric acid levels (5.8 ± 1.8 vs 5.2 ± 1.5 mg/dl, $p = 0.011$) and left ventricular mass index (LVMI) (115.7 ± 27.1 vs 103.7 ± 27.1 g/m², $p = 0.001$), whereas no difference was observed with respect to baseline office BP, renal function and lipid levels ($p = \text{NS}$ for all). Hypertensives who developed stroke (n = 24) compared to those without CAD at follow-up (n = 2391) were older (63 ± 8 vs 58 ± 11 years, $p = 0.006$), whereas no difference was observed with respect to baseline office BP, uric acid, renal function and lipid levels ($p = \text{NS}$ for all). Univariate Cox regression analysis revealed that baseline uric acid levels predicted CAD (hazard ratio = 1.219, $p = 0.013$) but not stroke. In multivariate Cox regression model baseline glomerular filtration rate (hazard ratio = 1.018, $p = 0.017$) LVMI (hazard ratio = 1.010, $p = 0.026$) and uric acid (hazard ratio = 1.226, $p = 0.016$) turned out to be independent predictors of CAD, while age (hazard ratio = 1.058, $p = 0.014$) predicted stroke.

Conclusions: In essential hypertensive patients uric acid predicts future development of CAD, whereas exhibits no prognostic value for stroke. These findings further support that uric acid estimation could improve overall risk stratification in essential hypertension.

CARDIOVASCULAR RISK FACTORS AND ARTERIAL STIFFNESS IN MEN AGED 41–43 YEARS

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Objective: To study the relationship of individual cardiovascular risk factors with arterial stiffness and subclinical atherosclerosis.

Design and method: The study is the part of a 32-year prospective cohort monitoring, beginning with childhood (11–12 years). The present cohort included 303 male subjects aged 41–43 years. Arterial stiffness (AS) was measured by aortic pulse wave velocity (PWV) and arterial wave reflections (augmentation index, Alx) with the use of SphygmoCor (AtCor Medical). Intima-media thickness (IMT) and subclinical atherosclerosis were estimated by ultrasonography methods both in left and right carotid arteries.

Results: Hypertension (H) was detected in 37.9%. PWV was significantly higher in the group with H. The risk of H development depended on hypertension presence in mother and did not depend on the presence of H in father. H was associated with the development of obesity, especially of the abdominal type and increased level of triglycerides. PWV was positively correlated with systolic ($r = 0.248$, $p < 0.001$) and diastolic blood pressure (BP) ($r = 0.220$, $p < 0.001$) measured on the brachial artery and with heart rate ($r = 0.164$, $p < 0.01$). A statistically significant positive correlation of the central aortic pressure ($r = 0.326$, $p < 0.001$) and central pulse pressure ($r = 0.225$, $p < 0.001$) with PWV was noted. When comparing arterial stiffness (AS) and duplex scan a correlation of mean IMT with the Alx ($r = 0.134$, $p < 0.05$) and augmentation pressure ($r = 0.127$, $p < 0.05$) was obtained, but no correlation between IMT and PWV was found. Correlation of AS with total cholesterol and glucose was also shown.

Conclusions: The AS is closely related with H and develops already in the early stages, in a fairly young age. The AS in men group was not associated with the presence of dyslipidemia and diabetes melitus. The interrelation of arterial stiffness and the degree of early atherosclerotic vascular lesions is ambiguous.

ACUTE DIETARY SALT MODULATION INDUCES CHANGES IN DYNAMICS OF MONOCYTES SUBSETS IN YOUNG HEALTHY WOMEN

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Objective: Our earlier studies have demonstrated that 7-days high-salt (HS) intake alters micro- and macrovascular response, and increases oxidative stress level in young healthy women independently of blood pressure (BP) changes. Still, it is not clarified whether such HS-induced endothelial dysfunction also involves changes in the immune system response which finally leads to vascular inflammation. Thus, the aim of this study was to assess the effect of 7-days salt intake modulation on monocyte subpopulations distribution and its activation in peripheral blood of young healthy women.

Design and method: 15 young healthy women who all took 7-days low-salt (LS) diet (<3.2 g salt/day) followed by 7-days HS diet (~14 g salt/day) participated in this study. Blood pressure (BP) was measured, and 24 h urine samples were analyzed for sodium, potassium, urea and creatinine levels before and after diet protocols. Flow cytometry analysis of circulating monocyte subpopulations distribution was assessed by determination of 'classical', 'non-classical' and 'inflammatory' monocytes based on CD14 and CD16 molecule expression in peripheral blood of young healthy women. Also, monocytes activation was assessed by measurement of lymphocyte function-associated antigen 1 (LFA-1, Cd 11a) expression which is known as ligand for endothelial cell adhesion molecules (ICAM-1).

Results: Changes in 24 h urinary sodium confirmed subjects conformed to the diet protocol. There was no change in BP after HS diet. CD14+CD16++ gated (non-classical) monocytes from peripheral blood significantly decreased after HS diet compared to the LS diet. Distribution of CD14++CD16+ (intermediate) and CD14++CD16- (classical) gated monocytes from peripheral blood did not change after HS diet compared to the LS diet. CD11a expression on all three gated monocyte subpopulations was significantly decreased after HS diet compared to LS diet measurement.

Conclusions: The results of the present study demonstrated that 7-days HS loading decreased CD14+CD16++ monocytes subpopulation (non-classical monocytes) which usually acts as endothelium housekeepers, and also decreased total monocytes (all three subpopulations) expressing high level of CD11a in young healthy women, probably due to activated monocytes adhesion and migration through endothelium layer to the place of endothelial injury.

IMPACT OF SLEEP DISORDERS ON THE PREVALENCE OF TARGET ORGAN DAMAGE IN ADULT HYPERTENSIVE PATIENTS

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Objective: Prolonged short sleep duration and poor sleep quality may lead to the onset and/or maintenance of arterial hypertension. Patients with obstructive sleep apnoea (OSA) and high blood pressure (BP), compared with hypertensive

subjects without OSA, show increased prevalence of left ventricular hypertrophy (LVH) and increased urinary albumin excretion (UAE). Nevertheless, data linking other common sleep disorders, such as insomnia and restless legs syndrome (RLS) and the onset of hypertensive-related organ damage (OD) are lacking. The aim of the present study was to assess the association of OSA, insomnia, and RLS with cardiac and renal OD in a cohort of adults with hypertension.

Design and method: In a prospective-observational study, we enrolled 160 consecutive patients aged between 18 and 60 years old, who underwent full assessment for OD by means of transthoracic echocardiography, UAE, and estimated glomerular filtration rate measurement. All patients were also screened to evaluate the risk of insomnia with the Insomnia Severity Index (ISI), OSA with the STOP-Bang, and RLS using the RLS Rating Score.

Results: 99 males and 61 females, with median age 47(11) years, body mass index 25.5(5.8) kg/m², office systolic BP 144(24) mmHg and diastolic BP 92(12) mmHg, have been studied.

In the group with high risk of OSA (STOP-Bang score ≥ 4) we observed an increased left ventricular mass index (LVMI) [119(35) vs. 104(26) g/m², $p = 0.002$] and diastolic dysfunction parameters [left atrium volume index 27.5(6.0) vs 24.0(5.0) ml/m², $p = 0.005$; mitral E/A ratio 1.1(0.2) vs 1.0(1.8), $p = 0.01$]. At multivariate analysis office systolic BP values and STOP-Bang score were independent predictors of LVMI ($b = 0.18$, $p = 0.023$ and $b = 0.23$, $p = 0.003$, respectively). No association with cardiac OD was seen in patients at increased risk of insomnia and RLS. No correlation was observed with renal OD for all subgroups.

Conclusions: The STOP-Bang, a simple, validated, and reproducible questionnaire, which predicts a high risk of OSA, is associated with hypertension-related heart remodelling in a cohort of hypertensive subjects and might be used to predict patients at risk of developing cardiac OD.

BLOOD PRESSURE CONTROL IN HYPERTENSIVE OUTPATIENTS: RESULTS OF A 2-YEAR OBSERVATIONAL STUDY

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Objective: Antihypertensive treatment lowers blood pressure (BP) and reduces cardiovascular, cerebral and renal risk of hypertension. In developed countries, BP control has increased over the past few decades and is now approaching 70% of patients. Herewith we report the results of an observational study carried out on hypertensive outpatients.

Design and method: In a cohort of 1,422 consecutive hypertensive outpatients (793 females, 629 males; mean age: 60.2 ± 12.3 years) evaluated from January 2015 to December 2016, the following parameters were assessed: age, sex, body-mass index (BMI), waist circumference (WC), smoking status, BP in the sitting position, estimated glomerular filtration rate (eGFR), serum glucose, glycosylated haemoglobin, lipid profile, antihypertensive drugs prescribed. In agreement with the European guidelines, hypertension was defined as sitting BP equal or higher than 140/90 mmHg or use of antihypertensive drugs. Patients whose sitting BP was lower than 140/90 mmHg were considered as having achieved BP control. Furthermore, in compliance with the new definition of hypertension suggested by the American College of Cardiology/American Heart Association (ACC/AHA), a second level of BP control (sitting BP below 130/80 mmHg) was evaluated.

Results: Overall, 76.3% of hypertensive patients achieved BP lower than 140/90 mmHg; 51.5% of them achieved BP lower than 130/80 mmHg. In both contexts, compared with patients whose BP was not controlled, those achieving the BP targets were younger, mainly females and showed a significantly lower BMI. No differences were in WC and eGFR. With regard to the major cardiovascular risk factors (smoking, diabetes mellitus and hypercholesterolemia), only diabetes resulted significantly higher in patients not achieving BP control. Finally, all patients achieving the BP target were prescribed significantly fewer antihypertensive drugs in comparison to those in whom BP was not controlled.

Conclusions: More than 76% of our outpatients achieved BP target of less than 140/90 mmHg, a figure that is higher than the objective of 70% of treated and controlled hypertensive patients set in Europe. Under the new definition of hypertension proposed by ACC/AHA, only 51.5% of our patients were below the threshold of 130/80 mmHg, a result that is however better than those recently reported.

HYPERTENSION AND CARDIOVASCULAR RISK FACTORS IN CROATIA. DATA FROM THE 2017. WORLD HYPERTENSION DAY

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Objective: The aim of this study was to obtain data on prevalence and awareness of hypertension, cardiovascular risk factors, and life-style habits in individuals (aged 18 years or older) participating in the 2017 World Hypertension Day in Croatia.

Design and method: Blood pressure (BP) was measured at 26 sites in 5 cities in Croatia. Along with BP measurement, a short questionnaire on hypertension awareness/salt intake/smartphone use was completed in the time of the interview. The average of two BP measurements, taken in seated position after a few minutes rest by a validated oscillometric device (Omron M6) was recorded. BP measurements were performed from 10 AM to 2 PM in hospital open points, central squares and pharmacies. BP was measured by physicians, trained nurses, pharmacist or medical students. This action was organized and supported by the Croatian Society of Hypertension.

Results: A total of 2175 subjects, 873(40.1%) men, 1211(59.9%) women were examined. Men were older, had higher BP, BMI and waist circumference (64.7(13.9)vs.61.8(14.5);142.9/85.4(19.8/11.7)vs.136.3/82.9 (21.2/11.3); 28.3(4.4)vs.26.7(5.4);103(12.2)vs.92.8(15.7), respectively). Proportion of patients with BMI over 25 and 25–30 kg/m² was 32.4% and 20% respectively. In the whole group there were 53.4% subjects with BP 140/90 mmHg or higher (women vs. men 54.1% vs. 45.9%, $p < 0.001$), 68.4% were aware of hypertension (men vs. women 66.9% vs. 67.8%, $p > 0.05$). Positive family history (FH) for hypertension, stroke and myocardial infarction was found in 46.7%, 17.9% and 23.5% subjects respectively. FH was more frequently positive in women than in men (51.0% vs. 40.3%, $p < 0.001$; 20.3% vs. 14.3%, $p = 0.008$, 26% vs. 19.6%, $p = 0.01$). We failed to find association between BP values and positive FH. There were 18.7% smokers (more women never smoked 66.5% vs. 57.1%, $p < 0.001$), average pack-years was 5. Only 9.4% of population declared regular physical activity (more than twice per week), and 49.7% were never physically active (no gender differences).

Conclusions: Prevalence of subjects with BP values in hypertensive ranges is high, awareness is insufficient, and high proportion of subjects is obese and physically inactive. There is an urgent need of education not only hypertensives but general population as a true measure of primordial prevention.

EVALUATION OF THE ASSOCIATION BETWEEN THE AGE AT ONSET OF HYPERTENSION AND DIFFERENT AFFECTIVE TEMPERAMENTS

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Objective: The age, when hypertension is initiated is influenced by different factors, but the role of personality traits in this regard is not clarified yet. Affective temperaments (depressive, cyclothymic, anxious, irritable and hyperthymic); which manifest early and are relatively stable in adulthood, have been associated with blood pressure and arterial stiffness. Our aim was to study the possible association between affective temperaments and the age at onset of hypertension.

Design and method: In this cross-sectional study 357 patients were included (302 and 55 with chronic and new hypertension, respectively). After the evaluation of history, patients completed the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A). Predictors of the age at onset of hypertension and that of the early onset (under the age of 40) were studied.

Results: The mean age of the subjects was 60.7 (± 12) years. The independent predictors of the age at onset of hypertension were male sex ($B = 4.67$, 95%CI = 1.44–7.9 $p = 0.005$), smoking ($B = -4.62$, 95%CI = -7.77–-1.46 $p = 0.004$) and positive family history ($B = -6.94$, 95%CI = -10.41–-3.48, $p < 0.001$). High cyclothymic affective temperament score tended to be an independent predictor, however, the association was not significant ($B = -0.48$, 95%CI = -1.07–0.11, $p = 0.110$). When the subgroup of patients with early onset hypertension was studied ($n = 73$), male sex, smoking and positive family history remained independent predictors,

however cyclothymic temperament score lost its predictive power ($B = 0.010$, $p = 0.86$).

Conclusions: Besides traditional factors, cyclothymic affective temperament might contribute to the initiation of hypertension, but not in the early decades of life.

EARLY VASCULAR AGEING SYNDROM: FROM RISK FACTORS TO THE DISEASE

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Objective: A clear correspondence of the age and state of the arteries is not always observed. The concept of early vascular aging syndrome acquires clinical significance. The aim of the study was to assess correlation between vascular stiffness, endothelial dysfunction, vascular age and biological age in healthy volunteers and patients with arterial hypertension (AH).

Design and method: Group I includes 63 healthy volunteers 24 M/39F, 33–55 years old, mean age 48.5 ± 7.6 . Group II includes 135 patients with AH 64 M/71F, 30–89 years old, mean age 54.8 ± 9.1 , duration of hypertension 8.6 ± 6.7 years. The following were measured: cardio-ankle vascular index (CAVI) and vascular age using VaSera VS-1500N (Fukuda Denshi, Japan); carotid femoral pulse wave velocity (PWV) and forearm blood flow (FBF) using Impeccard (Belarus).

Results: CAVI in group I – 7.59 ± 0.86 , in group II – 8.42 ± 1.31 , $P < 0.0001$; FBF in group I – $9.9 \pm 20.7\%$, in group II – $-0.9 \pm 26.2\%$, $P < 0.001$; PWV in group I – 6.5 ± 3.3 m/s, in group II – 12.3 ± 8.7 m/s, $P < 0.0001$. Vascular age in group I was 47.5 ± 10.4 years. Vascular age in group II was 58.3 ± 11.1 years, it is differ from biological age, $P < 0.05$. CAVI in group I correlated with age ($R_s = 0.47$, $P < 0.0001$), number of cigarettes ($R_s = 0.27$, $P < 0.05$), vascular age ($R_s = 0.88$, $P < 0.0001$) and SCORE rate ($R_s = 0.56$, $P < 0.05$). CAVI in group II correlated with age ($R_s = 0.54$, $P < 0.0001$), duration of AH ($R_s = 0.26$, $P < 0.01$), systolic blood pressure (SBP) ($R_s = 0.32$, $P < 0.001$), vascular age ($R_s = 0.85$, $P < 0.0001$). PWV in group II correlated with duration of AH ($R_s = 0.36$, $P < 0.0001$).

The multivariate analysis of variance in group I performed with vascular age as the dependent factor and CAVI ($F = 63.9$, $P = 0.0001$), $h = 64.1\%$; SBP ($F = 27.7$, $P = 0.048$), $h = 29.2\%$. The multivariate analysis of variance in group II performed with vascular age as the dependent factor and CAVI ($F = 83.4$, $P = 0.0001$), $h = 63.5\%$; SBP ($F = 5.1$, $P = 0.0003$), $h = 21.7\%$.

Conclusions: CAVI and vascular age increase in patients with AH. CAVI is more closely related to aging than PWV and FBF. Thus CAVI may be useful predictor of vascular ageing.

THE RELATIONSHIPS BETWEEN RENAL RESISTIVE INDEX AND CORONARY RISK FACTORS AND CORONARY HEART DISEASE

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Objective: Renal resistive index (rRI) can be measured in renal vascular echography and is reported to be associated with renal parenchymal damage. However, little is known about its clinical importance. In the present study, we investigated the relationships between rRI and coronary risk factors in the patients who were suspected or suffered from coronary heart disease (CAD) and stroke.

Design and method: We enrolled the patients who underwent renal vascular echography from September 2014 to August 2017, and excluded the patients with severe chronic kidney disease (estimated glomerular filtration rate (eGFR) < 15). The XarioXG (Toshiba Medical Systems, Tochigi, Japan) ultrasound device and a 3.5-MHz probe were used to obtain images for RI measurement. The rRI was defined as (peak systolic velocity - end diastolic velocity)/peak systolic velocity. In each patient, rRI at the interlobular was measured in the middle portions of the kidney in a supine position and was averaged for each kidney. The mean rRI value of both kidneys was used for analysis. We also examined the association with intima media thickness (IMT) of carotid artery, pulse wave velocity (PWV), and underlying clinical features and parameters.

Results: The number of patients was 331 (male/female = 225/106), and the mean age was 66.4 years old. The rRI was significantly increased with age, serum creatinine and decreased with eGFR. The patient with hyperlipidemia ($n = 204$, $p < 0.05$), hypertension ($n = 276$, $p < 0.01$), diabetes mellitus ($n = 81$, $p < 0.01$), CAD ($n = 125$, $p < 0.01$) or stroke ($n = 70$, $p = 0.01$) showed significantly higher rRI than the patients without these diseases. Disease severity of CAD assessed by the number of diseased vessels significantly associated with the rRI. ($p = 0.02$). Especially, the patients with three vessel diseases showed significantly higher rRI

than the patients without coronary disease or with single/double vessel diseases ($p < 0.01$). Furthermore, the rRI significantly associated with IMT ($p = 0.02$) but not with PWV ($p = 0.74$).

Conclusions: In the present study, we found that the rRI significantly associated with not only clinical feature and parameters but also IMT. These results revealed that the rRI had close relationships with coronary risk factors.

LEFT ATRIAL SIZE : DETERMINANTS USING NON-CONTRAST ENHANCED CARDIAC COMPUTED TOMOGRAPHY

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Objective: Left atrial (LA) size is a marker of diastolic dysfunction and is associated with cardio-vascular outcomes. A new method using a non contrast-enhanced cardiac computed tomography realised for the quantification of coronary artery calcium (CAC) allows to measure left atrial volume. The aim of this study was to determine the cardio-vascular risks factors associated with left atrial enlargement.

Design and method: 458 participants (mean age 59,4 years, 45,4% of women) at intermediate cardio-vascular risk benefited from a non contrast-enhanced cardiac computed tomography. Left atrial volume was performed by countouring the inner edges of LA in three shots of space.

Results: Mean LA volume was $76,7 \pm 18,6$ mL and $41,6 \pm 10$ mL/m² after adjustment with body area. Women had significantly largest LA volume ($p < 0,0001$). LA volume was strongly associated with body mass index and body area (beta coefficient = 0,27 et $p < 0,0001$ for both). Obesity (BMI > 30 kg/m²) was correlated with largest LA volume ($p < 0,0001$). Systolic blood pressure was associated with LA volume and adjusted LA volume (p respectively $< 0,01$ et $0,01$) but the association with hypertension was only found with non adjusted LA volume ($p = 0,003$). Dyslipidemia was correlated with smaller LA ($p < 0,01$). Smoking, diabetes and CAC was not associated with LA size. In a fully adjusted model, hypertension, female sex and dyslipidemia was still associated with adjusted LA volume.

Conclusions: LA volume determined using non contrast-enhanced computed tomography is associated with BMI, hypertension, female sex and dyslipidemia. This new technique allows to measure left atrial volume on a cardiac computed tomography used for the assessment of CAC to better predict the cardiovascular risk.

CHARACTERISTICS OF PATIENTS WITH ATRIAL FIBRILLATION. ESH-FA PROJECT – DATA ON CROATIAN COHORT

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Objective: The aim of the study was to analyze clinical characteristics of the consecutive sample of patients with atrial fibrillation (AFib) who were admitted to the UHC Zagreb Cardiology Clinic, part of the ESH Excellence centre of hypertension. This cohort is part of the ESH –FA project.

Design and method: Consecutive sample of 201 patients with AFib (115 M, 86 F; averaged age 71.6) was enrolled in period 2014–2016. Data were collected from medical records. BP was measured following the ESH/ESC guidelines. Hypertension (HT) was defined as BP $\geq 140/90$ mmHg and/or antihypertensive drugs treatment, chronic kidney disease (CKD) was defined as eGFR (CKD Epi < 60 ml/min).

Results: Average BP values and heart rate were $133.5/80.2$ mmHg, 82.2 bpm, and BMI was 31.1 kg/m², there were 19.6% and 11.5% smokers and ex-smokers, respectively. CHD, cerebrovascular disease, heart failure, valvular disease, PAD, hypothyreosis, and CKD were established in 52.7%, 17.9%, 49.3%, 29.3%, 13.9%, 14.4% and 52.5%, respectively. Family history for CVD was positive in 43.2% patients. Prevalence of HT was 83.5%, and 63.7% were treated, while 20% were newly diagnosed. Only 30.2% HT had BP $< 140/90$ mmHg. Most frequently used antihypertensive drugs were beta blockers (67.6%), loopD (54.7%), ACEi (50.7%), potassium-sparingD (22.8%) and thiazide-likeD (17.9%). LoopD were prescribed more frequently in patients with CKD than in non-CKD as well as in

HF than in non-HF patients. Hypokalemia was noticed in 18.9% patients and was mostly reported in non-HF patients (41.1%); it was associated with overuse of loopD and underuse of potassium-sparingD. First diagnosed, paroxysmal, permanent and persistent AFib were diagnosed in 5.4%, 33.3%, 51.2% and 10.4%, respectively. CHADVASC > 2 was determined in 78.9%; varfarin and NOAC were administered in 64.4% and 35.6% patients, respectively. In patients treated with varfarin INR > 2 was achieved in only 35.4%.

Conclusions: Better BP control and anticoagulation with more frequent use of NOACs is needed. Physicians must be aware of high prevalence of CKD in AFib patients and consequent drug dose adjustments.

COPEPTIN AS A RESEARCH MARKER IN CARDIOVASCULAR DISEASE

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Objective: Arginine vasopressin (ADH) is released from the neurohypophysis and regulates intravascular volume status. ADH activity is reflected by copeptin, the C-terminal peptide of pro-vasopressin. Elevated copeptin levels are associated with increased cardiovascular and all-cause mortality. The aim of this study is to compare copeptin levels in patients with different cardiovascular diseases.

Design and method: In this cross-sectional analysis we measured copeptin concentrations in 69 patients with diabetes mellitus type 2 (T2DM), 30 patients with primary hypertension stage 1 or 2 (HT1–2), 34 patients with treatment resistant hypertension (TRH) (21 of them with T2DM), and 28 healthy individuals, who participated in clinical trials. In 2 study groups we analyzed changes after therapeutic interventions. Patients with T2DM received 6 weeks of treatment with 25 mg empagliflozin or placebo. Patients with TRH underwent full four quadrant renal denervation (RDN) by an experienced interventionalist. Copeptin concentrations were measured before and after treatment using Time Resolved Amplified Cryptate Emission method.

Results: Patients with TRH showed higher copeptin levels than patients with HT1–2 (median 8.4 [interquartile range 3.6–14] vs. 4.2 [2.8–6.3] pmol/l, $p = 0.039$), patients with T2DM (4.5 [3.3–7.2] pmol/l, $p = 0.020$) and healthy individuals (5.7 [2.9–9.2] pmol/l, $p = 0.024$). There was no significant change in copeptin levels in patients with TRH before and 6 month after RDN (8.4 [3.6–14] vs 8.5 [4.5–13] pmol/l, $p = 0.334$), even though 24 h ambulatory blood pressure decreased from $154 \pm 15/87 \pm 12$ mmHg ($p = 0.001$) to $146 \pm 13/83 \pm 7.9$ mmHg ($p = 0.034$). In patients with T2DM (double blind randomized cross-over trial), no significant change in copeptin levels was observed in the placebo group compared to baseline (5.08 ± 2.83 vs 5.76 ± 4.05 pmol/l, $p = 0.09$), whereas treatment with empagliflozin increased copeptin levels compared to baseline (6.87 ± 3.89 pmol/l, $p = 0.001$). Patients receiving empagliflozin showed higher copeptin levels ($p < 0.001$) compared to placebo.

Conclusions: Patients with TRH showed higher copeptin levels than patients with HT1–2, T2DM and healthy individuals. RDN did not lead to any change of copeptin levels in patients with TRH, but empagliflozin, as expected induced an increase in copeptin levels due to volume contraction in patients with T2DM. Copeptin emerged as a valuable research marker in cardiovascular disease.

RELATIONSHIP BETWEEN SMOKING, ANGIOGRAPHIC SUBTYPES AND VASCULAR INVOLVEMENT IN PATIENTS WITH FIBROMUSCULAR DYSPLASIA - THE ARCADIA-POL STUDY

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Objective: To assess the relationship between smoking and angiographic subtypes and vascular involvement in patients with fibromuscular dysplasia (FMD) enrolled into ARCADIA-POL study.

Design and method: Out of 250 patients enrolled into ARCADIA-POL study since January 2015 (instituted on the basis of Polish-French collaboration) we analyzed 183 patients with confirmed FMD in at least one vascular bed. A standardized FMD data form was used for data collection. All patients underwent detailed clinical evaluation including ABPM, biochemical evaluation, biobanking, duplex Doppler of carotid and abdominal arteries and whole body angio-CT. For the purpose of this analysis we divided 183 patients into two groups according to the status – 79 ever smokers (current or ex-smokers) (66F, 13 M, mean age: 46.9 ± 12.9 years) and 104 non-smokers (84F, 20 M, mean age: 45.2 ± 16.5 years).

Results: As we compared smokers to non-smokers we found no statistically significant differences between the groups in age, gender, hypertension status (94.9% vs 87.5%, $p = 0.086$, respectively), nor in blood pressure values. Both groups did not also differ in terms of localization of vascular beds, nor number of vascular beds affected with FMD lesions. The most frequently FMD lesions were present in renal arteries (89.9% vs 82.7%, $p = 0.17$, respectively). There were also no differences between smoker and non-smoker in the number of vascular complications such as dissections (7.6% vs 8.7%, $p = 0.79$, respectively) and aneurysms (35.4% vs 28.8%, $p = 0.34$). In further analysis we also analyzed 41 FMD patients currently smoking and compared them to the never smokers and similarly we did not find differences between the analyzed groups. We also analyzed separately 157 consecutive patients with renal FMD dividing them into smoking and non-smoking individuals. We found no differences in terms of angiographic subtypes of renal FMD, number of complication, nor number of patients with history or currently significant renal artery stenosis.

Conclusions: Although smoking has been implicated as a potential contributing factor to the development of FMD we did not find the relationship between the smoking and vascular involvement and complications in patients with FMD.

CARDIAC ULTRASONOGRAPHY FINDINGS RELATED TO PREVALENCE OF ARTERIAL HYPERTENSION IN PERIPHERAL ARTERIAL DISEASE PATIENTS-HIGHLIGHT EVIDENCES

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Objective: The aim of this study was to evaluate the presence of cardiac ultrasound changes correlated with the prevalence of arterial hypertension (HT) in patients with peripheral artery disease (PAD) with critical leg ischemia (CLI) comparative with patients without CLI. LV hypertrophic remodeling related to HT prevalence is underdiagnosed in PAD patients, in whom the arterial imaging evaluation it is priority made.

Design and method: Our study enrolled 197 patients with PAD patients: 142 pts. (63.1 ± 9.4 yrs., 88% male, 70% smokers) with CLI and 55 pts. (60.4 ± 10.6 yrs., 85% male, 65% smokers) without CLI. After signing an informed consent, all patients were clinically evaluated, laboratory tested (glucose, cholesterol, triglyceride serum levels) and cardiac ultrasound was performed. The cardiac ultrasound parameters measurements were related to end-diastolic septum wall thickness (SWTd) and left ventricular (LV) posterior wall thickness (LVPWTd), LV relative wall thickness (RWT) and LV diastolic (LVD) function quantification. The study methodology was approved by the Ethical Committee. Statistical data processing was performed with SPSS.

Results: The prevalence of HT (66.3%) was higher than diabetes (50.2%, $p < 0.01$), hypercholesterolaemia (52.1%, $p < 0.01$), hypertriglyceridaemia (47.6%, $p < 0.01$) and it was higher in PAD patients with CLI (71.2%) comparative with PAD patients without CLI (53.4%, $p < 0.001$). We found symmetric or asymmetric concentric LV hypertrophy (RWT > 0.42) in 51.5% of PAD patients (53.6% in PAD patients with CLI versus 47.7% in PAD patients without CLI, ns). The prevalence of increase SWTd thickness (53.2%) was higher (53.8% in PAD patients with CLI versus 52.7% in PAD patients without CLI, ns; 10.6 ± 2.3 mm versus 10.5 ± 2.4%) than increase LVPWTd thickness (41.3%, $p < 0.01$), (38% in PAD patients with CLI versus 51.8% in PAD patients without CLI, $p < 0.001$; 10.1 ± 1.69 mm versus 10.2 ± 2.2 mm). LVD dysfunction was present in 36.2% of PAD patients (37.4% versus 35.1%, ns). The prevalence of diagnosed hypertensive cardiac disease in PAD patients increased from 3.1% on admission to 32.4% ($p < 0.001$).

Demographic and cardiac risk factors characteristics	PAD patients	PAD patients with CLI	PAD patients without CLI	Statistical significance CLI vs. non-CLI
Age (yrs.)	60.7±10.6	63.1 ± 9.4	60.4 ± 10.6	ns
Gender (male)	87.4 %	88.1%	85.8%	ns
Smoker	68.2%	70.3%	65.6%	$p < 0.1$
Diabetes mellitus	50.2%	63.5%	17.7%	$p < 0.001$
Hypertension	66.3%	71.2%	53.4%	$p < 0.01$
Hypercholesterolaemia (mg)	52.1%	47.7%	62.4%	$p < 0.01$
Hypertriglyceridaemia (mg)	47.6%	211 ± 46	220 ± 41	non-CLI vs. CLI
		56.8%	26.3%	$p < 0.001$
		129 ± 78	150 ± 59	

Cardiac ultrasound measurements	PAD patients	PAD patients with CLI	PAD patients without CLI	Statistical significance CLI versus non-CLI
LV hypertrophy	51.5%	53.6%	47.7%	ns
SWTd (mm)	53.2%	53.8%	52.7%	ns
		10.6 ± 2.3	10.5 ± 2.4	
LVPWTd (mm)	41.3%	38.5%	51.8%	$p < 0.01$
		10.1 ± 1.7	10.2 ± 2.2	
LVD dysfunction	36.2%	37.4%	35.1%	ns

Conclusions: High prevalence of HT in PAD patients (especially with CLI), correlated with the LV hypertrophy and diastolic dysfunction presence, reveal the need for sustained antihypertensive treatment in this usually undertreated group of patients.

CLINICAL CHARACTERISTICS, VASCULAR BED INVOLVEMENT AND VASCULAR COMPLICATIONS IN PATIENTS WITH FIBROMUSCULAR DYSPLASIA - POLISH REGISTRY FOR FIBROMUSCULAR DYSPLASIA (ARCADIA-POL)

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Objective: To assess the clinical characteristics, vascular bed involvement and vascular complications in patients with fibromuscular dysplasia (FMD) enrolled into on-going ARCADIA-POL study.

Design and method: Out of 250 patients enrolled into ARCADIA-POL study since January 2015 (instituted on the basis of Polish-French collaboration) we present 183 patients with confirmed FMD in at least one vascular bed. A standardized FMD data form was used for data collection. All patients underwent detailed clinical evaluation including ABPM, biochemical evaluation, biobanking, duplex Doppler of carotid and abdominal arteries and whole body angio-CT. In the following presentation we focused on data on the prevalence of vascular bed involvement and complications.

Results: In our analysis we included 183 patients with confirmed FMD (150F[82.0%], 33M[18.0%], mean age: 45.9 ± 15.0 years). 166 patients (90.7%) were hypertensives. The mean age at the diagnosis of hypertension was 35.6 ± 14.7 years and the FMD was diagnosed 6.8 ± 8.6 years later. In the analyzed group FMD was identified in renal arteries in 157 (85.8%) patient as well as in carotid, intracranial and vertebral arteries in 28(15.3%), 11(6.0%) and 15(8.2%) patients, respectively. FMD was also identified in celiac trunk and mesenteric, iliac and splenic arteries in 18(9.8%), 18(9.8%), and 4(2.2%) patients, respectively. Multisite FMD was found in 52 patients (28.4%). Two vascular beds were involved in 19.1%(35 pts), three in 4.9%(9 pts), four in 3.3%(4 pts), five and more in 1.0 % (2 pts). Arterial dissection(s) or aneurysms in various vascular beds were present in 15 (8.2%) and in 58 (31.7%) patients respectively. The most frequently dissections were found in carotid arteries (10 pts, 5.5%). Aneurysms were most often observed in renal and intracranial arteries, in 25 (13.7%) and 21 patients (11.5%).

Conclusions: The data of ARCADIA-POL registry showed that renal FMD was the most frequent, but also cerebrovascular FMD was found in relatively large proportion of patients. Our data revealed high incidence of FMD lesions coexisting in different vascular beds as well as relatively frequent occurrence of vascular complications.

YOUNG ISOLATED SYSTOLIC HYPERTENSION DIFFER ACCORDING TO THE LEVEL OF PHYSICAL ACTIVITY

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Objective: Little is known about the clinical significance and the management of isolated systolic hypertension in the young (ISHY). According to some authors ISHY is often associated with athletic participation and is considered at low cardiovascular risk whereas according to others ISHY subjects are characterized by increased BMI associated with metabolic abnormalities. The aim of the present study was to investigate whether in athletes ISHY has different clinical characteristics and better long-term evolution than ISHY in sedentary subjects.

Design and method: We examined 35 male athletes with ISHY (ISHY-Athl), with a mean age of 23.6 ± 7.0 years and blood pressure of 152.7 ± 12.0 mmHg and 35 age-matched sedentary ISHY subjects (ISHY-Sed). Thirty-five age-matched normotensives (NTs), and 35 subjects with systolic-diastolic hypertension- (SDH) were also enrolled. All these conditions were identified with ambulatory blood pressure (BP) monitoring. All data were re-measured after 8 years of follow-up.

Results: ISHY-Athl had lower 24 h heart rate than the other 3 groups (p for ANOVA = 0.001). In addition, they had higher stroke volume (89.2 ± 16.2 ml, $p < 0.01$ versus other 3 groups). Peripheral resistance was similar in ISHY-Athl and NT, whereas it was increased in the ISHY-Sed and SDH participants ($p < 0.05$). BMI and metabolic data at baseline did not differ between the 4 groups. After 8 years, changes in 24 h BP were similar in the ISHY-Athl and ISHY-Sed. Likewise, changes in BMI and metabolic data did not differ between these two groups.

Conclusions: Athletes with ISHY exhibited a different hemodynamic pattern characterized by elevated stroke volume and normal peripheral resistance compared to ISHY with sedentary habits. However, baseline BMI and metabolic profile and the evolution of BP and metabolic data in ISHY subjects did not differ according to physical activity habits.

ASSOCIATION OF NOVEL RISK FACTORS OF CARDIOVASCULAR DISEASE WITH BAPWV IN A LARGE COHORT OF ADULTS

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Objective: To clarify the association of triglyceride (TG), high- and low- density lipoprotein cholesterol (HDL-C and LDL-C), blood pressure, fasting plasma glucose (FPG), uric acid (UA), high sensitive C-reactive protein (hsCRP), and urine albumin-to-creatinine (UACR) with brachial ankle pulse wave velocity (baPWV), which has been reported as a potential surrogate marker of arterial stiffness, in the Japanese large cohort of adults.

Design and method: A total of 2,645 participants including 1,205 men (61.1 ± 9.9 years) and 1,440 women (61.2 ± 9.4 years) were enrolled in the present cross-sectional study. Systolic and diastolic blood pressure (SBP, DBP) were measured to obtain pulse pressure (PP). baPWV was measured using automatic device (BP-203RPE II form PWV/ABI, Omron Colin, Tokyo). Stepwise multiple regression analyses were performed adjusted for age, BMI, current smoking status, exercise habit, habitual alcohol consumption, and medication for hypertension, diabetes mellitus and dyslipidemia, including all indices shown above.

Results: Mean \pm SD of baPWV, SBP, DBP, PP, TG, FPG, hsCRP and UA were 1569.6 ± 366.1 (cm/sec), 131.2 ± 17.1 (mmHg), 77.3 ± 10.0 (mmHg), 54.0 ± 12.2 (mmHg), 139.8 ± 113.5 (mg/dL), 100.3 ± 20.3 (mg/dL), 0.09 ± 0.29 (mg/dL) and 5.8 ± 1.8 (mg/dL), respectively, in men, and 1486.6 ± 357.5 (cm/sec), 125.4 ± 18.1 (mmHg), 72.9 ± 10.0 (mmHg), 52.5 ± 12.5 (mmHg), 107.4 ± 68.2 (mg/dL), 94.7 ± 16.5 (mg/dL), 0.06 ± 0.19 (mg/dL) and 4.3 ± 1.3 (mg/dL), respectively, in women. In men and women, PP and FPG were significantly associated with baPWV ($P < 0.001$). In men, hsCRP showed significant association ($P = 0.002$). In women, TG showed significant association ($P < 0.001$). Since habitual alcohol consumption showed significant association in men ($P = 0.002$), those with or without this habit were analyzed separately. In men who drink alcohol beverage daily, UA showed significant association with baPWV besides PP and FPG ($P = 0.008$), whereas in men without this habit, hsCRP showed significant association besides PP and FPG ($P = 0.011$).

Conclusions: These results suggest that PP and FPG may correlate with arterial stiffness in both sex, and there may be sex differences in the influence-factors of arterial stiffness.

HYPERTENSIVE URGENCIES AFTER AN EMERGENCY CALL FOR A GENERAL PRACTITIONER HOME VISIT

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Objective: Research on hypertensive urgencies have been mainly studied after referral to the hospital. Their incidence, characteristics and management need to be investigated outside the hospital.

Design and method: Through a dedicated regional phone number (Urgentist general practitioner's), all people living in France may call for an urgency medical visit at home when considered as necessary by them or their family. These private Physicians associations cover 60% of the French territory. From January 1st 2010 to December 31st 2016, 15,095,682 emergency diagnostics at home visits have been performed after a telephone call.

Results: Among the 6,386,724 diagnostics concerning men, 20,762 have been attributed by the visiting physician to hypertension as the main cause of the urgency call (0.33%) versus 55,961 among 8,708,958 for women (0.64%). Median age of men was 68 years and of women 77 years. This sex difference persists over the time. It does not exist in hypertension population surveys. It is observed for hypertension as for most home visit causes and is more marked after an age of 62. Physicians requested hospitalizations for hypertension in 10.0% of these men and 9.1 % of these women. By comparison, during this seven-year interval, 12,697 (0.20%) diagnosis of cerebro vascular accident was made in men (hospitalization 68.3%) and 20,739 (0.24%) in women (hospitalization 64.5%). Diagnosis of coronary heart disease was made in 8,634 (0.14%) of men (hospitalization 65.0%), and in 9,631 (0.11%) of women (hospitalization 58.6%).

Conclusions: Despite a major decrease of undetected, untreated and uncontrolled hypertension in population surveys, hypertensive urgencies are not a rare cause of emergency home visit. Standardized procedures concerning the use of drugs and the decision of transferring patients to the hospital will be helpful for physicians and informative for patients.

PREVALENCE OF HYPERTENSION AND RISK FACTORS IN 47000 POPULATION FROM MULTI-ETHNIC RURAL, PASTORAL AND URBAN XINJIANG CHINA

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Objective: In China, estimated prevalence of hypertension is up to 41.9%, and the variations in demographic characteristics, cultural behaviors, and lifestyle habits vary substantially in different regions may result in differing disease prevalence in different populations. In remote less developed areas such as Xinjiang, patterns of hypertension may vary. In national sample analysis, it is difficult to perform strictly random proportional sampling, and to acquire a truly representative sample, given the vastness, the size of the population and multi-ethnic background. An accurate estimate of the hypertension prevalence and related risk factors is essential for the proper development of public health strategies by conducting regional studies.

Design and method: This is a cross-sectional study. This study, using population-based surveys of adults aged 18 years, was conducted in Xinjiang and the hypertension prevalence and associated risk factors in pastoral, rural and urban residents were compared.

Results: 47040 samples, with a response rate of 83.3%, were enrolled. The sex-age standardized hypertension prevalence was 25.4% in rural, 27.2% in pastoral and 28.2% in urban adults. Older age, overweight, obesity, non-agriculture or non- husbandry occupation, lower education, cigarette smoking and alcohol drinking were significantly associated with hypertension among pastoral, rural and urban adults. Nonetheless, females within rural setting were associated with higher hypertension prevalence. Kazakh and Mongolian subjects in rural setting were associated with higher risk for hypertension existence, and it was the same for Kazakh subjects in pastoral and urban Xinjiang, compared with Han subjects. The hypertension-associated risk was 1.74 times in urban area, compared with that of rural population.

Conclusions: The highest hypertension prevalence is observed in urban Xinjiang. Contributory factors for hypertension show some variations in pastoral, rural and urban settings. Taking into account the variations in the risk factors may provide greater insight into the design of future prevention strategies.

NATIONAL PREVALENCE OF HYPERCHOLESTEROLEMIA, TREATMENT AND CONTROL, IN FRANCE IN 2015 AND TEMPORAL TRENDS SINCE 2006

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Objective: The aims of this public-funded and representative study were to assess prevalence diagnosis, treatment and control of hypercholesterolemia LDL in the adult population in France in 2015 and to describe temporal trends between 2006 and 2015.

Design and method: The Esteban survey is a cross-sectional survey based on a multistage sampling design and conducted in continental France in 2015–2016. The design was the same as the one of the 2006-survey. Both samples were representative of the French adult population (18–74 years). Lipids concentrations were measured in a national sample of non-institutionalized adults during a health examination. LDL-cholesterol (LDLc) was determined by the Friedewald equation only if triglycerides were lower than 3.4 g/l. Sociodemographic characteristics and risk factors were collected by questionnaires. Lipid-lowering treatments during the year preceding the survey came from the reimbursement databases of the national health insurance inter-scheme information system. Hypercholesterolemia LDL was defined as LDLc greater than 1.6 g/l, or a reimbursement for lipid-lowering drugs. Analyses were weighted and adjusted.

Results: LDLc was determined in 2,074 adults (44.8% of men). The mean LDLc was 1.30 g/l (CI95% [1.28–1.32]). One adult in five had LDLc > 1.6 g/l and 8.8% had a reimbursement for lipid-lowering drugs (statins: 7.5%). The prevalence of hypercholesterolemia LDL was 27.0% [24.5–29.5] and increased with age, reaching 48.4% in adults aged 65–74 years, and was higher in men (29.7%) than in women (24.5%). Between 2006 and 2015, mean LDLc and the proportion of adults with a LDLc > 1.6 g/l were stable ($p = 0.5$ and $p = 0.09$, respectively). We observed a 18% decrease in the prevalence of hypercholesterolemia LDL ($p < 0.001$) and a 33% decrease in the proportion of adults having a reimbursement for lipid-lowering drugs ($p < 0.0001$).

Conclusions: Despite a significant decrease in the prevalence of hypercholesterolemia LDL observed during the past decade, it remains high in France. Our study suggested that this decrease could be linked to changes in the lipid-lowering drugs prescription. Further analyses are necessary to investigate this hypothesis.

THE 22-YEAR PROSPECTIVE QUEBEC (PROQ) STUDY ON WORK AND HEALTH CONDUCTED AMONG 9000 WHITE-COLLAR WORKERS

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Objective: Cardiovascular diseases (CVD) are the leading cause of mortality worldwide accounting for 17.7 million deaths per year. Mental health problems (MHP) are the first cause of disability worldwide. Their prevalence, long duration and high risk of recurrence place a considerable burden on health and social care systems and important productivity losses for employers. The PROspective Quebec (PROQ) Study on Work and Health is a prospective cohort initiated in 1991–93 to further extend our comprehension of the effect of work stressors on cardiovascular and mental health outcomes.

Design and method: At baseline (1991–1993), the study population involved 9,189 white-collar workers aged 18 to 65 years-old employed by 19 specific public organizations in Quebec City. At the first follow-up, 8 years later (1999–2001), 8,121 workers agreed to participate again corresponding to 89% of the initial sample. The 22-year follow-up (2015–18) is currently ongoing. This second follow-up includes measurements at later life of a large number of cardiovascular and mental health outcomes as well as their major risk factors, including blood pressure.

Results: Data collection procedures are a self-reported questionnaire, an interview, biological variables and medico-administrative databases extractions. This prospective cohort will fill important research gaps related to: 1) the pathways by which adverse psychosocial work stressors cumulated over the working life could lead to higher risk of cardiovascular diseases (CVD) and mental health problems (MHP) at older ages, 2) the effects of psychosocial work stressors on novel subclinical markers of disease risk (aortic stiffness, inflammatory markers, telomere length, cognitive function) and 3) the costs of CVD and mental health problems attributable to work stressors.

Conclusions: This cohort is one of the most rigorous and extensive occupational cohorts in the world. The results will contribute substantially to the primary prevention of CVD and MHP.

INCREASED ALL-CAUSE MORTALITY, TOTAL CARDIOVASCULAR DISEASE AND MORBIDITY IN HOSPITALIZED OCTOGENARIANS WITH ORTHOSTATIC HYPOTENSION

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Objective: Orthostatic hypotension is a common finding in elderly patients and is associated with significant morbidity and mortality. Most of the knowledge on orthostatic hypotension and cardiovascular endpoints and mortality comes from prospective cohort data and there are few clinical studies performed in octogenarians.

Design and method: From the year 2014 until May of the year 2017 a team composed of a physiotherapist and an occupational therapist supervised by a medical doctor visited newly hospitalized patients at Lund's University Hospital. The team measured BMI, blood pressure, pulse, saturation and registered the patients' age, sex, number and types of medications and symptoms for admittance. They were also able to register blood tests taken, the patients' final diagnosis, the number of days in hospital, the number of medications at discharge, the number of re-hospitalizations and the number of deaths at follow-up after 6 months. Patients with complete blood pressure measurements both in the lying position and standing position were included in our study ($n = 210$). These patients were divided into two groups, the orthostatic hypotension group ($n = 119$) and the normotensive group ($n = 91$). Mean age was 83 years.

Results: During follow-up 14 of 91 patients died in the normotensive group compared to 32 of 119 in the orthostatic hypotension group ($p < 0.05$). At discharge 41 of 91 patient had been diagnosed with cardiovascular disease in the normotensive group compared to 70 of 119 patients in the orthostatic hypotension group ($p < 0.05$). The patients in the normotensive group stayed at the hospital for a mean of 8,38 days compared to the patients from the orthostatic hypotension group whom stayed for a mean of 9,86 days ($p < 0.05$).

Conclusions: This study has shown that there is increased cardiovascular disease, morbidity and mortality in elderly patients with orthostatic hypotension compared to patients without orthostatic hypotension in a hospital setting. The study results indicate the importance of taking orthostatic blood pressure tests in elderly patients.

ASSOCIATION BETWEEN SLEEP COMPLAINTS AND CAROTID ATHEROSCLEROTIC LESIONS

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Objective: Sleep deprivation is discussed as a cardiovascular risk factor, however, its association with cardiovascular mortality and morbidity is controversial. We assessed the relation between self-reported sleep complaints and carotid atherosclerotic lesions.

Design and method: In this analysis, we included 861 (320 males, 37.2%) out of 1600 participants of the St Petersburg population-based sample (within the ESSE-RF study) without previously known cardio/cerebrovascular events. Mean age – 44.9 ± 11.9 years old. Mean body mass index: 26.9 ± 5.3 kg/m². All participants underwent a structured interview regarding their lifestyle, complaints, medical history, and sleep complaints. In this analysis, we considered the following questions: “How often did you have difficulties in falling asleep for > 30 minutes after going to bed in the last month?”, “How often did you have difficulties in falling asleep after midnight awakening in the last month?”. The answers “> 1/week” were considered symptomatic. In addition, we measured office blood pressure (BP) and performed a standard duplex ultrasound protocol (My Sono U6, Samsung, Korea) to evaluate carotid intima-media thickness (IMT) (normal: < 0.9 mm, abnormal: 0.91–1.29 mm) and atherosclerotic plaques (local thickening > 1.3 mm). We applied parametric statistics (t-Student, chi-square tests), Spearman correlation analysis.

Results: In total, 362 subjects (42%) reported at least one sleep complaint. The atherosclerotic plaques were found in 15 subjects (1.7%). The plaques presence was associated with awakenings (chi-square 9.04, $p = 0.005$). Abnormal IMT was found in 83 subjects (9.6%). Subjects with sleep-related complaints showed higher IMT values (0.71 ± 0.18 vs. 0.67 ± 0.16 in insomniacs vs. non-insomniacs, $p = 0.001$). However, there was no association between the rates of sleep complaints and abnormal IMT ($p = 0.24$). Correlation analysis demonstrated a weak association between mean IMT and sleep complaints ($r = 0.11$, $p = 0.001$), which disappeared after adjustment for age and BP.

Conclusions: In a large epidemiology cohort, we demonstrated an association between sleep complaints and carotid atherosclerosis. However, their role seems to be minor compared to the traditional cardiovascular risk factors, although potential mechanisms and benefits of insomnia treatment deserve further investigation.

THE INFLUENCE OF ANNOYANCE DUE TO NOISE ON RENAL HEMODYNAMIC

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Objective: Epidemiological studies have found a link between noise exposure and increased incidence of arterial hypertension and cardiovascular disease. The kidney as long-term regulator of blood pressure might play a role in the underlying pathophysiological mechanism. The aim of this study is to investigate the influence of annoyance due to noise on renal hemodynamic in hypertensive and healthy subjects.

Design and method: We analysed the influence of annoyance due to noise on renal hemodynamic (measured using steady state input clearance with infusion of paraaminohippuric acid and inulin, respectively) in 79 healthy normotensive subjects (NT) and 34 drug-naïve subjects with hypertension stage 1 or 2 (HT). All subjects ranked subjective annoyance due to noise in everyday life on a 7 grade likert scale. The median of all rankings was used as cut off point to divide the group into annoyed and non-annoyed subjects.

Results: The prevalence of subjects with annoyance due to noise was higher in HT (25 out of 34 [73.5%]) compared to NT subjects (33 out of 79 [41.8%], $p = 0.04$). There was no difference in office blood pressure ($124 \pm 8.2/75 \pm 7.8$ vs $124 \pm 7.4/73 \pm 6.4$ mmHg, $p = 0.52/0.32$) and heart rate (69 ± 1.4 vs 66 ± 9.0 bpm, $p = 0.09$) between annoyed and not-annoyed NT subjects. Annoyed NT subjects showed lower renal plasma flow (635 ± 95.7 vs 685 ± 116 ml/min, $p = 0.04$) compared to not-annoyed subjects. There was no difference in glomerular filtration rate between annoyed and not-annoyed NT subjects (133 ± 12 vs 138 ± 15 ml/min, $p = 0.12$). There was also no difference in office blood pressure ($145 \pm 8.4/87 \pm 11$ vs $148 \pm 11/72 \pm 11$ mmHg, $p = 0.34/0.07$) and heart rate (73 ± 13 vs 72 ± 8.5 bpm, $p = 0.76$) in annoyed and not-annoyed HT subjects. In HT subjects there was no difference in renal plasma flow (553 ± 102 vs 552 ± 106 ml/min, $p = 0.99$) and glomerular filtration rate (132 ± 12 vs 136 ± 14 ml/min, $p = 0.52$) between annoyed and not-annoyed subjects.

Conclusions: Annoyance due to noise in everyday life was found more frequently in HT compared to NT subjects and was associated with lower renal plasma flow in NT but not HT subjects. Our data suggest the hypothesis that annoyance due to noise triggers early renal changes in NT subjects potentially leading to hypertension.

FEASIBILITY OF ESTIMATING FIBROMUSCULAR DYSPLASIA PREVALENCE USING HEALTH ADMINISTRATIVE DATABASE: A NATIONWIDE STUDY

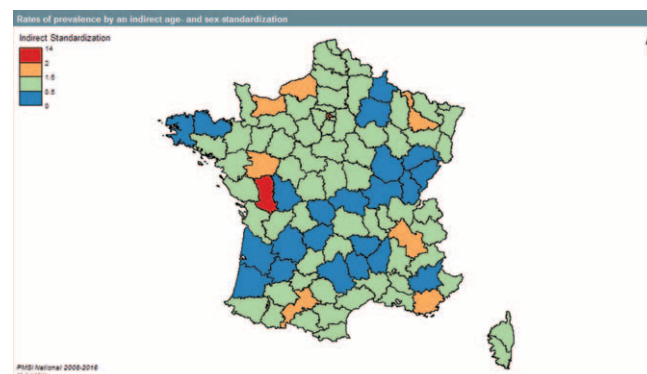
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Objective: Fibro-muscular dysplasia (FMD) is a non-atherosclerotic and non-inflammatory vascular disease, occurring mainly in women aged 30–50 years. Its prevalence is not well-known and possibly underestimated due to asymptomatic forms. Our aim was to determine whether the French national summary discharge database could be used to estimate the prevalence of FMD.

Design and method: Patients were selected by the first occurrence of the I773 ICD-10 code. This code was chosen after an exploratory analysis and advice from national hypertension specialists. In the French national summary discharge database system, all hospitalizations can be linked for a given patient. The zip code of residence was used for geographical analysis. We computed rates of prevalence by an indirect age- and sex-standardization.

Results: Between 2008 and 2016, we identified 2798 patients (65.2% female; median age 55y IQR = [43.0–67.0]), for a total of 10835 stays (74.9% of patients had less than 2 stays) of which only 4061 contained the I773 code. No major change in annual incident cases was observed between 2008 to 2016: 317 (11.3%), 342 (12.2%), 292 (10.4%), 309 (11.0%), 299 (10.7%), 319 (11.4%), 294 (10.5%), 279 (9.97%) and 347 (12.4%), respectively. The most common associated codes were

I10 (hypertension, 49.0%), I15.0 (vascular/renal hypertension, 19.7%) and E780 (essential hypercholesterolemia, 11.9%). Among all French hospitals, the largest number of patients was identified in the Paris University Hospitals, especially ESH excellence centers (15.7%) and 8 additional University Hospitals belong to the 'top 10' recruiting centres. Using indirect standardization, we observed a geographical disparity with a low prevalence in the East/South-West part of France, which may indicate under-diagnosis of the disease and a very high unexplained prevalence in a single hospital.



Conclusions: Both the stable estimate of yearly incident cases and demographic characteristics of the population study are consistent with the literature. Nevertheless, the observed geographical disparity suggests a diagnostic bias. We conclude that the use of the French national summary discharge database alone cannot provide a reliable estimation of the FMD prevalence. Both harmonization of diagnosis procedures and hospitalization coding could help identifying FMD patients in addition to existent multicentric registries.

TRENDS IN THE USE OF CARDIOVASCULAR PREVENTION TREATMENTS IN FRANCE BETWEEN 2007 AND 2017 USING THE FRENCH LEAGUE AGAINST HYPERTENSION SURVEYS

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Objective: To observe the trends in the use of cardiovascular treatments for hypertension, dyslipidemia and diabetes resulting of consecutive French League against hypertension surveys.

Design and method: The FLAHS surveys are carried out by self-questionnaire sent by mail to individuals from the Kantar Health (representative panel of the population living in metropolitan France) sampling frame. Three surveys have been carried out in 2007, 2012 and 2017 in subjects aged 35 years and older. The questionnaire included questions related to treatment of hypertension, dyslipidemia and diabetes with medications. Number of participants in FLAHS 2007, 2012, and 2017 were 3229, 3462 and 4783 respectively.

Results: Results: In 2007, prevalence in subjects aged 35 years and older for treated hypertension was 32% [IC 95, 30–34], for treated dyslipidemia was 22% [IC 95, 19–25], for treated diabetes was 8% [IC 95, 5–11]. In 2012, prevalence were respectively: 30% [IC 95, 28–33], 22% [IC 95, 20–25], and 8% [IC 95, 5–11]. In 2017, prevalence were respectively: 28% [IC 95, 26–30], 17% [IC 95, 14–19], and 9% [IC 95, 6–11]. Calculated on the French national census in 2017, the number of subjects treated for hypertension and/or dyslipidemia and/or diabetes in 2007 was 13.6 millions [IC 95, 12.8–14.6]. Between 2007 and 2017, number of treated patients decreased from 8.3 to 6.4 millions for dyslipidemia and from 11.2 to 10.8 millions for hypertensives.

Conclusions: In France, the use of cardiovascular treatments for hypertension, dyslipidemia and diabetes has changed between 2007 and 2017. A decrease in the prevalence of treatments for hypertension and dyslipidemia is observed in the population of 35 years and older. Monitoring of cardiovascular morbidity and mortality indicators will make it possible to judge the consequences on the health of the population.

AN EDUCATIONAL THERAPEUTIC PROGRAM OF THE FRENCH NATIONAL HEALTH INSURANCE FUND (CNAM) FOR HYPERTENSIVE AND/OR DYSLIPIDEMIC FRENCH PATIENTS: FIRST RESULTS

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Objective: Aim: to improve the hypertensive and/or dyslipidemic French patients' awareness in their health problems and to favor a healthier life-style, a better Blood Pressure (BP) and lipid control, and a better patient's compliance.

Design and method: Methods: this educational program realized by the CNAM in association with the French Federation of Cardiology and the French National Committee Against Hypertension contains an educational assessment, four workshops: cardiovascular risk, physical activity and nutrition, stress and tobacco, treatment and home BP measurement, and an individual follow-up of 18 months.

Results: this program has been proposed to 2343 patients distributed in 16 centers, 844 (44 %) agreed to participate. Average age: 61 years, 52 % of women, 21 % workers, 65 % couple living, 60 % of the patients had one or two cardiovascular risk factors and 40 % both (hypertension and dyslipidemia).

The office BP control (<140/90 mm Hg) was 31 % for men and 42 % for women. The abdominal obesity (BMI > 30) occurred in 41 % for men and 26 % for women. LDL control (<1,3 g/l) under treatment was obtained in 52% in men and 38% in women. 12 % of the subjects are smokers, 30 % felt moderate stress. A good therapeutic observance assessed by a specific questionnaire was found in only 44 %.

Conclusions: Conclusion: BP and lipid controls are insufficient in this French cohort at the beginning of the program, associated with a poor observance. These results emphasize the need to provide more systematically a specific therapeutic education program to moderate risk patients (European score risk). An evaluation of the first 1000 patients will be made in 2018 to improve data collection and to perhaps allow an extension of this national program by CNAM.

FEATURES OF 24-HOUR BLOOD PRESSURE PROFILE, VASCULAR WALL STIFFNESS PARAMETERS AND MARKERS OF VASCULAR INFLAMMATORY REACTION IN POSTMENOPAUSAL FEMALE PATIENTS

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Objective: To study the relationship of 24-hour blood pressure profile, vascular wall stiffness parameters, sex hormone profile, parameters of lipid profile and vascular inflammatory markers in postmenopausal female patients with arterial hypertension (AH).

Design and method: 57 postmenopausal women (mean age 58.23 ± 6.45 years) with AH of moderate and high cardiovascular risk were included in the study. All patients underwent 24-hour blood pressure monitoring and sphygmography. Pulse wave velocity for elastic arteries on the right or the left (PWV-R/L), cardio-ankle vascular index (CAVI), ankle-brachial index (ABI); parameters of the lipid profile; inflammatory markers and sex hormone profile were measured.

Results: AH in postmenopausal female patients are associated with increase in blood pressure variability, increased pressure loading, disturbance of 24-hour blood pressure rhythm, great vessels rigidity ($p < 0.05$), low level of estrogen ($p < 0.001$) and increased level of total cholesterol, triglycerides, LDL-cholesterol, APO-B ($p < 0.01$), C-reactive protein, TNF-alpha, endothelin-1, IL-6 and uric acid ($p < 0.05$). The following positive correlations were found: between PWV-R and systolic blood pressure and diastolic blood pressure variability at night and systolic blood pressure variability in the daytime, IL-6, ($p = 0.047$), homocysteine ($p = 0.015$), APO-B ($p = 0.048$), age ($p = 0.01$); negative correlation with progesterone. In addition, positive correlations were found between ABI-R and uric acid ($p = 0.05$), systolic blood pressure variability in the daytime ($p = 0.02$).

Conclusions: The parameters of 24-hour blood pressure profile are associated with target organ damage, in particular, with vascular wall stiffness, sex hormone profile and vascular inflammatory reaction in postmenopausal female patients, which can determine the course of hypertension and the development of cerebral and cardiovascular complications.

AUTONOMIC DYSREGULATION IN PRIMARY HYPERTENSION

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Objective: Introduction: Would cardiovascular autonomic reflexes help in understanding the diagnosis and the management of primary hypertension (PHT). The purpose of this study was to evaluate the cardiovascular autonomic reflexes in patients with primary hypertension (PHT), including masked hypertension (MHT), hypertension with type 2 diabetes (DHT), orthostatic hypertension (OHT) and orthostatic hypotension (OHypT).

Design and method: Patients and Methods. This prospective study included two groups: normotensive group, NT (N = 120) and primary hypertensive group, PHT (N = 120). The PHT group was divided in different subgroup: N1 = subgroup of MHT, N2 = subgroup of DHT, N3 = subgroup of OHT and N4 = subgroup of OHypT. The PHT group as well as the subgroups were compared to NT group. The cardiovascular autonomic tests performed in these groups, included deep breathing (DB), hand-grip (Hg), mental stress (MS) and orthostatic (Orth) tests. Statistical analysis was done using the Student's t-test.

Results: Results. Cardiovascular autonomic reflexes responses were as follows: Compared to NT,

1. Central alpha adrenergic response to mental stress test was of $20.0 \pm 9.8\%$ vs $15.2 \pm 8.6\%$ ($p < 0.001$) in PHT; $24.7 \pm 7.2\%$ vs $15.2 \pm 4.5\%$ ($p < 0.001$) in MHT; and $23.48 \pm 9.82\%$ vs $20.28 \pm 9.60\%$ ($p = 0.243$) in DHT.
2. Peripheral alpha adrenergic response to hand grip test of $16.7 \pm 7.5\%$ vs $13.3 \pm 6.5\%$ ($p < 0.001$) in PHT; $27.0 \pm 5.4\%$ vs $16.4 \pm 4.5\%$ ($p < 0.001$) in MHT; and 20.03 ± 8.05 vs $21.71 \pm 11.23\%$ ($p = 0.588$) in DHT.
3. Vagal response to deep breathing test was of $30.2 \pm 8.1\%$ vs $46.1 \pm 2.1\%$ ($p < 0.001$) in PHT; $30.5 \pm 10.4\%$ vs $32.7 \pm 11.3\%$ ($p = 0.1$) in MHT; and $23.09 \pm 11.06\%$ vs $34.15 \pm 17.7\%$ ($p < 0.001$) in DHT. Of interest orthostatic test showed that 70% of PHT had orthostatic hypertension and 15% orthostatic hypotension.

Conclusions: Conclusion. PHT, hypertensive with type 2 diabetes, MHT have a significantly higher sympathetic response when compared to controls and vagal response significantly lower. The latter is accentuated by the association of diabetes to hypertension. The results attest that cardiovascular autonomic reflexes study is of high interest in assessing PHT

AN EASY STRATEGY TO MANAGE NIGHT CRAMPS ASSOCIATED TO STATIN ASSUMPTION: RESULTS FROM A REAL PRACTICE STUDY

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Objective: Night cramps associated to statin assumption are a relatively frequent adverse event, strongly disturbing and often cause of statin interruption. The aim of our study was to evaluate if the displace of statin assumption from evening (conventional one) to morning has been associated to change in night symptomatology.

Design and method: For the purpose of this study, we retrospectively evaluated 3200 ambulatory CRFs. Selection criteria were: patients claiming night cramps since the assumption of statins at evening, modification of the statin prescription (molecule or timing of administration), verification of the symptomatology at a next visit.

Results: In total we identified 129 patients claiming cramps from the statin assumption at evening. 64 of them also claimed cramps or myalgia during the day. 68 patients interrupted the treatment. We identified two main management strategy: 62 patients were prescribed the same statin at the same dosage but displacing its assumption at morning (group A). 67 patients were prescribed a different statin (lower power or lower dosage) at evening (group B). The result was that in the group A 53 subjects declared the disappearance of the night cramps, while the remaining 9 ones just a reduction in frequency and intensity (all of these subjects were also claiming daily cramps and/or myalgia). No significant change in LDL-cholesterolemia control was observed. In group B, cramps were maintained (same intensity and frequency) in the 50% of cases (24 of them interrupting again the treatment before the control visit). The ones experiencing a reduction of the

symptomatology however also experienced a small but significant increase in LDL-Cholesterol level.

Conclusions: In conclusion, shifting the statin assumption from evening to morning time improve symptomatology and persistence in therapy in patients with night cramps related to evening assumption of the statin, without a worsening of the LDL-cholesterol control.

PREVALENCE AND CONTROL OF HYPERTENSION WITH THE USE OF AMBULATORY BLOOD PRESSURE RECORDING IN HEMODIALYSIS PATIENTS

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Objective: To date, there is no commonly accepted definition for hypertension in patients with chronic kidney disease undergoing hemodialysis. A recent expert consensus suggests hypertension in dialysis to be defined based on ambulatory blood pressure monitoring (ABPM). The aim of this study is to evaluate the prevalence and control of hypertension using ABPM in a large hemodialysis population according to the latest definitions.

Design and method: A total of 160 hemodialysis patients underwent 48-hour ABPM, during a regular hemodialysis session and the subsequent interdialytic interval. Hypertension was defined as (i) pre-hemodialysis BP > = 140/90 mmHg or use of antihypertensive agents (ii) ambulatory BP > = 130/80 mmHg (over 44-hours or over the second 24-hour period) or use of antihypertensive agents. Phenotypes of hypertension control were defined as: 1) concordant control (pre-hemodialysis BP < 140/90 mmHg and ambulatory-BP < 130/80 mmHg), 2) concordant lack of control (pre-hemodialysis BP > = 140/90 mmHg and ambulatory-BP > = 130/80 mmHg), 3) "white coat" phenomenon (pre-hemodialysis BP > = 140/90 mmHg and ambulatory-BP < 130/80 mmHg) and 4) masked hypertension (pre-hemodialysis BP < 140/90 mmHg and ambulatory-BP > = 130/80 mmHg).

Results: Based on pre-hemodialysis BP levels, the prevalence of hypertension was 91.3%. Based on the ABPM covering the total 44-hour or the 2nd 24-hour interdialytic period, the prevalence was 88.8%. The proportion of hypertensive

patients receiving treatment was 124 (84.9%). With the use of pre-hemodialysis BP and ABPM during 44-hours, 12 (10.1%) of hypertensive patients had concordant BP control, 87 (58.8%) of patients had lack of control, 29 (19.6%) had a white-coat phenomenon, and 17 (11.5) masked hypertension, respectively. In multivariate logistic regression analysis, only use of antihypertensive agents was independently associated with increased odds for lack of control (reverse causation).

Conclusions: Hypertension prevalence in hemodialysis patients is overwhelmingly high. The rates of control rates are different when calculated from office and ambulatory BP recordings. In the population studied, almost one out of three patients had white-coat or masked hypertension.

THE EFFECT OF GENDER ON RIGHT VENTRICULAR DEFORMATION IN UNTREATED HYPERTENSIVE PATIENTS

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Objective: The purpose of this investigation was to evaluate the effect of gender on right ventricular (RV) strain in hypertensive individuals.

Design and method: This cross-sectional investigation involved 178 untreated hypertensive subjects and 94 normotensive controls. All study participants underwent 24-hour ambulatory blood pressure monitoring and detailed echocardiographic assessment that included strain evaluation.

Results: The difference in 24-h blood pressure was not found between hypertensive men and women. RV wall thickness was higher among hypertensive participants, but there was no significant difference between hypertensive women and men (4.7 ± 0.5 vs. 4.9 ± 0.7 mm, $p = 0.108$). RV global longitudinal strain was significantly lower in hypertensive subjects comparing with controls (-22.8 ± 2.6 vs. -25.6 ± 3.4 %, $p < 0.001$). RV global longitudinal strain was significantly lower in hypertensive men than in women (-21.4 ± 2.1 vs. -24.0 ± 3.1 %, $p < 0.01$). Layer-specific RV strain showed that endocardial and mid-myocardial longitudinal strains were significantly lower in hypertensive population. Additionally, RV endocardial longitudinal strain was significantly lower in hypertensive men than in hypertensive women (-23.2 ± 2.8 vs. -25.8 ± 3.4 %, $p < 0.001$). Female gender and arterial hypertension and their interaction were related with reduced RV global and endocardial longitudinal strain.

Conclusions: RV longitudinal strain and RV layer-specific endo- and mid-myocardial strains were significantly reduced in hypertensive patients. Female gender was associated with significantly higher risk of decreased RV longitudinal and endocardial strain.

POSTER SESSION

POSTERS' SESSION PS02:

PHARMACOLOGICAL TREATMENT

ASSESSMENT OF SUITABLE ANTIHYPERTENSIVE THERAPIES: COMBINATION WITH HIGH DOSE AMLODIPINE/IRBESARTAN VS. TRIPLE COMBINATION WITH AMLODIPINE/IRBESARTAN/INDAPAMIDE (ASAHI AI STUDY)

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Objective: Angiotensin receptor blockers (ARBs) plus calcium channel blockers (CCBs) are a widely used combination therapy for hypertensive patients. This study aimed to determine which combination was better as the next step therapy: a combination with high dose CCBs or a triple combination with diuretics.

Design and method: We conducted a prospective, randomized, open-label trial. Hypertensive outpatients who did not achieve their target blood pressure (BP < 140/90mmHg) with usual dosages of ARBs and amlodipine 5 mg were randomly assigned to switch treatment to Irbesartan 100 mg/amlodipine 10 mg (group ARB+C: n = 30, aged 65 ± 14 years) or indapamide 1 mg in addition to ARBs+ amlodipine 5 mg (group ARB+C+D: n = 29, aged 68 ± 9 years). The primary endpoint was any change in the systolic blood pressure (SBP) and diastolic blood pressure (DBP) after the 3-month treatment period, while secondary endpoints were any change in the BP after the 6-month treatment period and laboratory values. We also evaluated the blood pressure variability including the seasonal variation in both groups.

Results: At three months, the SBP/DBP significantly ($p < 0.01$) decreased from 150/80 ± 8/12mmHg to 132/73 ± 13/11mmHg in group ARB+C and 153/81 ± 11/14mmHg to 129/74 ± 16/12mmHg in group ARB+C+D. Similarly, at six months, the SBP/DBP significantly decreased to 132/74 ± 12/10mmHg in the ARB+C group, and to 128/73 ± 12/12mmHg in the ARB+C+D group. The serum potassium tended to decrease and uric acid to increase in the ARB+C+D group. When each treatment group was subdivided into four seasonal groups according to the season in which patients were assessed, there were no significant differences in the BP values between the four treatment groups. On the other hand, the visit-to-visit variability, evaluated by the SD or CV for the systolic BP, was higher in the ARB+C+D group than ARB+C group especially in the summer.

Conclusions: High dose CCBs combined with ARBs and a triple combination with diuretics combined with CCB/ARBs produced a similar efficacy in reducing the BP. However, the change in the laboratory data and blood pressure variability were advantageous in the ARB+C group. The results from the ASAHI AI trial will provide new evidence for selecting optimal combination therapies for uncontrolled hypertensive patients.

CARDIOPROTECTIVE EFFECT OF THE RED PALM OIL SUPPLEMENTATION ON THE CARDIAC OXIDATIVE STRESS, NITRIC OXIDE SYNTHASE AND HEART FUNCTION IN THE RATS SUFFERING FROM HYPERTENSION

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Objective: We know from our previous study that myocardial protein connexin 43 (Cx43), responsible for intercellular communication, and protein kinase C epsilon which directly phosphorylates Cx43 on the serine 368, were significantly decreased in spontaneously hypertensive rats (SHR) what was also associated with increased incidence to malignant arrhythmias. Antioxidant rich red palm oil (RPO) significantly normalized all of these parameters. Therefore, we further aimed to investigate whether intake of RPO may affect endothelial dysfunction, antioxidant enzymes and heart function in SHR.

Design and method: In accordance with the rules issued by the State Veterinary Administration of the Slovak Republic and European Union Council Directive 86/609/EEC we used in our experiment 3-months-old, male SHR and normotensive Wistar-Kyoto control rats fed standard rat chow without or with RPO (0.2 ml/day/5 weeks). Left ventricular tissue was used to examine expression of anti-oxidant enzymes such as superoxide dismutases (SOD1, SOD2) and glutathione peroxidases (GPx) as well as activity of nitric oxide synthase (NOS). Functional parameters of the heart were measured during basal conditions and at the early-phase of post-ischemic reperfusion by Langendorff-perfused system.

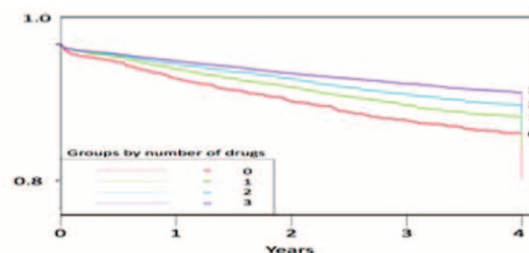
Results: RPO supplementation significantly normalized higher blood pressure and total NOS activity as well as increased lowered expression of mitochondrial SOD2 in SHR hearts during basal condition. RPO intake resulted in the suppression of elevated heart rate, increase of reduced coronary flow and enhancement of systolic and diastolic heart function at the early-phase of post-ischemic reperfusion.

Conclusions: We can conclude that SHR benefit from RPO intake due to its apparent anti-arrhythmic effects by Cx43 modulation, reduction of blood pressure, enhancement of oxidative stress and protection of heart function that was deteriorated by post-ischemic reperfusion.

IMPACT OF CARDIOVASCULAR DRUG ON ALL-CAUSE MORTALITY IN SECONDARY PREVENTION. A POPULATION STUDY

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Objective: Drug treatment for secondary prevention of cardiovascular disease is an establish 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 impact on mortality of the gap in subjects after stroke or transitory ischemic attack (TIA), myocardial infarction (MI) or coronary revascularization (REV) based on Electronic Health Records (EHR).



NUMBER DRUGS	SUBJECTS	CASES	HR (CI 95%) Model 1	HR (CI 95%) Model 2	HR (CI 95%) Model 3
0	3803	313	Ref.	Ref.	Ref.
1	18714	1203	0.84 (0.75, 0.96)	0.81 (0.71, 0.93)	0.83 (0.73, 0.95)
2	30440	1604	0.71 (0.63, 0.80)	0.67 (0.58, 0.77)	0.70 (0.60, 0.82)
3	39479	1544	0.61 (0.54, 0.70)	0.57 (0.49, 0.66)	0.61 (0.51, 0.74)

Design and method: Subjects and methods: Patients with a diagnosis of stroke, TIA, MI or REV after January 1st, 2012 were selected from the EHR of the Valencia Community which contain 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. All cause mortality was obtained from official sources during 1.7-1.5 years. In order to compare the survival time by groups, according the number of class of drugs, we used Cox proportional hazards models. The mortality in each group and the HR were adjusted for group of number of class of drugs (group 0, group1, group 2, group 3), age (continuous), gender (male, female), systolic blood pressure (continuous), LDL-cholesterol (continuous), HDL-cholesterol (continuous), diabetes treatment (yes, no) and diabetes (yes, no) (Model 1). We further adjusted for hypertension treatment (yes, no) and hypertension (yes,

no) (Model 2). We further adjusted for dyslipidemia treatment (yes, no) and dyslipidemia (yes, no) (Model 3).

Results: A total of 92436 patients (62% men, mean age 72 yr) were included, 55319 with stroke or TIA, MI 28311 and REV 8059. Among them, 4% were not taking drug of the three groups, 20% one, 33% two and 43% three. The HRs are in the table and the survival curves in the figure

Conclusions: In conclusion, the gap between guidelines and reality in the use of cardiovascular protecting drugs largely influence all cause mortality.

BISOPROLOL BETTER THAN ATENOLOL AS ADD ON THERAPY TO ACE INHIBITORS IN BLOOD PRESSURE CONTROL

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Objective: ACE-inhibitors (ACEi) are a first choice treatment in arterial hypertension as reported in European and American guidelines. However, in order to reach the optimal target blood pressure (BP), frequently adding another drug is needed.

The aim of this study is to evaluate whether the addition of a beta-blocker (BB) can lead BP to target and whether there is a difference between BBs

Design and method: We have recruited 2 groups of patients (pts) treated with ACEi who weren't to BP target. First group (Group A), (50 pts 23 F; 27 M, age 62,6) has started treatment adding atenolol while second group (group B), (50 pts 21 F, 29 M, age 62,12) bisoprolol. Comorbidities (hypercholesterolemia, diabetes and use of tobacco) were similar in the 2 groups. The doses of BBs were determined by the achievement of a 60 bpm mean heart rate. All pts monitored their BP at home (twice a day during a week) and 24 hours ambulatory monitoring (ABPM) was performed before and 1 month after the treatment.

Results: After 1 month 38 pts of the group A and 43 pts of the group B were to BP target. Furthermore, the systolic BP in group A decreased from 142,38 mm Hg to 131,17 mm Hg (-7,9%, p ns) and the diastolic BP from 89,44 mm Hg to 79,89 mm Hg (-10,7%); in group B systolic BP decreased from 142,83 mm Hg to 126,05 mm Hg (-11,7%) and the diastolic from 89,39 mm Hg to 75,04 mm Hg (-16,05%).

Pts didn't experience any side effects.

Conclusions: Our study demonstrated that adding bisoprolol to a ACEi reduced BP in more pts compared to atenolol allowing to reach target.

PPAR GAMMA STIMULATION BY ROSIGLITAZONE DECREASES BLOOD PRESSURE AND RENAL APOPTOSIS IN A RAT HYPERTENSION MODEL SECONDARY TO AORTIC COARCTATION

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Objective: Rosiglitazone (RGZ), a peroxisome proliferator-activated receptor gamma (PPARγ) ligand, has been reported to function like an insulin sensitizer and exerts cardiovascular actions. The activation of PPARγ has been described to have antiapoptotic effects in renal ischemia-reperfusion models. We hypothesized that RGZ exerts a PPARγ-dependent regulation of blood pressure and decreases kidney apoptosis in an experimental model of hypertension.

Design and method: We performed the experiments in normotensive (sham) and aortic coarctation (AoCo)-induced hypertensive male Wistar rats. Both sham- and AoCo rats were treated for 7 days with vehicle (V), RGZ (5 mg/kg/day) or RGZ plus BADGE (120 mg/kg/day). After treatment, we measured blood pressure and vascular reactivity on aortic rings as well as the expression and activity of renin-angiotensin system (RAS) components. To study the effect on renal apoptosis, we isolated the kidneys, separated both, cortex and medulla, and evaluated the expression of apoptotic (Bax) and anti-apoptotic proteins (14-3-3e, p-Akt and Bcl2) in both regions.

Results: RGZ in AoCo group decreased blood pressure values and improved vascular response to ACh in a PPAR dependent manner. RGZ lowered serum AngII but increased Ang-(1-7) levels. Also, RGZ decreased oxidative stress markers and improved antioxidant capacity. Regarding protein expression of ACE and AT1, it was lower in RGZ- than in vehicle-treated rats but the expression of ACE2,

MAS, and AT2 receptors was increased. Regarding renal apoptosis, in the cortex from AoCo-ischemic kidney Bax was increased, while 14-3-3e and PPARγ proteins were decreased. Treatment with RGZ, prevented PPARγ and 14-3-3e lower expression, however, it had no effect on Bax expression. With respect Bcl-2 expression was slightly increased in RGZ-treated group. These effects were not observed in medulla where proteins evaluated presented no differences in expression in all four groups.

Conclusions: We conclude that RGZ lowers blood pressure values by reducing the expression of ACE, decreasing the levels of AngII, and increasing levels of Ang-(1-7) in a PPARγ-dependent manner. RGZ decreases apoptosis in renal cortex and medulla in hypertensive rats. The increase of PPARγ, Bcl-2 and 14-3-3e observed in renal cortex could contribute to this effect.

CONTRIBUTION OF ENVIRONMENTAL POLLUTANTS TO EPIGENETIC MODIFICATION IN RAT VASCULAR SMOOTH MUSCLE CELLS

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Objective: More than a quarter of human diseases have been linked to exposure to environmental pollutants. These pollutants can exacerbate disease conditions through labile epigenetic modifications and directly result in changes in gene transcription. The most commonly reported epigenetic changes are acetylation and methylation of histone lysine. Contribution of acrolein, an environmental pollutant and a major component of cigarette smoke, to cardiovascular diseases and several neurological disorders has been reported. We have previously reported toxicity of acrolein in rat's vascular smooth muscle cells (VSMCs) and the effect of precursor of glutathione transferase, N-acetyl cysteine (NAC), in prevention of acrolein toxicity. In the present study, modification of histones and their effect on protein expression was further investigated in rat's VSMCs in the present/absent of acrolein and NAC.

Design and method: Design and method: VSMCs were treated with 3 mg/ml of acrolein for 6 and 24 hours in the present/absent of 0.2 mM NAC. At the end of the treatment, MTS assay, ELISA, western blot analysis, immunofluorescence, and LC/MS/MS analysis were used to check cells viability, superoxide dismutase (SOD) activity/expression, reactive oxygen species (ROS) generation, expression and cellular localization of H3K9 tri-methylation and acetylation, and identification of proteins affected by these changes.

Results: Results: Acrolein treated VSMCs exhibited the highest toxicity after 6 hours. Acrolein increased generation of ROS, reduced SOD activity and expression. There was 52% induction of acetylation and 62% in tri-methylation. Addition of N-acetyl cysteine reduced ROS, induced SOD (45%), reduced H3K9 acetylation by 102% and tri-methylation by 120%. These changes were confirmed with immunofluorescence staining. LC/MS/MS analysis revealed increased in actin protein and a significant decreased in annexin, heat shock cognate, and myosin 9 proteins.

Conclusions: Based on our data we are concluding that effect of acrolein on VSMCs is partially due to alterations of H3K9 methylation/acetylation, resulting in overexpression of actin and significant reduction of annexin, heat shock cognate, and myosin 9 proteins. Addition of 0.2 mM NAC resulted in prevention of toxicity by acrolein by reducing ROS, improving SOD and preventing changes in H3K9 acetylation and methylation.

EFFECTS OF GANAXOLONE ON BLOOD PRESSURE AND STRESS IN FEMALE BPH/2J GENETICALLY HYPERTENSIVE MICE

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Objective: Dysfunctional forebrain gamma-aminobutyric-acid type-A receptors (GABAARs) have been suggested to contribute to neurogenic hypertension in Schlager BPH/2J mice. Ganaxolone is a synthetic-form of the progesterone metabolite, allopregnanolone, an allosteric modulator of GABAARs that has reduced blood pressure (BP) in male BPH/2J mice. However, it is unknown whether ganaxolone is suitable to treat hypertension in females mice due to its related structure to progesterone.

Aim: To determine the cardiovascular effects of ganaxolone treatment in female BPH/2J mice.

Design and method: Female 12–13-week-old BPH/2J (n = 20) and normotensive (BPN/3J; n = 19) mice were implanted with a telemetry probe to record BP and heart rate. Cardiovascular responses to stress tests and pentolinium were measured before and after administering vehicle or ganaxolone (5 mg/kg/day via

subcutaneous minipumps) for two weeks. Vascular reactivity was measured using myography.

Results: Ganaxolone reduced BP of 9.9 mmHg ($P < 0.001$) in BPH/2J mice but there were no effects of vehicle or ganaxolone in BPN/3J mice. Depressor responses to pentolinium decreased by 32% ($P = 0.02$) and pressor responses during restraint (-40% , $P < 0.001$) and feeding (-40% , $P = 0.04$) stresses were reduced in ganaxolone-treated BPH/2J mice compared with pre-treatment. Whilst there were no differences in 24-hour BP in BPN/3J mice, there was an increased pressor response to dirty-cage switch stress ($+50\%$, $P < 0.001$).

Conclusions: Ganaxolone is effective in reducing hypertension and the cardiovascular response to stress in female BPH/2J mice but also appears to impair endothelial function. Therefore, targeting GABAARs with ganaxolone presents a novel treatment for stress-related hypertension.

PROSPECTIVE COMPARISON BETWEEN ADDITIONAL CCB OR DIURETICS ON TOP OF COMBINATION OF ARB AND CCB IN UNCONTROLLED HYPERTENSIVES (CHAT-ANA TRIAL)

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Objective: We investigated which choice will be more effective whether additional calcium channel blocker (CCB) or diuretic, even administration of routine dose CCB and angiotensin II receptor blocker (ARB) as a multi-center, prospective study.

Design and method: Hypertensives whose blood pressure (BP) couldn't achieve target BP referred to guideline were recruited. These patients already took routine dose ARB and Amlodipine (AM) 5 mg were divided into two groups. The patients were changed from combination of routine dose ARB and AM 5 mg to combination of Irbesartan 100 mg and AM 10 mg were defined as Group-1. The patients were changed to combination of Irbesartan 100 mg, AM 5 mg and Indapamide were defined as Group-2. Selection of assign depended on decision of each attending physician. These patients were followed for 6 month to monitor office BP.

Results: 85 Group-1 and 49 Group-2 patients were enrolled. After modification, systolic and diastolic BP decreased through 6 month in both groups ($p < 0.001$, respectively). In the same periods, depressor change of Group-1 SBP was greater compared with that of Group-2 in 1 and 6 month later ($p < 0.05$, $p < 0.05$, respectively). Although uric acid in Group-2 was increased in 3 month, this change disappeared in 6 month.

Conclusions: Although both choices demonstrated useful antihypertensive effect, loading AM to 10 mg might be respectable strategy for the uncontrolled hypertensives without serum uric acid increase.

EVALUATION OF THE EFFECTS OF MONACOLIN K ON LIPID PROFILE AND ARTERIAL FUNCTION IN DYSLIPIDEMIC PATIENTS

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Objective: dyslipidemia is the major Cardio-Vascular (CV) risk factor after hypertension. Some natural derivative molecules are able to improve the lipid profile, including monocolin K. This substance, which inhibits cholesterol synthesis, is produced by the fermentation of the red rice by a mycetes (Monascus Purpureus). Monocolin K is also known as lovastatin, but recent data show that compared to classic lovastatin, monocolin K would have a higher bioavailability, a greater efficacy at the same dosage and a satisfactory tolerability. Its role as an hypolipidemic therapy is accounted in guidelines but, to date, the effect on arterial functional and structural parameters has never been evaluated.

Design and method: we evaluated 20 patients (11 females) with mild to moderate dyslipidemia (LDL cholesterol between 100–160 mg/dL) before and after three months from monocolin therapy starting. Obesity, hypertension (defined as BP values $> 140/90$ mmHg or anti-hypertensive therapy) and alterate glycemic state Inclusion criteria were Patients were non-obese, normotensive and normoglycemic. Serum lipids, Blood Pressure (BP) and Pulse Wave Velocity (PWV – Complior).

Results: at baseline mean age was 43.4 ± 10.2 , BP $121 \pm 14/76 \pm 9.3$ and Heart Rate (HR) 67.2 ± 7.6 . Treatment lead to a significant reduction of total and

LDL cholesterol (total: 258.4 ± 25.9 versus 228.5 ± 28.4 mg/dL after 3 months, $p < 0.001$; LDL: 167.3 ± 31.2 versus 140.8 ± 25.2 mg/dL after 3 months, $p < 0.001$) and a significant improvement of arterial stiffness (PWV: 8.0 ± 1.4 versus 7.6 ± 1.2 m/s after 3 months, $p = 0.02$). No significant differences were seen for Systolic BP (121 ± 14 versus 118.3 ± 15.5 mmHg after 3 months, $p = ns$) and HR (67.2 ± 7.6 vs 69 ± 5.1 bpm after 3 months, $p = ns$) while a slight improvement for Diastolic BP (76 ± 9.3 vs 72.8 ± 8.3 mmHg after 3 months, $p = 0.004$) was found.

Conclusions: the results of the present study confirm that the treatment with monocolin K reduces significantly the levels of total and LDL cholesterol. They also show that a so brief treatment course of only 3 months induces an improvement in arterial function as showed by the reduction in pulse wave velocity without changes in BP and HR.

EFFECT OF SUPPLEMENTATION OF FRUIT EXTRACT (CRANBERRY, BLUEBERRY AND POMEGRANATE) ON INSULIN RESISTANCE AND OXIDATIVE STRESS IN HYPERTENSIVE PATIENTS

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Objective: The purpose of this study was to determine if antioxidants (fruit extract) supplementation interfere with insulin resistance and oxidative stress in hypertensive patients.

Design and method: A clinical trial was conducted with 59 individuals, 30 hypertensive patients (group A) and 29 normotensive controls (group B). Study participants received placebo capsules for 4 weeks and then received the fruit extract capsules (blueberry, cranberry and pomegranate), one capsule each day for 4 weeks. Oxidative stress was evaluated by the catalase, TBARS, SOD, carbonyl and FRAP methods. Anthropometric assessment (weight, height, and body mass index), systolic BP, diastolic BP, heart rate, and biochemistry were evaluated at baseline, after 4, and 8 weeks. The comparisons between groups were held with the GLM repeated measures.

Results: The mean age among hypertensive participants was 49.3 ± 9.3 years, of which 33 (55.9%) were female. BMI, blood pressure and heart rate did not differ between groups. HOMAIR decreased significantly in both groups. Oxidative stress analysis showed increased catalase in both groups and reduced TBARS, carbonyl, and FRAP in the hypertensive group.

Table 1: Hemodynamic, anthropometric, and biochemistry data

Variables	Baseline	4 weeks	8 weeks	P value
Group A				
BMI (kg/m ²)	28.6±3.9	28.7±4.1	28.8±4.1	0.452
Systolic BP (mmHg)	141.7±22.6	143.4±28.6	137.0±21.9	0.113
Diastolic BP (mmHg)	83.6±13.9	86.3±17.9	79.7±15.5	0.137
HR (bpm)	63.7±10.0	60.6±10.5	61.7±9.0	0.081
HOMA (units)	3.6±2.8	3.0±2.6	1.3±1.4	0.001
Glucose (mmol/L)	107.4±42.4	103.2±33.1	106.1±35.1	0.603
Catalase (nmol/mg prot)	1.06±0.3	1.1±0.6	1.70±1.0	0.018
TBARS (nmol/mg prot)	0.90±0.7	1.0±0.9	0.5±0.1	0.002
SOD (U/mg protein)	3.05±0.5	3.2±1.0	3.0±0.6	0.847
Carbonyl (nmol/mg prot)	2.41±0.6	1.96±0.7	1.8±0.8	0.014
FRAP (mM Fe(II)/L)	1.3±0.4	1.4±0.5	1.3±0.4	0.035
Group B				
BMI (kg/m ²)	27.9±3.8	28.0±3.8	27.9±3.7	0.045
Systolic BP (mmHg)	121.8±15.6	122.0±13.4	120.3±11.7	0.557
Diastolic BP (mmHg)	74.2±9.6	74.3±9.4	71.9±8.7	0.124
HR (bpm)	64.7±11.2	66.0±12.0	67.3±10.7	0.179
HOMA (units)	2.6±1.2	2.5±0.7	1.0±0.7	0.000
Glucose (mmol/L)	90.7±6.9	91.0±8.7	90.3±7.3	0.848
Catalase (nmol/mg prot)	1.5±1.1	0.91±0.5	1.89±1.4	0.003
TBARS (nmol/mg prot)	0.67±0.4	0.58±0.3	0.55±0.3	0.657
SOD (U/mg protein)	3.2±0.5	3.1±0.4	0.6±1.3	0.135
Carbonyl (nmol/mg prot)	1.9±0.2	1.9±0.5	2.1±0.6	0.618
FRAP (mM Fe(II)/L)	1.16±0.5	1.4±0.5	1.3±0.4	0.213

BP = Blood Pressure; HR = Heart Rate, TBARS = thiobarbituric acid reactive substances; SOD = Superoxide dismutase; FRAP = Ferric Reducing Antioxidant Power.

Values are expressed as medians (±SD)

Conclusions: The results of this study suggest that supplementation with fruit capsules rich in antioxidants for 4 weeks significantly reduces insulin resistance and improves oxidative stress in hypertensive patients.

SAFETY AND EFFICACY OF INDAPAMIDE SUSTAINED RELEASE/ AMLODIPINE FIXED-DOSE COMBINATION IN ESSENTIAL HYPERTENSION

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Objective: To assess safety and efficacy of indapamide/amlodipine in single-pill (Ind/Aml) versus free combination of indapamide + amlodipine (Ind+Aml).

Design and method: International, randomized, open-label, controlled, 12-week phase III trial. After a run-in period on their previous antihypertensive drug (if any), patients with mild to moderate systolic and diastolic or isolated systolic uncontrolled hypertension (SBP 140–180 mmHg and DBP < 110 mmHg) were randomized and received Ind/Aml 1.5/5 mg single-pill or free combination at the same dose, potentially up-titrated to 1.5/10 mg after 6 weeks.

Assessment criteria: Office systolic blood pressure (BP) in all patients, office diastolic BP in patients with systolic and diastolic hypertension, home BP monitoring (HBPM), control rate, safety.

Results: 154 patients (77 per group) with similar baseline BP (154/97 mmHg), mean age 58 years, mostly previously treated for hypertension (92%) were included. At the office, after 12 weeks, a large BP decrease (-20 mmHg in systolic and -15 mmHg in diastolic) was obtained on the fixed-dose combination allowing BP control in most patients (69%). A large decrease was already observed after 6 weeks (-18/-13 mmHg). The titration to Ind/Aml 1.5/10 mg, in patients not controlled at 6 weeks, allowed additional BP decrease (-11 mmHg in systolic and -6 mmHg in diastolic), while efficacy of the first dose was maintained in the patients already controlled at week 6 (51%). Similar results were observed in terms of BP decrease (-22/-12 mmHg) and control rate (64%) in the free combination group at 12 weeks. HBPM data corroborated these findings. Treatment was well tolerated regarding adverse events or laboratory testing. Peripheral edema and hypotension or orthostatic hypotension remained low, even with the highest dose. The safety profile was similar in the two treatment groups.

Conclusions: Indapamide/amlodipine in a single pill was as effective on BP reduction as the free combination in patients with uncontrolled hypertension, allowing a blood pressure control rate of 69% after 12 weeks. Up-titration to Ind/Aml 5/10 mg was associated with an incremental reduction of BP. The safety profile was good and similar in both groups.

CARDIAC MYOSIN-ISOFORM SHIFT IS ACCOMPANIED BY STABLE MUSCLE-SPECIFIC MICRORNAS IN MONOCROTALINE-INDUCED PULMONARY HYPERTENSION

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Objective: During cardiac hypertrophy, a shift in distribution of myosin heavy chains (MHC) isoforms occurs, namely MHC-b (coded by Myh7 gene) increases at the expense of MHC-a (coded by Myh6 gene). MicroRNAs are small, non-coding RNAs which are involved in gene expression regulation. Muscle-specific miR-1 and miR-133a have a pivotal role in heart development and cardiac disease, miR-208a and miR-499 directly control MHC gene expression and cardiac remodelling. The epigenetic regulation of right ventricular remodelling in pulmonary hypertension is poorly understood.

Design and method: Male Wistar rats were subcutaneously injected either with 60 mg/kg monocrotaline (MCT) or with vehicle (CON). One, two and four weeks after the MCT injection, vital functions and right ventricular pressure were measured in three different periods of disease development (after one week MCT+1W, two weeks MCT+2W and in the fourth week MCT+4W). Gene expression of brain type natriuretic peptide (Nppb), Myh6, Myh7, miR-1, miR-133a, miR-208a and miR-499 in right (RV) and left ventricle (LV) were determined by qRT-PCR.

Results: MCT injection led to expected significant isolated right ventricular hypertrophy, decreased oxygen saturation and increased right ventricular pressure in MCT+4W group ($P < 0.05$). Nppb was significantly increased in RV in MCT+2W rats (by 154%) and in MCT+4W (by 312%) and, paradoxically, also in non-hypertrophied LV of MCT+4W (by 30%) when compared to age-matched controls ($P < 0.05$). Myh6 was significantly decreased in RV in MCT+4W (by 14%). Interestingly, we noted significant increase in Myh7 also in non-hypertrophied LV in MCT+2W (by 58%). These alterations were independent from microRNAs (miR-1, miR-133a, miR-208a and miR-499) expressions, which remained stable (the only exception was a moderate, but significant decrease in miR-133a in RV of MCT+4W by 13%).

Conclusions: MCT-induced pulmonary hypertension was accompanied by increased Nppb expression and myosin isoform shift, however no change in muscle-specific microRNAs was observed. Our findings suggest a missing epigenetic regulation of particular MHC genes and hypertrophic remodelling by respective microRNAs in experimental pulmonary hypertension.

SMOOTHNESS INDEX OF CENTRAL BLOOD PRESSURE AND PARAMETERS FOR VASCULAR STIFFNESS AFTER 20 WEEK TREATMENT WITH LOSARTAN PLUS AMLODIPINE VS. THIAZIDE RANDOMIZED TRIAL

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Objective: With limitation of clinic and brachial BP, central BP and vascular parameters have known to be better to probe efficacy of antihypertensive drug. Because vascular parameters are measured at resting state, role of ambulatory central BP and vascular parameters to explain the difference in clinical efficacy between renin angiotensin system inhibitor in combination with amlodipine versus hydrochlorothiazide was uncertain.

Design and method: As sub-study of multicenter randomized double blinded, losartan based therapy combined with amlodipine (LA) versus hydrochlorothiazide (LH), 143 patient (LH:73, LA:70) out of 220 patients with 80% or more valid readings in 24 hour ambulatory monitoring using Mobile-O-graph which provide ambulatory central BP and vascular stiffness data were analyzed. Smoothness index (SI) of SBP, central SBP(ACSBP), pulse pressure amplification(APPA), augmentation index(AAIx@75), and carotid femoral pulse wave velocity(AcfPWV). APPA was calculated by the ratio of SBP to ACSBP.

Results: Age was 58.9 ± 12.3 years and female was 25.9%. Prevalence of drinking and current smoking were 51.5% and 21.7%, respectively. Diabetes mellitus was noted in 14.7%. Clinic BPs were $153.8 \pm 10.2/92.4 \pm 8.5$ mmHg. Ambulatory 24 hour SBP and ACSBP were 136.5 ± 11.7 mmHg and 126.6 ± 11.0 mmHg. Changes in office BP was not different (LH: -15.2 \pm 15.0/-7.8 \pm 8.0 vs. LA: -14.9 \pm 13.7/-9.2 \pm 7.5 mmHg). Reductions of 24 hour SBP were greater in LA than LH (-10.3 \pm 12.6 vs. -6.6 \pm 10.2 mmHg, $p = 0.0478$). Only nocturnal ACSBP reduction was significant (LH:4.1 \pm 12.2 vs. LA:9.4 \pm 12.2, $p = 0.01$). And only nocturnal AcfPWV reduction was significant (LH:0.09 \pm 0.41 vs. LA: 0.26 \pm 0.44 m/sec, $p = 0.023$). Intra-individual SIs for SBP and ACSBP were higher in LA than LH (SBP:-0.57 \pm 0.78 vs. -0.39 \pm 0.57, $p = 0.0196$; ACSBP:-0.57 \pm 0.74 vs. -0.40 \pm 0.57, $p = 0.022$). Intra-individual SI for AcfPWV were marginally significant (LH:0.31 \pm 0.58 vs. LA:0.54 \pm 0.77, $p = 0.053$). SIs for APPA and AAIx75 were not different. Intra-individual TP ratios were higher in LA than LH group but the differences are not significant for both SBP(0.30[95%CI, -0.07~1.30] and ACSBP(0.24[95% CI, -0.51~3.80]).

Conclusions: LA combination seems to be superior to LH combination in reduction of ambulatory SBP. But for the reduction of ACSBP or AcfPWV was significant only in nighttime. Difference in intra-individual SI was significant both in SBP and ACSBP but not in AcfPWV. Further larger sample size studies are need

IMPACT OF THE TRIPLED FIXED-DOSE COMBINATION OF ANTIHYPERTENSIVE DRUGS ON CARDIAC ORGAN DAMAGE REGRESSION

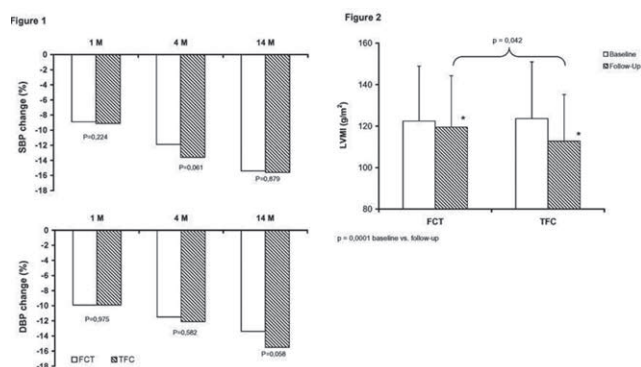
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Objective: The increase of left ventricular mass index (LVMI), a marker of cardiac end-organ damage, is frequently found in hypertensive patients (HTs) and is associated with high risk of cardiovascular and cerebrovascular events. Therefore, LVMI reduction is an important treatment goal. Few specific studies on LVMI have been reported to date about the effects of tripled fixed-combination (TFC) of antihypertensive drugs.

Design and method: The data shown herein are a part of a clinical prospective, open-label study performed in 2016 (see reference below), involving 92 HTs with essential hypertension randomized to 4-month treatment with the TFC of perindopril + indapamide + amlodipine and a comparable sample of HTs taking a free tripled combination therapy (FCT) with ACE-inhibitor + diuretic + calcium channel blocker. The study was aimed to clarify whether TFC treatment was as effective as FCT in reducing echocardiographic LVMI in a 14-month of follow-up. The changes of office systolic (SBP) and diastolic (DBP) blood pressure (BP) at the follow-up (FW) from baseline (BL) were calculated according this formula: $((BP_{FW} - BP_{BL}) / BP_{BL}) \times 100$. Analysis of variance for repeated measures was performed. Ref. Mazza A et al. Adv Ther 2017; 34:975–985.

Results: During the follow-up, BP lowering was comparable in the two groups, with a positive but non-significant trend for TFC (Figure 1). Compared to baseline, both treatments reduced LVMI, but the reduction was significantly greater with TFC than with FCT (Figure 2).

Conclusions: A TFC of antihypertensive drugs was found to be effective in improving LVMI and could be considered a new important tool in modulating the cardiovascular continuum from cardiac organ damage to events.



CONTRIBUTION FACTORS ON ACHIEVEMENT RATE OF TREATMENT GOALS OF BP AND LDL-C BY 3 MONTHS' THERAPY OF ROVELITO (FIXED DOSE COMBINATION PILL OF IRBESARTAN AND ATORVASTATIN)

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Objective: Coexistence of hypertension (HTN) and hypercholesterolemia is the major synergistic and modifiable risk factor for cardiovascular disease (CVD). A fixed-dose combination (FDC) of anti-HTN drug and statin may be valuable in terms of improving drug compliance especially for statin. Because renin-angiotensin system activation and hypercholesterolemia are accompanied with obesity and angiotensin receptor blocker is more advantageous for Asians as it does not cause dry cough due to the angiotensin converting enzyme inhibitors, FDC of irbesartan and atorvastatin (Rovelito) may improve the treatment success rate.

Design and method: Patients with comorbid HTN and hypercholesterolemia were screened for this prospective, observational, descriptive, multi-center, phase IV study. Eligible patients were administered with Rovelito for 3 months. Dose adjustment was allowed per physician's discretion. Primary purpose of this study was to evaluate the variables that affect treatment success rate for blood pressure (BP) and/or LDL-cholesterol (LDL-C). In addition, the compliance with the therapeutic lifestyle modification and the safety of the study drug were evaluated.

Results: Among the total of 2,801 patients enrolled in the study, 945 patients were analyzed for clinical efficacy. BP and LDL-C goals were achieved in 813 (86.03%) and 811 (85.82%), respectively. Higher baseline BP and body mass index (BMI) were the factors for poor treatment success rate of BP goal. Baseline LDL-C level, number of concurrent medications and drinking status were the factors for poor

treatment success rate for LDL-C goal. Of the total of 945 study participants, 706 (74.71%) reached the both treatment goals BP and LDL-C, diabetes and higher baseline LDL-C levels and number of concurrent medications were the factors for poor treatment success rate for both BP and LDL-C. Adherence with Rovelito was 97.87 ± 6.06% and incidence of AEs was 4.15%.

Conclusions: FDC of irbesartan and atorvastatin (Rovelito) can be very helpful for managing patients with both HTN and hypercholesterolemia in Asian perspectives. Poor metabolic profile itself is as well the reason to choose Rovelito as the factor for poor treatment success rate. Therapeutic life style modification still should be underscored even with 75% treatment success rate for both conditions.

INFLUENCE OF ANTIHYPERTENSIVE TREATMENT ON MMP-9 LEVELS IN CONTROLLED HYPERTENSIVE INDIVIDUALS

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Objective: Ambulatory blood pressure monitoring (ABPM), in addition to peripheral blood pressure (BP) measurements, provides data on central hemodynamic, such as pulse wave velocity (PWV), augmentation index (AI 75%) and central pressure, which are associated with arterial stiffness. The development of arterial stiffness is related to an extracellular matrix enzyme called metalloproteinase-9 (MMP-9). The aim of the current study is to evaluate the correlation between the variables obtained by ABPM and levels of MMP-9 at different BP levels.

Design and method: On-hundred and one individuals were enrolled: 21 normotensive (NT), 36 prehypertensive (PH), and 44 controlled hypertensive (CHT). Peripheral and central BP parameters were evaluated by ABPM using Mobil-O-Graph® 24-hour monitor and MMP-9 levels were determined in all participants. The levels of MMP-9 were assessed using the Human Matrix metalloproteinase-9 Quantikine ELISA kit (R & D Systems, Inc., Minneapolis, MN, USA) with a calculation of medians being presented as nanograms per milliliter (ng/mL). Subsequently, MMP-9 values were transformed into logarithms to reflect normal distribution for statistical analysis.

Results: Age of the participants ranged from 30–71 years. MMP-9 concentration was significantly higher in the PH (log 4.74 ± 0.5) compared to CHT group (log 4.41 ± 0.5; p = 0.02). Mean PWV was greater in CHT than PH (8.1 ± 1.2 m/s vs. 6.9 ± 1 m/s; p-value = 0.0003, respectively), but no differences were found in AI 75% between CHT and PH groups. On the other hand, PH individuals had higher mean PWV than NT individuals (8.1 ± 1.2 m/s vs. 6.9 ± 1 m/s; p-value = 0.0003, respectively). MMP-9 levels correlated with cardiac output and peripheral vascular resistance in the three periods evaluated by ABPM (24 h, wakefulness and sleep).

Conclusions: Prehypertensive individuals present greater arterial stiffness and MMP-9 levels than normotensive subjects, fact that demonstrate already structural alterations in this group. In its turn, higher levels of MMP-9 are observed in prehypertensive compared to controlled hypertensive subjects, suggesting that antihypertensive therapy may reduce MMP-9 plasma levels.

SELECTIVE DOWNREGULATION OF STROMAL CELL DERIVED FACTOR-1 ALPHA IN THE RIGHT VENTRICLE PRECEDES THE DEVELOPMENT OF PULMONARY HYPERTENSION IN MONOCROTALINE-TREATED RATS

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Objective: Stromal cell derived factor-1 alpha (SDF-1) is chemoattractive for stem cells, it inhibits cardiomyocyte apoptosis and promotes vascularization via CXCR4 receptor. SDF-1 is inactivated by dipeptidylpeptidase-4 (DPP-4). Albeit cardioprotective, SDF-1 was proposed to play a pathogenic role in hypoxic pulmonary hypertension (PH), antagonism of SDF-1 in the monocrotaline PH model improved pulmonary remodeling, and increased SDF-1 in human PAH was associated with an unfavourable outcome. However, the status and role of local SDF-1 in right ventricular (RV) damage in PH is unknown.

Design and method: We treated male 12 weeks old Wistar rats with monocrotaline (60 mg/kg, s.c., MON) or vehicle (CON), (n = 7–10 per group at the end of experiment). The rats were sacrificed after 1, 2 or 4 weeks after monocrotaline or vehicle injection. Hemoglobin oxygen saturation, heart rate were measured using pulse oximetry in conscious rats, RV pressure was measured by right ventricular catheterisation under anesthesia. Gene expressions of SDF-1 alpha (SDF-1), CXCR4 and DPP4 in left ventricle (LV) and RV samples from separate groups of rats sacrificed by CO2 were analyzed by qRT-PCR.

Results: Haemoglobin oxygen saturation decreased (–3.2%, P < 0.05) and breath rate increased (+40%, P < 0.05) after 4 weeks, heart rate was unaffected by MCT.

RV pressure markedly increased after 4 weeks (CON: 25.4 \pm 2.3 mmHg, MON: 50.8 \pm 4.6 mmHg, $P < 0.05$). Left ventricular SDF-1 remained unaltered, while the expression of SDF-1 decreased in the RV at weeks 2 and 4 (-41% and -47%, respectively, both $P < 0.05$ vs CON). CXCR4 decreased in both ventricles at week 1 (-26% and -25%, $P < 0.05$ vs CON) and it increased in LV at week 4 (+36%, $P < 0.05$ vs CON), with a trend only in the RV (+42%, $P = 0.07$). DPP-4 expression was unaltered by MON at weeks 1 and 2 and we observed a clear downregulation in MON group at week 4 in both ventricles (-53% and -55%, respectively, both $P < 0.05$ vs CON).

Conclusions: Selective downregulation of SDF-1 in the right ventricle temporally preceded the establishment of PH and indicates a possible role for local SDF-1 in right ventricular damage in the MON model.

AGE-DEPENDENT HYPERTENSION AND VASCULAR REMODELING IN DAHL-S RATS ARE ASSOCIATED WITH ELEVATED LEVELS OF MARINOBUFAGENIN AND COGNITIVE DECLINE

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Objective: Age-associated hypertension and central arterial stiffening contribute to cognitive impairment. Increase in blood pressure (BP) and aortic remodeling occur in Dahl salt-sensitive rats (Dahl-S) with an advancing age even on a normal salt intake. Marinobufagenin (MBG), a novel pro-hypertensive factor, is implicated in Dahl-S hypertension. Here we determined whether age-associated arterial remodeling and hypertension implicate in cognitive decline in Dahl-S and whether these changes are accompanied by an increase in pro-hypertensive and pro-fibrotic factor MBG.

Design and method: Male Sprague-Dawley rats (S-D) and Dahl-S were kept on a normal 0.5% NaCl intake ($n = 8/14$ per group) for the duration of the study. Systolic BP (SBP), pulse wave velocity (PWV), MBG, aortic collagen, and behavioral tests (open field test (OFT); novel object test; redundant place-cue version of the Morris water maze test (MWM); rotarod test) were assessed in 3-mo and 12-mo animals.

Results: At 3-mo Dahl-S had higher SBP, PWV and aortic wall remodeling vs. 3-mo S-D. Between 3 and 12-mo both S-D and Dahl-S exhibited an increase in SBP, PWV, MBG and aortic wall collagen deposition. These parameters were significantly higher in 12-mo Dahl-S than in age-matched S-D (Table). MBG correlated with SBP in Dahl-S only (Pearson $R = 0.52$, $p = 0.04$), and with PWV in both S-D (Pearson $R = 0.37$, $p = 0.01$) and Dahl-S (Pearson $R = 0.54$, $p = 0.04$). Behaviorally, in an MWM, 12-mo DSS demonstrated impaired spatial hippocampal memory vs. 12-mo S-D. Compared to 3-mo, both 12-mo S-D and Dahl-S demonstrated an age-dependent decline in OFT activity, but 12-mo Dahl-S were more active in OFT, had more endurance during the rotarod test indicating non-impaired motor coordination, and showed increased object exploration vs. age-matched S-D (Table). Performance in behavioral tests by 12-mo hypertensive Dahl-S may suggest the development of age-associated anxiety and change in emotional status, and a decline in their spatial hippocampal memory.

Conclusions: Cognitive deficit in aged hypertensive Dahl-S is limited to hippocampal-dependent spatial memory. In Dahl-S, development of age-dependent hypertension and aortic wall remodeling, occurred in context with an increase in MBG, may contribute to hippocampal spatial memory impairment, and suggested a possible implication of MBG in these declines.

	Sprague-Dawley rats (S-D)		Dahl-S rats	
Age (months) and number	3 (n=8/11 ⁵)	12 (n=8)	3 (n=8/14 ⁵)	12 (n=8)
Body weight (BW) (g)	452 \pm 10	754 \pm 24 ^{***}	329 \pm 7 ^{**}	470 \pm 8 ^{***}
SBP (mmHg)	128 \pm 2	140 \pm 3 ^{***}	142 \pm 2 ^{**}	170 \pm 5 ^{***}
PWV (m/s)	2.4 \pm 0.1	4.7 \pm 0.1 ^{***}	4.2 \pm 0.8 [*]	7.6 \pm 0.7 ^{***}
Urine MBG (pmol/24 hr)	17 \pm 3	33 \pm 2 ^{***}	19 \pm 2	55 \pm 8 ^{***}
Aortic wall collagen (%)	8.0 \pm 1.2	9.6 \pm 0.7	14.9 \pm 3.0 [*]	20.8 \pm 1.7 ^{**}
OFT, total distance traveled day 1 first 5 mins (m)	6.7 \pm 0.4	3.9 \pm 0.4 ^{***}	6.9 \pm 0.3	5.2 \pm 0.3 ^{***}
OFT, vertical activity day 1 first 5 mins (n)	329 \pm 25	106 \pm 13 ^{***}	345 \pm 15	229 \pm 29 ^{***}
Rotarod, max latency (sec)	88 \pm 15	36.3 \pm 9	119 \pm 15	164 \pm 25 ^{**}
Object recognition, novelty preference at 2 hours (%)	64 \pm 2	72 \pm 7	63 \pm 3	74 \pm 5
Novel object, time investigating objects during familiarization (sec)	37 \pm 4	21 \pm 2 ^{***}	36 \pm 3	34 \pm 2 [*]
MWM, time spent to find a platform (sec)	17 \pm 4	19 \pm 2	16 \pm 2	31 \pm 1 ^{***}
Mean \pm SE. * $p < 0.05$, ** $p < 0.01$, age-matched S-D vs Dahl-S; # $p < 0.05$, ## $p < 0.01$, 3-mo vs. 12-mo, by 2-way ANOVA. *More animals were used in behavioral tests at 3-mo.				

QUERCETIN INCREASES NITRIC OXIDE-DEPENDENT DILATION IN RAT THORACIC AORTA

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Objective: Endothelial dysfunction plays an important role in development and progression of arterial hypertension. In recent years there was reported that polyphenolic compounds improve the function of endothelium, however, their molecular mechanisms on endothelial cells remain unclarified. Purpose of study was to determine whether polyphenols (quercetin, caffeic acid or resveratrol) are able to improve NO-dependent vasodilation in rat aortic rings.

Design and method: Male Wistar rats were anaesthetized by chloralhydrate over dose and decapitated. Descending thoracic aorta was carefully excised and cut into ring segments 3 mm in length and then transferred into organ baths containing Krebs solution bubbled with mixture of 95% O₂ and 5% CO₂. Rings were precontracted with 0.3 μ M Phenylephrine and increasing concentrations of acetylcholine (ACh, 0.001 μ M - 30 μ M) were cumulatively added to organ bath. At the beginning of each experiment, all rings were pretreated with diclofenac for 30 minutes to prevent the generation of vasoactive prostanoid metabolites. Quercetin, caffeic acid or resveratrol (10 μ M) was added to organ baths for 20 minutes before investigation of relaxant responses to ACh. Some rings were incubated in the DMSO (solvent, control).

Results: ACh elicited a concentration-dependent relaxation of rat aortic rings. After exposure to quercetin the relaxant responses to all concentrations of ACh were markedly potentiated. There was no significant relaxant response to ACh in caffeic acid and resveratrol groups. Maximum relaxation (E max, %) was increased from 54.6 \pm 3.3 in control group to 67.3 \pm 3.8 in quercetin group, and 63.4 \pm 4.8 and 62.4 \pm 5.1 in caffeic acid and resveratrol group, respectively ($P < 0.05$). Negative logarithm of EC₅₀ (pD₂) value in control study was 5.2 \pm 0.28. After pretreatment with quercetin, caffeic acid and resveratrol pD₂ values were 6.1 \pm 0.16, 5.6 \pm 0.18 and 5.4 \pm 0.32, respectively ($P < 0.005$ vs. control).

Conclusions: Our results demonstrate that quercetin improves endothelial dysfunction due to increased NO-dependent vasodilation. This mechanism could be associated with decrease in the ROS level and related decrease in inactivation of NO, or with activation of eNOS and related increase in NO synthesis in the endothelium.

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POSTER SESSION

POSTERS' SESSION PS03:

RESISTANT HYPERTENSION

PREVALENCE AND RISK FACTORS OF RESISTANT HYPERTENSION IN THE RENAL TRANSPLANT RECIPIENT

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Objective: Arterial hypertension (HT) is common in renal transplant recipients (RTRs) and control of HT is not optimal in this high risk population. Previous study showed that metabolic syndrome is emerged as strong predictors of poor HT control. Also, also persistent hyperparathyroidism is common in RTRs and elevated serum parathyroid (PTH) levels are related with an increased risk of HT development. RTRs, regardless of achieved renal function, may experience resistant hypertension (RH). The aim of this a cross-sectional was to analyse the prevalence of RH and identified possible factors associated with resistant HT in RTRs.

Table 1. Difference between renal transplant recipients with arterial hypertension who were taking < 3 antihypertensive drugs (N=85) and those renal transplant recipients who were taking ≥ 3 antihypertensive drugs (N=104) (Student's t-test for independent data, one-tailed significance), significant correlations are marked

	Patients with arterial hypertension who were taking < 3 antihypertensive drugs (N=85)		Patients with arterial hypertension who were taking ≥ 3 antihypertensive drugs (N=104)		
	Mean ± SD		Mean ± SD		P
Body mass index (kg/m ²)	25.42 ± 3.50		26.92 ± 3.07		0.005*
Systolic blood pressure (mmHg)	137.26 ± 18.72		146.10 ± 18.19		0.001*
Diastolic blood pressure (mmHg)	81.25 ± 9.24		83.23 ± 8.90		0.077
Urea (mmol/L)	9.28 ± 3.97		11.08 ± 5.21		0.005*
Creatinine (mmol/L)	126.25 ± 47.78		149.17 ± 89.86		0.019*
Glucose (mmol/L)	5.47 ± 1.43		5.86 ± 1.74		0.050*
Total cholesterol (mmol/L)	4.12 ± 0.71		4.82 ± 1.52		0.019*
LDL cholesterol (mmol/L)	3.19 ± 0.92		3.50 ± 0.97		0.019*
Calcium (mmol/L)	2.41 ± 0.21		2.43 ± 0.16		0.251
Phosphorus (mmol/L)	0.99 ± 0.24		0.99 ± 0.24		0.500
Parathyroid hormone (pmol/L)	11.65 ± 8.46		19.81 ± 14.08		0.023*
Uratex (mmol/L)	397.85 ± 91.75		438.49 ± 84.52		0.001*

*P < 0.05; LDL cholesterol: low density lipoprotein cholesterol

Design and method: The 198 RTRs (aged 58.07 ± 12.07 years) were investigated. For each RTRs patient data about number of antihypertensive drugs were collected by interviewing participants, as well as by reviewing participants' medical records. Serum urea, creatinine, glucose, total cholesterol, low density lipoprotein (LDL) cholesterol, calcium, phosphorus, PTH and urates were measured for each RTRs. Therefore, the systolic (SBP) and diastolic blood pressure (DBP) was measured and body mass index (BMI) was calculated for each patient.

Results: The results showed that 189 (95.45%) RTRs have HT and 85 (44.97%) RTRs were taking less than 3 antihypertensive drugs and 104 (55.03%) were taking 3 or more antihypertensive drugs (one of these was diuretic). Also, when we divided RTRs in two groups according number of antihypertensive drugs (<3 or ≥ 3 antihypertensive drugs) statistically significant difference in BMI, SBP, creatinine, urea, glucose, total cholesterol, LDL cholesterol, PTH and urate level was found as shown in Table 1.

Conclusions: These data suggested that RH is prevalent in RTRs and that elevated serum PTH levels might be related with RH in RTRs. Also, features of metabolic syndrome and other comorbidity that are common in RTRs (diabetes, chronic graft failure, hyperlipidaemia, hyperuricemia) might be related for increased risk of RH in RTRs. A careful approach to detect true RH and rule out all this potential causes is warranted. Also, further studies should determine if persistent hyperparathyroidism or its treatment influences blood pressure and long-term post transplantation clinical outcomes.

PREDICTION OF LONG-TERM RENAL DENERVATION EFFICACY

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Objective: Diversity of blood pressure response and great variability within studies emphasise the need to identify predictors of renal denervation efficacy. Previous studies identified various predictors within periods of 3–6 months.

Design and method: The goal of the current study is to examine the possible predictors of sustained decline of blood pressure after renal denervation in a long-term period of 2 years.

Evaluated patients were either randomised in the original Prague-15 study or were pilot patients, meeting the same inclusion criteria of true-resistant hypertension. Patients were considered as responsive when the decline of 24 h systolic blood pressure > 10 mmHg was present 6, 12 and 24 months after the procedure. In addition, analysis for separate visits was performed. Denervation was performed using the unipolar Symplicity® Renal Denervation System. Extensive assessment of computed tomography angiography by numerous measurements including morphology of the renal arteries was performed.

Results: A total of 48 patients were analysed with 27 patients suitable for long-term prediction. According to the protocol of the study, spironolactone was added at 12-month follow-up as a crossover and these patients were excluded from long-term analysis.

Five of the 27 patients were identified as long-term responders with average 24 h blood pressure decline of 20/9 mmHg. Strongest predictors of BP decline were higher baseline 24 h systolic blood pressure (p = 0.01) and higher diameter of the left renal artery (p = 0.04).

Conclusions: Only a minority of denervated patients exhibited sustained blood pressure decline. Higher baseline blood pressure and higher renal artery diameter were the strongest predictors. Our findings thus might theoretically support the actual hypothesis of the necessity to ablate the distal parts of the renal artery (these conditions might allow such ablation to be performed).

EFFECTS OF TNF-ALPHA INHIBITOR ON HEMODYNAMIC PARAMETERS AND BIOMARKERS IN RESISTANT HYPERTENSION

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Objective: Currently it has been largely discussed the influence of inflammation in resistant hypertension (RH). The blood pressure (BP) variation promotes increased expression of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), interleukins -1 and -6. It was showed that treatment with TNF-α inhibitor improves BP and endothelial function, and reduces arterial stiffness in patients with rheumatoid arthritis. Recently, it was demonstrated that TNF-α levels are increased in RH subjects compared to normotensives. The purpose of this study was to assess whether the acute inhibition of TNF-α (using infliximab infusion) changes hemodynamic parameters, as well as biomarkers in RH.

Design and method: This crossover, double-blind study included 10 RH subjects – regularly followed at the Outpatient Resistant Hypertension Clinic (UNICAMP/Brazil) – which were randomized assigned to either (1) serum infusion followed by infliximab infusion (TNF-α inhibitor, 3 mg/kg) or (2) infliximab followed by serum infusion, for two hours and a washout period of 40 days between the infusions. Office, central and ambulatory BP levels, and biomarkers were determined before and after 7 days of infusions. Hemodynamic parameters (determined by Finometer device) was simultaneously assessed during infusions. The plasma concentrations of TNF-α, ILs-1, -6, -10, adiponectin, aldosterone, renin, cortisol were determined by ELISA.

Results: Treatment with infliximab increased the delta values of cortisol (3.45 vs. 0.24 ug.dL⁻¹; p = 0.01) and decreased delta renin levels (0.05 vs. 0.25 ng.mL⁻¹; p = 0.03) compared with placebo. Also, TNF-α levels increased after 7 days of infliximab infusion (37.93 ± 38.49 to 110.18 ± 19.54 pg.mL⁻¹; p = 0.01), but did not change with placebo. Delta heart rate values increased after infliximab when

compared to placebo (0.89 vs. -1.04 bpm; $p = 0.006$). No statistical changes were found in either BP parameters evaluated in the study.

Conclusions: Our data suggest that the acute inhibition of TNF- α changes hormonal and inflammatory biomarkers although did not modifies hemodynamic parameters in RH subjects.

CARDIOPROTECTIVE EFFICACY OF RENAL DENERVATION: INFLUENCE OF BLOOD PRESSURE VARIABILITY

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Objective: To study influence of BP variability on cardioprotective efficacy of renal denervation using cardiac contrast-enhanced magnetic resonance.

Design and method: 26 patients with resistant hypertension, giving informed consent, were enrolled in the study. RDN was done to all patients. All patients were divided into two groups, according to BP variability (systolic standard deviation SSD > 15 mm Hg): the 1st group – with normal 24-h BP variability ($n = 10$) and the 2nd – with high 24-h BP variability ($n = 16$). Initially, at 6 and 12 months after treatment, patients were measured 24-h ambulatory BP and cardiac contrast-enhanced magnetic resonance (MR). Left ventricular mass (LVM) and the volume of subendocardial damage, detected as summary volume of contrast uptake in myocardium on post-contrast MR study, were measured.

Results: All baseline parameters were similar in comparison groups: for ambulatory BP $151.9 \pm 13.4/84.5 \pm 9.7$ and $157.0 \pm 14.9/88.9 \pm 16.2$ mm Hg ($p = 0.4$), age 58.4 ± 5.2 and 56.1 ± 7.7 years ($p = 0.4$); for LVM 231.7 ± 67.2 and 250.3 ± 79.3 g ($p = 0.5$). Subendocardial damage was detected in 100% patients of both groups in the absence of coronary atherosclerosis (2.04 ± 0.97 and 1.76 ± 0.85 sm³, $p = 0.5$). BP wasn't reduced at 6 ($151.5 \pm 14.3/82.4 \pm 11.8$ mm Hg, $p > 0.05$) and 12 month ($148.5 \pm 17.7/80.4 \pm 14.3$ mm Hg, $p > 0.05$) in the 1st group and reduced significantly in the 2nd group at 6 ($140.5 \pm 14.0/81.1 \pm 13.5$ mm Hg, $p = 0.02$) and 12 month after RDN ($142.6 \pm 14.9/81.5 \pm 11.9$ mm Hg, $p = 0.03$). LVM was significantly reduced at 6 month by 9.3% (231.8 ± 58.9 g, $p = 0.02$), at 12 month by 23.1% (196.4 ± 41.6 g, $p = 0.003$) in the 2nd group. The volume of subendocardial damage also was reduced in the 2nd group at 12 month (1.23 ± 0.72 sm³, $p = 0.03$). There were no significant changes in the 1st group neither for LVM (216.7 ± 82.0 g, $p = 0.23$) nor for volume of subendocardial damage (1.70 ± 1.39 sm³, $p = 0.93$) at 12 month.

Conclusions: In patients with high BP variability LVM and subendocardial damage were reduced better than in patients with normal variability.

IMPROVING AN EFFICIENCY OF RESISTANT HYPERTENSION TREATMENT WITH FIXED DOSE COMBINATION OF 3-COMPONENTS ANTIHYPERTENSIVE MEDICATION

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Objective: Improving an efficiency of resistant hypertension treatment with fixed dose combination of 3-components antihypertensive medication

Table 1. The dynamics of blood pressure under 3-components FDC treatment

BP, mmHg	CAH pts n = 102		RAH pts n = 78	
	Before treatment	After treatment	Before treatment	After treatment
Office SBP	161,6 ± 1,7	127,7±0,9	176,7 ± 2,0***	153,4±2,4***
Office DBP	98,3 ± 1,5	79,2±0,9	97,1 ± 1,8	88,5±1,7***
Average daytime SBP	154,1 ± 1,5	130,8±1,1	174,5 ± 1,5***	154,6±1,9***
Average daytime DBP	92,3 ± 1,4	79,4±1,3	98,2 ± 1,8**	89,7±1,5***
Average nighttime SBP	136,1 ± 1,9	113,5±1,5	159,7 ± 1,8***	142,1±2,2***
Average nighttime DBP	78,3 ± 1,3	65,5±1,0	85,6 ± 1,6***	76,9±1,3***

*, the significance of the differences between the groups before and after treatment: ** - $p < 0.01$, *** - $p < 0.001$.

Design and method: 180pts with the preliminary diagnosis of RAH, which was confirmed by 24-h ambulatory blood pressure monitoring (ABPM), were included in the study. All pts received an average of 4.1 ± 0.3 antihypertensive drugs, mainly in free combinations. After ABPM pts were started treatment with 3-component fixed dose combination (FDC) of antihypertensive drugs: the FDC of perindopril 10 mg/indapamide 2.5 mg/amlodipine 10mg (108pts) or the FDC of valsartan 320 mg/hydrochlorothiazide 25 mg/amlodipine 10mg (72pts). The adherence to the treatment was evaluated by the Morisky-Green test (MGT) at the initial examination and after 3 months of treatment with the FDC of antihypertensive drugs.

Results: The average level of office systolic BP (SBP) and diastolic BP (DBP) was 158.1 ± 1.2 and 91.03 ± 0.9 mmHg respectively. After 3 months of treatment with 3-components FDC, according to the results of office and ambulatory BP measurements, RAH was confirmed at 78pts and 102pts achieved the target blood pressure level (these pts were classified as pts with controlled arterial hypertension (CAH)).

RAH pts were older than CAHpts: 52.4 ± 1.2 vs 49.8 ± 1.6 years ($p = 0.02$). Both groups were dominated by men: 60.5% among RAH pts and 62.6% among CAH pts. But initial BP levels (office and ambulatory) were higher in RAH group (tab. 1). In the CAH group the office SBP decreased by 21%, DBP by 19.5%, the average daytime SBP and DBP by 15.2 and 14% respectively, the average nighttime SBP and DBP by 16.7 and 16.4% respectively. In the RAH group BP lowering was smaller: the office SBP decreased by 13.2%, DBP by 9%, the average daytime SBP and DBP by 10.3 and 8.7% respectively, the average nighttime SBP and DBP by 11.1 and 10.2% respectively. All pointed changes of BP were significant ($p < 0.001$) (tab. 1).

The results of the Morisky-Green tests show that treatment with FDC of antihypertensive drug led to improvement of the adherence to therapy. The initial Morisky-Green rate, which was assessed retrospectively, at RAH pts was 1.3 ± 0.1 points and at CAH pts 1.4 ± 0.1 ($p > 0.05$), after 3 months of treatment with 3-components FDC it elevated to 2.5 ± 0.2 and 2.6 ± 0.2 points, respectively, in both groups ($p < 0.005$).

Conclusions: Thereby, administration of 3-components FDC (RAAS blocker/diuretic/calcium channel blocker) improves the adherence to treatment, which can probably ameliorate the efficacy of antihypertensive treatment. Perhaps, the use of 3-component FDC in patients with a diagnosis of RAH could help to achieve the effective BP control and reduce the necessity of adding the 4-th antihypertensive drug for achieving of goal BP.

EFFECTS OF RENAL DENERVATION ON BLOOD PRESSURE IN PATIENTS WITH END-STAGE RENAL DISEASE: A SINGLE CENTER EXPERIENCE

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Objective: Sympathetic nerve activity is a hallmark of hypertension in end-stage renal disease (ESRD). An initial proof-of-concept study implies that renal denervation (RDN) is feasible and safe in RDN, but overall data are limited.

Design and method: In this single-center prospective pilot study 6 patients with ESRD and treatment resistant hypertension were consecutively included. Ambulatory blood pressure (ABP) was measured before and 6 months after RDN (Symplicity Flex[®], Medtronic Inc., Santa Rosa, CA). Moreover, hemodialytic parameters which may impact on BP-reduction were monitored closely.

Results: In all patients bilateral RDN was successfully done, without documentation of peri- or postprocedural complications. There was a significant reduction in 24-h ABP by $-20 \pm 17/15 \pm 12$ mmHg 6 months after RDN (systolic: 163 ± 16 vs. 143 ± 9 mmHg, $p = 0.043$; diastolic: 96 ± 9 vs. 81 ± 15 mmHg, $p = 0.043$), with similar results for day-, and nighttime values, respectively. Antihypertensive medication was kept stable as well as there was no change in hemodialysis parameters during follow-up. In addition, ultrafiltration/week (1.4 ± 1.4 versus 2.2 ± 1.4 l, $p = 0.08$) as well as hematocrit (measured at baseline and 6 months after RDN) (33.7 ± 4.3 versus 33.1 ± 3.9 %, $p = 0.715$) revealed no change in volume status.

Conclusions: Our single-center pilot study supports current data on renal safety of RDN even in small arteries of patients with ESRD, but also expands the knowledge towards an effective ABP-reduction.

A STANDARDIZED TRIPLE THERAPY COMBINED WITH ELECTRONIC MONITORING OF ADHERENCE NORMALIZES 24 H ABPM IN AT LEAST ONE THIRD OF PATIENTS WITH RESISTANT HYPERTENSION

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Objective: Poor adherence to drug therapy is one of the most common factors explaining a poor blood pressure (BP) control in patients with apparent resistant hypertension. Few studies have used a standardized treatment coupled to electronic adherence monitoring in patients with apparent resistant hypertension. The objective of this study was to determine the rate of BP control when prescribing a standardized triple therapy associated with electronic monitoring of drug intake for 3 months and assessing BP control using 24 h ambulatory BP monitoring (ABPM).

Design and method: Patients with 3 antihypertensive drugs and residual hypertension on 24 hr ABPM (excluding white coat hypertension) were recruited. A single pill combination of olmesartan 40 mg and amlodipine 10 mg was prescribed together with 25 mg chlorthalidone for 3 months. Medications were provided in 2 separated electronic pills boxes (MEMS®) recording the date and time of each opening. Patients were seen at 6 and 12 weeks. At 3 months, we analyzed MEMS® data and performed a second ABPM.

Results: 49 patients (36% women) were included: 36 had complete data sets. Mean age was 56.5 ± 11.9 y, BMI was 31.2 ± 5.1 kg/m². Overall, mean 24 h systolic BP (SBP) decreased from 148 ± 19 mmHg to 129 ± 16 mmHg ($p < 0.001$) and diastolic BP (DBP) decreased from 89.0 ± 16.1 mmHg to 77.5 ± 10.5 mmHg ($p < 0.001$). Overall 50 % of patients normalized SBP and 36% normalized both SBP and DBP. Median taking adherence (%) was respectively 92.5 % (interquartile range (IQR) 84.0–100) and 91.9 % (IQR 83.0–100) for the fixed combination and chlorthalidone. When analyzed according to tertiles of adherence, decreases in SBP were respectively 27 ± 16.6 mmHg in tertile 1 (99–100%), 20 ± 31 mmHg in tertile 2 (89–98.9%) and 9.1 ± 15.4 mmHg in tertile 3 (0–88%) ($p = 0.027$ for trend).

Conclusions: A simplified standardized antihypertensive therapy together with an electronic monitoring of adherence enables to normalize BP in more than 1/3 of patients with apparent resistant hypertension and no white coat effect. BP reduction correlates with the level of adherence. This diagnostic and supportive strategy may prevent from expensive and unnecessary investigations.

REFRACTORY HYPERTENSION, ASSOCIATED AND TYPE 2 DIABETES MELLITUS: DIFFERENCE WITH RESISTANT HYPERTENSION

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Objective: Refractory hypertension (RfH) is an extreme phenotype of antihypertensive treatment failure and a specific subgroup of resistant hypertension (RH). Type 2 diabetes mellitus (T2DM) is associated with both of RfH and RH, but features of diabetic patients with RfH have not been established. The purpose of this study was to determine the difference in clinical characteristics of diabetic patients with RfH in comparison with those with RH.

Design and method: We examined 64 diabetic patients with RHT (mean age 59.0 ± 8.4 years; 24-hour BP (systolic/diastolic) $153.9 \pm 17.0/81.4 \pm 12.4$ mmHg; 25 men (39%)), eGFR 77.1 ± 21.9 mL/min/1.73m², duration of hypertension 22.4 ± 10.3 years, duration of DM 7.9 ± 5.2 years, body mass index (BMI) 34.5 ± 5.7 kg/m²), among them 15 patients (23.4%) met the criteria for RfH. RH was defined as uncontrolled blood pressure (BP) ($\geq 140/90$ mm Hg), despite the use of ≥ 3 antihypertensive drugs, or controlled requiring use of ≥ 4 drugs. RfH was defined as uncontrolled BP on ≥ 5 antihypertensive drug classes. All patients were underwent clinical examination, laboratory evaluation (basal and postprandial plasma glucose and insulin levels, calculation of HOMA- index, HbA1C, serum aldosterone, plasma renin activity (PRA), creatinin, adipokines (adiponectin, leptin and resistin), microalbuminuria (MA)), and 24 –hour ABPM.

Results: Diabetic patients with RfH and RH did not differ in age, male sex, BP (according to office measurement and ABPM), BP dipping status, BMI, duration of hypertension and duration of DM, frequency of visceral obesity, type of hypoglycemic therapy. In addition, patients with RfH and those with RH had the same levels of aldosterone and PRA, the average levels of eGFR, MA, HbA1C, glucose and insulin levels. At the same time, patients with RfH compared with RH had a significantly higher value both of HOMA index (8.3 ± 3.1 vs. 4.6 ± 3.2 , $p = 0.02$), and plasma resistin level (6.0 ± 1.1 vs. 4.5 ± 1.4 ng/mL, $p = 0.02$).

Conclusions: Subjects with RfH characterized by a higher level of HOMA- index and plasma resistin level, despite the absence of differences in clinical phenotype with RH. Our results indicate important pathogenetic role of the severity of insulin resistance and deregulation of adipokines in the development of refractory hypertension in patients with T2DM.

DOES HYPERURICEMIA INFLUENCE ON EFFICACY OF RADIOFREQUENCY SYMPATHETIC DENERVATION OF THE RENAL ARTERY?

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Objective: Hyperuricemia is a risk factor for chronic renal insufficiency and is frequently encountered in patients with arterial hypertension (AH). However the impact of hyperuricemia on efficacy of radiofrequency sympathetic denervation

(RFD) of the renal artery in patients with resistant AH (RAH) has not been fully appreciated. The objective of the study was to assess the efficacy of RFD of the renal artery in patients with RAH and hyperuricemia one year after the procedure.

Design and method: 15 patients with RAH and hyperuricemia were examined while a comparison group consisted of 12 patients with RAH and without hyperuricemia. All patients received five antihypertensive drugs including diuretics. At baseline and one year after RFD of the renal artery the following parameters were assessed: 24-hour blood pressure monitoring, glomerular filtration rate (GFR) based on Modification of Diet in Renal Disease (MDRD) equation, 24-hour microalbuminuria and left-ventricular myocardial mass index (LVMMI).

Results: In one year after RFD of the renal artery the significant decrease in mean 24-hour systolic and diastolic BP was detected in both groups according to 24-hour blood pressure monitoring. GFR level significantly decreased in main group of patients. No changes in microalbuminuria were found. LVMMI did not reach significant differences in patients with RAH and hyperuricemia while significant decrease was observed in a comparison group.

Conclusions: In patients with RAH and hyperuricemia one year after RFD of the renal artery along with identical hypotensive effect the significant reduction in GFR was observed. Moreover, no decrease in LVMMI was detected that might be caused by a latent kidney disease providing additional factors for maintenance of AH.

PATIENTS WITH RESISTANT HYPERTENSION AND NORMAL NOCTURNAL BLOOD PRESSURE DIPPING SHOW BETTER INFLAMMATION AND CARDIORESPIRATORY FITNESS

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Objective: Introduction: Inflammation seems to play an important pathophysiological role in the development of arterial hypertension namely resistant hypertension (RH). Studies have pointed out the importance of immunity and inflammation in hypertension and cardiovascular prognosis, yet progress has been slowed by limited experimental tools and conflicting results.

Objective: to determine if night time blood pressure dipping is associated with inflammation, body composition and cardiorespiratory fitness in patients with RH.

Design and method: Seventeen patients (age, 59.1 ± 7.3 years; weight, 78.5 ± 10.1 kg; height, 1.64 ± 0.10 m) with RH participated in this cross-sectional study. Outcome measures included clinical data, cardiorespiratory fitness (VO2peak), casual and ambulatory blood pressure (BP), and plasma levels of high-sensitivity C-reactive protein (hsCRP). The night time BP dip was calculated as the difference between daytime mean pressure and night time mean pressure expressed as a percentage of the day value. Correlation analysis was conducted to assess the association between variables; independent t-tests were conducted to compare variables between those with hsCRP levels $<$ and ≥ 3 mg/L, and between dippers and non-dippers.

Results: Patients were mostly men (10 men, 7 women), overweight (body mass index, 29.2 ± 3.0 kg/m²), with a casual systolic and diastolic BP of 144.0 ± 3.8 mmHg and 82.0 ± 1.9 mmHg, respectively. The mean night time systolic blood pressure dipping was not correlated with age ($r = -0.015$, $p = 0.955$), body mass index ($r = -0.458$, $p = 0.075$) nor VO2peak ($r = 0.198$, $p = 0.446$), but was correlated with hsCRP ($r = -0.561$, $p = 0.024$); this correlation remained significant when controlling for age and body weight ($r = -0.617$, $p = 0.019$). Patients with lower values of CRP ($n = 9$) showed higher night systolic (14.4 ± 1.2 vs. 7.3 ± 1.7 mmHg, $p = 0.022$) and diastolic (18.7 ± 2.3 vs. 11.9 ± 1.7 mmHg, $p = 0.035$) BP dipping than those with values of hsCRP ≥ 3 mg/L. Systolic dipping pattern occurred in 10 patients (58.8%); when comparing with non-dippers, the systolic dippers showed significantly better VO2peak (36.4 ± 1.6 vs. 29.4 ± 2.3 mL O₂/kg/min, $p = 0.021$) and hsCRP (2.2 ± 0.4 vs. 6.9 ± 2.2 mg/L, $p = 0.026$) than non-dipper.

Conclusions: Patients with RH with a normal night time systolic dipping showed lower levels of low grade inflammation and better cardiorespiratory fitness, an independent predictor of mortality, than non-dippers RH patients.

SHORT- AND LONG-TERM SAFETY AND EFFICACY OUTCOMES OF SPIRONOLACTONE IN RESISTANT HYPERTENSION

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Objective: We aimed to evaluate short- and long-term outcomes of spironolactone as add-on antihypertensive treatment for resistant hypertension (RH).

Design and method: We evaluated 202 patients with RH consecutively attended by hypertension specialists, who started spironolactone as additional antihypertensive treatment. Blood pressure and laboratory parameters (serum creatinine (SCrea), estimated glomerular filtration rate by CKD-EPI equation (eGFR) and serum potassium (Kp)) were analysed at 3, 6 and 12 months.

Results: The variation of SBP (mean and 95% CI) was -10.7 mmHg [-13.5 to -7.8] and -12.7 mmHg [-15.8 to -9.6] at 3 and 12 months, respectively. The variation of DBP was -4.0 mmHg [-5.6 to -2.3] and -5.4 mmHg [-7.2 to -3.6] at 3 and 12 months. $P < 0.001$ in all cases. These BP values were confirmed by 24-h ABPM at 12 months, the variation of SBP 24 h was -11.8 mmHg [-17.2 to -6.3] and the variation of DBP was -6.6 mmHg [-9.6 to -3.5] ($P < 0.001$). The variation of eGFR was -6.4 ml/min/1.73m² [-9.0 to -3.9] and -9.4 ml/min/1.73m² [-12.0 to -6.7] at 3 and 12 months, respectively ($P < 0.001$). The variation of Kp was 1.0 mmol/l [0.2 to 1.8] at 3 months ($P = 0.02$) and 0.4 mmol/l [-0.5 to 1.2] at 12 months ($P = 0.4$). The eGFR significantly decreased ($p = 0.046$) between 3 and 12 months. There were no statistically significant differences in BP, Kp and SCrea between 3 and 12 months. Seventy-seven patients out of the whole cohort were prospectively evaluated. Spironolactone was withdrawn in 7 patients (9.09%) due to adverse effects, including 1 due to excessive eGFR decrease and 1 due to hyperkalemia. The analysis of the remaining 70 patients parallels the results of the whole cohort.

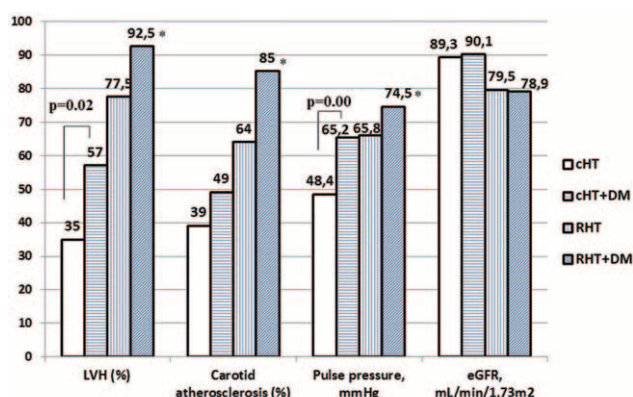
Conclusions: 1) Spironolactone significantly decreased BP at 3 and 12 months. 2) Likewise, we observed a decrease in eGFR at 3 months and 12 months. 3) In 9% of RH patients, spironolactone was withdrawn due to adverse effects. Spironolactone seems a safe and effective add-on treatment for RH, although it requires a close monitoring of renal function.

PREVALENCE OF TARGET ORGAN DAMAGE IN PATIENTS WITH RESISTANT HYPERTENSION, ASSOCIATED WITH DIABETES MELLITUS TYPE 2

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Objective: To assess the frequency of target organ damage (TOD) in diabetic patients with resistant hypertension (RHT).

Design and method: 332 essential hypertensive patients were included in the study (47 patients with controlled hypertension (cHT) without diabetes mellitus (DM), 100 diabetic patients with cHT (cHT+DM), 120 RHT patients without DM (RHT) and 65 diabetic patients with RHT (RHT+DM). Patients were underwent ambulatory blood pressure monitoring, ultrasonography of heart and carotid arteries, laboratory tests (estimated glomerular filtration rate (eGFR)). All groups were comparable in male gender.



Results: Patients of RHT+DM group were older than patients of all other groups (57.9 ± 7.9 vs. 52.8 ± 8.9 y.o. in RHT pts.; 51.2 ± 6.8 y.o. in cHT+DM pts. and 50.8 ± 9.6 y.o. in cHT pts., $p < 0.05$). Diabetic patient had higher frequency of LVH, carotid atherosclerosis (CA) and average value of 24h-pulse pressure (PP) than non-diabetic patients with the same blood pressure control ($p < 0.05$) (Fig.1). Diabetic patients with RHT had maximal frequency of LVH, CA and values of PP ($p < 0.05$). Values of eGFR were similar in RHT patients and were lower than in cHTN patients ($p < 0.05$) independently of presence of DM ($p < 0.05$).

Conclusions: DM contributes to more frequently TOD with maximal prevalence of those in diabetic patients with RHT, which can be the cause of a very high rate of cardiovascular complications. At the same time, decline the renal function is common feature in patients with RHT independently of DM.

RESISTANT HYPERTENSION ASSOCIATED WITH TYPE 2 DIABETES MELLITUS, CLINICAL CHARACTERISTICS

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Objective: Diabetes mellitus (DM) increases risk of resistant hypertension (RHT) but phenotype of RHT associated with DM has been poorly characterized. The aim of this study was to investigate the clinical characteristics of diabetic patients with true RHT.

Design and method: We examined 65 diabetic patients with true RHT (with office systolic blood pressure (BP) > 140 mmHg despite the use of 3 and more antihypertensive agents in optimal dosages, one of them being a diuretic) and 67 diabetic patients with controlled HT (with target BP on less than three drugs). Office and ambulatory 24 hour-BP measurements, evaluating of body mass index (BMI), serum HbA1c, aldosterone and creatinine levels with calculation of estimated glomerular filtration rate (eGFR) according to MDRD formula were performed.

Results: The number of male gender (36% in RHT patients vs. 34% in control group) and body mass index (35.9 ± 5.5 in RHT+DM group vs. 34.5 ± 6.4 kg/m² in control group) were similar. Compared with patient of control group, diabetic patients with RHT were not only older (by 7.9 years, $p < 0.001$), had longer duration of HT (by 13.8 years, $p < 0.001$) and DM (by 2.4 years, $p = 0.01$), but also had earlier onset of HT (by 5.6 years, $p < 0.000$) and later onset of DM (by 5.7 years, $p < 0.000$). Average serum aldosterone level in diabetic patients with RHT was higher (by 168.2 pg/mL, $p < 0.000$) and eGFR was lower (by 10.7 ml/min/1.73m², $p = 0.03$) than in patients with controlled HT. Frequency of insulin therapy in RHT patients were higher (25% vs. 10%, $p = 0.02$) and level of HbA1c was lower ($7.1 \pm 1.6\%$ vs. 8.2 ± 1.4 , $p = 0.004$) than those in control group.

Conclusions: Clinical characteristics of diabetic patients with RHT include older age, long duration and early onset of HT, association with increase of aldosterone level and progression of chronic kidney disease. Diabetic patients with RHT characterized by long duration of but late onset of DM that may reflect difference in mechanisms of development DM in patients with RHT and controlled HT. Higher frequency of insulin-requiring patients in RHT can particularly explain better glycaemic control in pts with RHT than in patients with controlled HT.

NEED OF ANTIHYPERTENSIVE ADJUSTMENT THROUGHOUT THE ONCOLOGIC TREATMENT

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Objective: Use of some antitumor drugs which are directed against vascular endothelial growth factor (VEGF) and tyrosine-kinase inhibitors has induced an immediate vital risk due to blood pressure sudden rising and a cause to limit both the dosage and the exposure to the chemotherapy.

Aims: To evaluate the implementation of a protocol for preferential derivation between the Oncology and Hypertension Units in order to decrease the incidence of severe hypertension and therefore to avoid oncologic therapy interruption. We created a preferential derivation (less than 48 h) between both units for these clinical reasons: recent hypertension diagnosis or severe hypertension diagnosis not responding to conventional antihypertensive treatment

Design and method: Data about patients gathering above mentioned criteria was evaluated. Collection of epidemiological, clinical variables, number of blood pressure-lowering drugs at initiation and final of oncologic treatment and number of needed treatment modifications.

Results: 42 patients, aged 37–81 yo (24 women, 26 with background of hypertension, 13 dyslipidemia, 6 diabetics) were included. Regarding the type of cancer, all of them in stage IV: 19 digestive, 14 gynaecological, 5 urological and 4 others.

VEGF inhibitors were used in 26 patients, tyrosine-kinase in 13 and both in the remaining 3. At the Hypertension Unit arrival, only 5 patients were free of antihypertensive drugs, 13 were under monotherapy, 12 bi-therapy, ⁹with triple therapy and 3 with 4 or more drugs. This treatment was maintained in 2 patients while 35 of them needed and adjustment with a maximum of 10 modifications throughout the follow-up period. 10 of them needed with 3 or more antihypertensive drugs. Hypertension Unit follow-up lasted for 1–43 months (mean 12.5). It was not necessary oncologic treatment withdrawal in any patient. 12 died during this period.

Conclusions: Specific derivation protocol/circuit has improved the tolerability to anti-angiogenic drugs. The multi-disciplinary approach of oncologic patients allows treatment optimization. The possibility of antihypertensive therapy adjustment (posology and dosage) across the anti-angiogenic treatment is associated with excellent results. No patient needed definitive withdrawal of oncology treatment throughout our follow-up period.

THE IMPACT OF CHRONOTHERAPY OF FIXED-DOSE TRIPLE-COMBINATION ON BLOOD PRESSURE TARGETS IN RESISTANT AND CONTROLLED HYPERTENSION PATIENTS

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Objective: to evaluate different effects on blood pressure (BP) control depending on the time of administration of antihypertensive treatment in resistant (rHTN) and controlled (HTN) hypertension patients.

Design and method: We studied 51 patients with true rHTN confirmed by the office and ambulatory BP monitoring (ABPM) despite the use of 3 antihypertensive medications with diuretic and 58 participants with HTN by triple therapy. Two groups of patients were comparable for age, sex and body mass index. All patients at baseline were randomized to ingest fixed-dose triple-combination (FDTC) upon awakening or at bedtime. Office BP and 24-h ABPM were evaluated at baseline and after 3 months. The analysis of the influence of chronotherapy on the reduction of BP was studied separately in the groups of patients with rHTN and HTN.

Results: There were no significant differences in adherence to therapy, office BP and average daytime and nighttime BP between the patients of the bedtime compared with the morning-treatment group in HTN and rHTN. In HTN patients normalization of clinic BP and ABPM values were observed at month 3 of follow-up, relative to baseline regardless of the time administration of FDTC. There was attenuated prevalence of non-dipping at the final evaluation (43 % vs 14 %, $P < 0.01$) in bedtime treatment, but some non-dipper patients (75 %) had over-dipping pattern. In rHTN patients reduction in average 24-h BP was greater with night-time administration than morning ($-23.8/-16.7$ mmHg vs. $-16.1/-9.4$ mmHg, $P < 0.05$) both due lowering effect to daytime and nighttime BP. However, the decrease in office BP did not differ between the groups. Bedtime treatment was associated with restoring the dipping BP profile in nondipping rHTN patients (80 % vs 33 % in patients on morning treatment, $P < 0.01$).

Conclusions: In rHTN patients ingestion of FDTC at bedtime compared with ingestion of medication upon awakening results in improved ambulatory BP control during day and night and restored normal dipper-type circadian BP rhythm. In HTN patients, bedtime dosing of FDTC demonstrated extreme dipping BP patterns even in patients with a blunted fall in night-time BP.

LONG ANTIHYPERTENSIVE EFFECT OF RENAL DENERVATION TO 3 YEARS OF FOLLOW-UP

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Objective: To determine the degree of reduction of arterial pressure and dynamics of the circadian profiles in patients with resistant arterial hypertension 3 years after renal denervation

Design and method: The study included 30 patients (average age 53.7 ± 9.6) with arterial hypertension resistant to drug therapy. All patients underwent office blood pressure measurement and ambulatory monitoring of blood pressure at baseline and after 1 and 3 years of renal denervation. The number of antihypertensive drugs throughout the study were not changed

Results: According to office measurements, baseline blood pressure made $168.4/95.0$ mmHg with reduction on $-27.0/-14.9$ mmHg after 1 year and $-27.5/-15.5$ mmHg after 3 years of denervation ($p < 0.05$). The average daily level of blood pressure source made up $159.2/87.3$ mmHg, with a decrease on $-11.0/-7.3$ mmHg after 1 year and on $-17.3/-9.2$ mmHg towards the end of the study ($p < 0.05$). Similar improvement is observed when comparing the average daily and average night of blood pressure and is $-17.6/-9.4$ mmHg and $-16.4/-8.1$ mmHg respectively ($p < 0.05$) by the end of the 3 years of observation. The decrease of the

temporary load index pressure in the daytime and at night on $-31\% -17\%$, respectively ($p < 0.05$). No patient included in the study were not recorded unwanted side effects connected with carrying out renal denervation. Negative dynamics of the level of blood creatinine or signs of stenosis of the renal arteries after ablation have not been identified

Conclusions: In patients with resistant arterial hypertension conducting renal denervation contributes to a pronounced and persistent decrease in the level of office blood pressure levels and indicators of ambulatory monitoring. This effect persists for 3 years observation of patients and evidence the positive impact of renal denervation on the hypertension, reducing the burden on target organs due to long-term lowering blood pressure, reducing the risk of developing cardiovascular complications

THE EFFICACY OF FIXED TRIPLE COMBINATION THERAPY IN ROUTINE CLINICAL PRACTICE

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Objective: Treatment of arterial hypertension reduces cardiovascular mortality and morbidity. Currently, the majority of patients during the treatment does not reach the target blood pressure (BP). One common cause of reaching the target pressure is poor adherence to treatment, which can improve the use of fixed combination therapy. The aim of our work is to analyze the effect on office blood pressure and influence of the number of antihypertensive medications deployment of fixed triple combination therapy (perindopril/indapamide/amlodipine)

Design and method: We enrolled 194 patients (122 men, average age 63.9 years). All patients underwent a clinical examination and office blood pressure measurements. It was subsequently modified antihypertensive therapy according to current guidelines ESH/ESC using a fixed combination of perindopril/indapamide/amlodipine. The effect of changes in therapy was evaluate the next clinical control, with an average interval of 15 weeks.

Results: Mean baseline office BP values were $168.9 \pm 22.1/87.9 \pm 12.6$ mmHg. Patients received treatment prior to the change was averaged 3.9 ± 1.4 antihypertensive drugs, which represented 3.3 ± 2.0 daily tablet antihypertensive drugs. After adjusting treatment insignificantly increased the number of daily used antihypertensive agent by 0.2 ± 1.0 ($p = 0.099$) and significantly reduced the number of antihypertensive tablets per day 1.2 ± 1.4 ($p < 0.001$). Systolic blood pressure after changing average decreased by 23.6 ± 3.7 mmHg ($p < 0.001$) and diastolic blood pressure by 9.7 ± 2.3 mmHg ($p < 0.001$). The average office blood pressure achieved after treatment therapies were $132.7/83.0$ mmHg.

Conclusions: The use of fixed triple combination therapy of arterial hypertension significantly reduced systolic and diastolic office blood pressure. At the same time there is a significant decrease in the number of antihypertensive tablets per day, which probably contributes to better adherence to treatment.

USE OF TRIPLE FIXED-DOSE ANTIHYPERTENSIVE DRUG COMBINATIONS IN RESISTANT HYPERTENSION – AMBULATORY BLOOD PRESSURE MONITORING RESULTS

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Objective: To check the efficacy of triple fixed-dose antihypertensive drug combination as continuation of separate drug regime during the follow-up at repeated ambulatory blood pressure monitoring (ABPM) in out-patient clinic.

Design and method: Triple fixed dose antihypertensive combination of perindopril, amlodipine and indapamide in four different dosage combinations is now available for 4 years. During years 2015 to 2017 we analysed 23 patients with resistant hypertension (16 men, 7 women) who had repeated ABPM procedures with time gap from 3 to 24 months, replacing separate drugs.

Results: Patients' age was 60 ± 11 years (37–79 years). During 1st ABPM average antihypertensive drug use was 3.3 ± 1.4 drugs (1–7 drug groups) with 61% of patients already taking the 3 studied drug groups separately (ACE inhibitor, diuretic and calcium channel blocker), or in double fixed combinations. 26% of patients were taking additional antihypertensive drug groups (e.g. beta blockers, alpha blockers, centrally acting drugs, spironolactone).

During 2nd ABPM triple fixed-dose perindopril /indapamide/amlodipine was prescribed ($10/2.5/10$ mg in 78%, $10/2.5/5$ mg in a single patient – 4% and $5/1.25/5$ mg in 18% of patients). Drug usage was intensified to 4.2 ± 1.3 antihypertensive drugs (3–7 drugs). Additional drug groups were prescribed in 22% of patients (beta blockers in 2, alpha blocker in 3 patients) and in 2 patients drug regimen could be simplified with discontinued drug groups (beta blocker and alpha blocker).

Average blood pressure during ABPM lowered from 151/84 mmHg to 135/73 mmHg (16/11 mmHg, $p < 0.047/p < 0.000$), during awake period from 154/87 mmHg to 137/76 mmHg ($p < 0.001/p < 0.030$) and during sleep from 136/72 mmHg to 131/68 mmHg (NS/NS). During 2nd ABPM adequate blood pressure control was achieved in 35% of patients. Systolic blood pressure control improved from initial 4% of patients to 39% and for diastolic blood pressure from 43% to 74%, respectively.

Conclusions: Intensive triple fixed dose antihypertensive drug combination, with prescription of additional antihypertensive drug groups when necessary, is effective way to simplify and improve control of resistant hypertension. Although blood pressure in our group of patients was significantly reduced, adequate blood pressure control still wasn't achieved in a majority of patients.

THE ROLE OF HIGH DIETARY SALT INTAKE IN DEVELOPMENT OF RESISTANT HYPERTENSION

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Objective: Aim of the study: evaluate salt-taste sensitivity and daily salt intake in patients with resistant arterial hypertension (RAH) during antihypertensive treatment (AHT).

Design and method: The study included 137 patients with high risk arterial hypertension in average age 56.6 ± 9.8 years. All patients took triple combination AHT with diuretic, RAAS-blocker and calcium antagonists during 3 months. After 3 months therapy 83.2% patients were achieved goal BP, 16.8% of them were resistant to triple combination AHT. Thus, patients divided into 2 groups: RAH ($n = 23$) and non-RAH ($n = 114$) and continued AHT with recommendation to reduce dietary salt intake to 5–6 g/24 h. Salt-taste sensitivity (STS) evaluation, implemented R.Henkin method with using sodium chloride in different concentration: from 0.01% to 1.28%. The patients divided to 3 STS thresholds: low (0.01%–0.08% NaCl), medium (0.16% NaCl), and high thresholds ($>0.32\%$ NaCl). Daily salt intake was calculated by urinary sodium excretion level multiply 2.55, before and after treatment.

Results: Patients with RAH characterized with significantly high systolic and diastolic BP (SBP/DBP): $178.1 \pm 15.4/103.3 \pm 10.1$ mmHg vs. $158.9 \pm 13.3/98.7 \pm 7.25$ mmHg in non-RAH group ($p = 0.0001$). STS test was shown prevalence high threshold of STS in RAH patients (high/medium $90.5\%/9.5\%$ $\chi^2 = 46.7$, $p = 0.0001$) in comparison with non-RAH group (high/medium/low $74\%/12\%/14\%$ $\chi^2 = 130.4$, $p = 0.0001$) with significant difference in sodium chloride concentration: $0.41 \pm 0.17\%$ vs. $0.3 \pm 0.18\%$, $p = 0.01$, for RAH and non-RAH groups respectively. Before AHT daily urinary sodium excretion rate was high in RAH patients (5.66 ± 2.49 g/24 h vs. 4.5 ± 2.54 g/24 h, $p = 0.056$), that corresponded to 14.4 g and 11.47 g daily salt intake in RAH and non-RAH respectively. During 6 months therapy BP significantly decreased in both groups, but in non-RAH group BP reducing was better with statistical difference: $128.3 \pm 11.46/80.8 \pm 7.9$ mmHg vs. $122.4 \pm 6.0/76.36 \pm 8.5$ mmHg, $p = 0.0001$ and $p = 0.022$ for SBP and DBP respectively. Daily urinary sodium excretion rate was significantly decreased only in non-RAH patients in comparison with RAH patients with statistical difference: 3.8 ± 2.29 g/24 h vs. 5.46 ± 2.7 g/24 h ($p = 0.006$).

Conclusions: Patients with RAH characterized with high STS threshold and dietary salt intake. During six monthly optimal AHT, BP significantly reducing in both groups, but in non-RAH patients BP and daily urinary sodium excretion was statistically lower.

COMPARATIVE EVALUATION OF RESISTANT AND REFRACTORY HYPERTENSION: CLINICAL AND ABPM DATA

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Objective: Background: Resistant hypertension (RHT) is defined as failure in control of hypertension despite of using three antihypertensive agents in maximal dose including a diuretic. Refractory hypertension (RFHT) is defined variably as either failing treatment after at least 3 months or failing to control blood pressure with use of over 5 different classes of antihypertensive agents. RHT is multifactorial in cause: excess fluid retention, older age, obesity, chronic kidney disease, diabetes are well-recognized causes. The underlying mechanisms of RFHT are not clearly established, but some data suggest a possible role of increased sympathetic tone. The aim of this work was to evaluate the real prevalence of RHT and RFHT using arterial blood pressure monitoring (ABPM) in patients with clinical suspicion of RHT and a comparative evaluation of clinical and ABPM derived parameters including blood pressure variability (BPV) in this two special group of hypertensives.

Design and method: Material and methods: Approximately 600 hypertensive patients were evaluated. Clinical blood pressure, age, sex, BMI, smoking status, associated diabetes and target organ damage were evaluated. ABPM monitoring on patients with clinical suspicion of RHT and a repeated second ABPM on patients with suspicion of RFHT (after 3 month of treatment optimization) were performed.

Results: RFHT has apparently high prevalence among hypertensive patients with RHT, but after treatment optimization the real prevalence is around 2–3%. RHT is more often in males, older and with higher BMI. RFHT patients are younger, without differences between sexes and with higher prevalence of comorbidities (renal, cardiovascular) Additional ABPM indices as high pulse pressure and pressure load, non-dipping or rising pattern, morning surge are present in RHT and RFHT patients with unfavorable prognostic significance and predictors of high cardiovascular risk

Conclusions: The high systolic blood pressure, higher heart rate values and the low variability present in RFHT patients suggests an increased sympathetic activity in these patient. This could be a new therapeutic on this special group of hypertensive pathology.

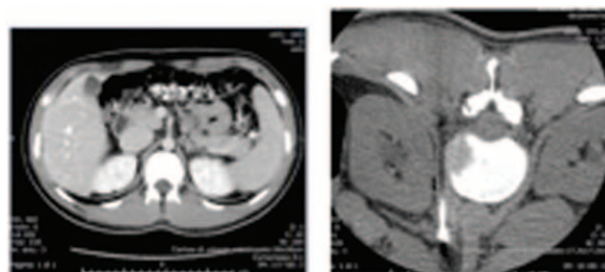
SEVERE HYPERTENSION IN A YOUNG BOY WITH PARAGANGLIOMA OF THE ORGAN OF ZUCKERKANDL TREATED WITH THERMOABLATION

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Objective: Paragangliomas are tumors of the paraganglia, chromaffin tissue complexes of the neuroendocrine system distributed along the paravertebral and para-aortic axes. A small number of these tumors arise from the organ of Zuckerkandl that is the smallest endocrine gland, composed by paraganglia. These organs are accessory tissues of the autonomic nervous system that undergo involution during childhood. By adulthood distinct microscopic groups of extra-adrenal chromaffin cells endure and have the potential to develop into tumors that are rare cases of secondary hypertension.

Design and method: A 19-year-old professional footballer, since two years, developed severe symptomatic hypertension forcing him to stop all activities. During each episode he reported headache, sweating, tachycardia, blurred vision and paradoxical hypotension. No drugs were effective to lower blood pressure. Laboratory hormonal assessment were discordant, with high daily urinary catecholamines but daily adrenaline, noradrenaline and dopamine in range.

We performed a CT scan and a MRI of the abdomen that showed a nodular lesion of 7 mm near the left crus of diaphragm, where the left superior mesenteric artery originates (Figure 1). An iodine-123-meta-iodobenzylguanidine scan revealed an abnormal radiotracer uptake in the region of the mass identified by CT.



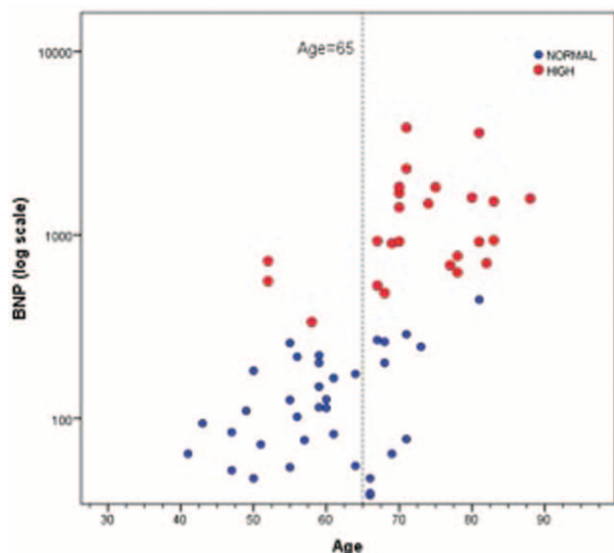
Results: A multidisciplinary team composed by cardiologist, anesthesiologists and interventional radiologist, previous a particular preoperative management, performed an innovative surgical technique consisting in a two-steps CT-guided percutaneous radiofrequency ablation of the mass (Figure 2), at 65 and 100 W of energy for 5 minutes, after appropriate hydrodissection of perilesional tissues. A small tissue sample was obtained and pathology found the tissue was suggestive of an organ of Zuckerkandl.

Conclusions: This is absolutely the first case in literature, since exist only few cases of robot-assisted laparoscopic excision, laparoscopic resection or laparotomy. The patient recovered well from the operation and was eventually discharged in a stable state. He's no longer suffering from hypertension and he started playing football again. 24-hour ambulatory blood pressure monitoring, after 15 days from discharge, shows satisfying blood pressure values (Figure 3).

RESISTANT HYPERTENSION IN ELDERLY: A CLINICAL MANIFESTATION OF HFPEF ? RETROGRADE SINGLE CENTER ANALYSIS

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Objective: Resistant hypertension is defined as high blood pressure despite treatment with at least 3 different class of antihypertensive drugs at best tolerated doses. Resistant hypertension is a common clinical problem and has not been studied widely. The present study has investigated the diagnostic differences and the relationship between resistant hypertension and the N-terminal pro-brain natriuretic peptide (NT-proBNP) level, which is a marker of heart failure among the resistant hypertensive patients according to age retrospectively.



Design and method: The outpatient data of 957 patients, who applied to the hypertension specialty clinic of Izmir Kemalpaşa State hospital between 1st of January and 30th of June 2015, has been reviewed retrospectively. The patients with pseudo-resistant hypertension and secondary hypertension are excluded. All the resistant hypertensive patients have had an echocardiogram, renal Doppler ultrasonogram, NT-proBNP and thyroid function tests in addition to the electrocardiogram (ECG), routine biochemistry and urine exam, which have been performed for every resistant hypertensive patient according to the clinic's algorithm, 68 patients have been identified as true resistant hypertensive with an ejection fraction (EF) > 50, no moderate to severe valvular disease and serum creatinine level < 1.5. The present study has investigated the relationship between resistant hypertension and the NT-proBNP level, which is a marker of heart failure.

Results: The mean age was 58.94 ± 11.81 years. Among 68 patients, 49 were female and 19 were male. Only 9 patients had atrial fibrillation and 59 were on sinus rhythm. Instead of a common cut-off level for NT-proBNP, age (decades) and gender related cut-off levels have been used for each patient. NT-proBNP levels were disproportionally high in elderly patients (<0.001) and high NT-proBNP levels in resistant hypertensive patients were related to a larger left atrial diameter (<0.001).

Conclusions: Resistant hypertension could be the clinical manifestation of various diseases with different etiology. Resistant hypertension in older patients can be a clinical presentation of heart failure with preserved ejection fraction (HFpEF). Elderly patients with resistant hypertension should be investigated for HFpEF and treated accordingly. Because of one-center results and limited number of patients, further studies are needed.

CORRELATION RELATIONSHIPS AGES, OFFICE BLOOD PRESSURE, EGFR, RENIN, ALDOSTERONE, METANEPHYRYS LEVELS IN PATIENTS WITH RESISTANT HYPERTENSION

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Objective: The purpose of this analysis was to determine factors that contribute to poor blood pressure lowering in patients with resistant hypertension.

Design and method: We examined and treated 1146 patients with AH and take 3 or more antihypertensive drugs (62.7% - women, 37.3% - men). Mean age was 57.9 ± 0.4 years, weight - 87.7 ± 0.6 kg/m². At baseline mean office blood pressure (BP) was $174.6/100.5 \pm 0.6/0.4$ mmHg.

Results: Mean office BP after treatment was $131.3/80.1 \pm 0.4/0.6$ mmHg. Patients had dyslipidemia - 65%, type 2 diabetes - 16.6%, cerebrovascular disease - 15.8% (ischemic stroke - 12.8%), thyroid disease - in 10.4%, including hypothyroidism - 2.8%, chronic pyelonephritis - 16.3%, obstructive sleep apnea - 3.3%, chronic kidney disease - 3.3%. Ages was correlation with weight ($r = -0.255$, $p < 0.01$), triiodothyronine ($r = -0.40$, $p < 0.01$), thyroid-stimulating hormone ($r = 0.169$, $p = 0.01$), eGFR ($r = -0.551$, $p < 0.01$), SBP after treatment ($r = -0.081$, $p < 0.012$), DBP after treatment ($r = -0.230$, $p < 0.01$), glucose ($r = 0.125$, $p < 0.01$), left ventricular myocardial mass index ($r = 0.159$, $p < 0.01$), potassium ($r = 0.077$, $p = 0.01$), takes beta-blockers ($r = 0.128$, $p < 0.01$), takes calcium antagonists ($r = -0.126$, $p < 0.01$). BMI was correlation with aldosterone levels ($r = -0.190$, $p = 0.04$), urine metanephryls ($r = -0.247$, $p = 0.02$). Renin level was correlated with total cholesterol ($r = -0.319$, $p = 0.002$), TG ($r = -0.267$, $p = 0.02$), office SBP after treatment ($r = -0.243$, $p = 0.03$), office DBP after treatment ($r = -0.230$, $p = 0.04$). SBP after treatment was correlated with men ($r = 0.135$, $p = 0.001$), eGFR ($r = -0.132$, $p = 0.01$), high density lipoproteins ($r = -0.170$, $p = 0.007$). DBP after treatment was correlated with potassium ($r = -0.066$, $p = 0.041$).

Conclusions: Patients whose taken 3 or more antihypertensive drugs less decreased BP was associated with male sex, less of renin level, less eGFR, bigger body mass index, was younger, less level of high density lipoproteins, less of potassium level, higher left ventricular myocardial mass index.

ENDOVASCULAR RENAL DENERVATION EFFICACY AND FEASIBILITY IN END-STAGE KIDNEY DISEASE WITH RESISTANT HYPERTENSION

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Objective: Sympathetic neural activation is markedly increased in end-stage kidney disease or in dialysis treatment, making hypertension difficult to control. Nephrectomy should be considered to remove the reflex pressor effects of the afferent fibers originating in renal parenchyma, but - due to the high risk of morbidity and mortality associated with the surgical procedure - endovascular renal denervation (RDN) may be an alternative therapeutic strategy to improve blood pressure levels.

Figure 1

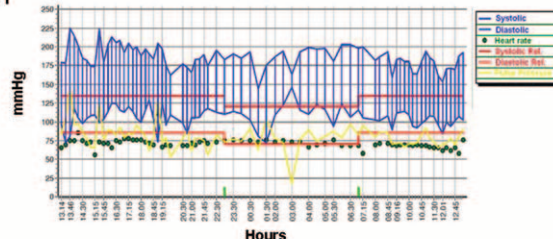
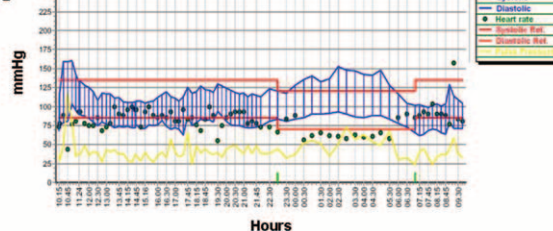


Figure 2



Design and method: A 47-year-old male, with a long history of hypertension complicated by renal amyloidosis diagnosed in 2009, was admitted to our emergency department 3 times in the last 2 months for hypertensive crises with initial

signs of encephalopathy. He followed a dialysis program 3 times a week. At the last admission, his blood pressure was in average 256/142 mmHg under up to 10 antihypertensives medications (nifedipine 120 mg/day, ramipril 20 mg/day, furosemide 500 mg/day, doxazosine 12 mg/day, valsartan 320 mg/day, and hydrochlorothiazide 25 mg/day). Resistant hypertension was confirmed by the 24-h ambulatory blood pressure measurement (Figure 1). Patient underwent bilateral RDN using a 3rd-generation Spyral™ catheter, a device with multi-electrode configuration that is associated with a reduced procedural time, contrast use and radiation exposure.

Results: The procedure was completed without complications. After 48 hours office systolic blood pressure was 40 mmHg lower, and controlled

with 4 antihypertensive drugs 1 month later (Figure 2) through the 24-h ambulatory blood pressure measurement.

Conclusions: Bilateral RDN procedure in dialyzed patients with resistant hypertension was feasible without complications and produced an acute and long-term significant decrease in blood pressure. End-stage kidney disease might be the source of a persistently elevated activity of afferent signals to sympathetic nervous system, and the interruption of this loop may favour blood pressure reduction. This may be obtained by RDN with no need of surgical kidney removal.

POSTER SESSION

POSTERS' SESSION PS04:

HEART

THE PATHOGENESIS OF HYPERTENSIVE HEART IN EXTREME NORTH CONDITIONS

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Objective: To study the relationship between the autonomic nervous system dysfunction (ANSF) with circadian BP disorders and structural changes of the heart in patients with AH in Far North conditions.

Design and method: 373 patients engaged in monthly round-trip sojourns to the Arctic with arterial hypertension (AH) of 1–2 stages (Gr.1) and 144 inhabitants of moderate climate zone with AH of 1–2 stages (Gr.2) were examined. The groups were matched for age ($p = 0.4450$), AH experience ($p = 0.7333$), office SBP ($p = 0.3222$); DBP ($p = 0.0640$).

All patients underwent ABPM, echocardiography, 24-hour heart rate variability and vegetative status using the questionnaire offered by A.M.Vayne.

Results: ANSD was detected significantly more often in Gr.1 compared to Gr.2 according to the survey ($p = 0.0279$) and according to the physical examination ($p = 0.0001$). Heart rate (HR) variability (SDNN and SDNN5 indices) in Gr.1 was significantly lower than in the Gr.2 ($p = 0.0266$) with significantly low circadian index (CI). Higher 24-hour DBP was detected in Gr.1 due to high night-time DBP and day/night BP variability ($p < 0.00001$). 24 h HR, daytime HR and night-time HR in Gr.1 were significantly higher than in Gr.2. In Gr.1 compared to Gr.2 diurnal SBP and DBP were significant lower as well as CI ($p < 0.0001$). With equal office BP values in both groups, LVM and LVMI were higher in Gr.1 as compared with Gr.2 (LVM: 281.5 ± 90.4 g., LVMI 130.3 ± 26.2 g. vs 247.5 ± 76.6 , $p = 0.0002$ and 128.8 ± 36.4 , $p = 0.0024$). The most prevalent type of LV structural changes in Gr.1 was concentric LV hypertrophy ($p = 0.0014$). Higher LVM and LVMI values were due to thicker inter-ventricular septum ($p < 0.0001$) and LV posterior wall ($p < 0.0001$) as well as large left atrium ($p = 0.0088$).

Conclusions: Thus, in Arctic monthly round-trip sojourns conditions the influence of exogenous factors can cause in autonomic and neurohumoral BP regulation mechanisms the circadian-dependent changes that modulate the circadian rhythm of BP and structural changes in the heart. As a result, metabolic disorders and hemodynamic alterations towards increasing BP with severe LV hypertrophy occur.

LABORATORY PREDICTORS OF THE RISK OF RECURRENT CARDIOVASCULAR EVENTS IN PATIENTS WITH UNSTABLE ANGINA AND ARTERIAL HYPERTENSION AND STENTING OF THE CORONARY ARTERIES

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Objective: To determine independent laboratory predictors of the risk of developing repeated cardiovascular events in patients with unstable angina (UA) and arterial hypertension (AH) and stenting of the coronary arteries for 1 year of follow-up.

Design and method: 143 patients with UA who underwent stenting of the coronary arteries by 3.6 ± 1.2 days after admission. 1 Group 63 (44%) patients mean age 61.2 ± 6.5 years without AH, 2 group 80 (56%) patients mean age 63.5 ± 4.5 years with AH. All patients initially, at discharge, at 6 and 12 months of follow-up was performed aggregation, coagulation tests, levels of troponin I, C-reactive protein, myeloperoxidase, BNP.

Results: Over the 1 year of follow-up, repeated cardiovascular complications developed in 10 patients G1 (15.9%) and 21 G2 (26.3%) ($p = 0.048$). After 12 months a large-heart attack of myocardial infarction developed in 1 patient (1.6%) from G1 and in 3 patients from G2 (3.7%), in 27 cases recurrent angina developed (9 persons G1 (14.3%) and 18 G2 (22.5%). There were no death.

Independent laboratory predictors of the risk of recurrence of cardiovascular events (MI, recurrent angina pectoris) after UA with AH are: baseline von Willibrand factor $> 149\%$ (sensitivity-73.6%, specificity 84.6%), myeloperoxidase level > 348 mmol/l (sensitivity - 80.3%, specificity 81%), platelet volume- MPV > 9.8 fl (sensitivity - 86.0%, specificity - 90%) AUC value of the ADR test > 68 U.

Independent predictors of the risk of developing cardiovascular complications after UA without AH are: baseline CRP > 6.8 g/l (sensitivity 84.4%, specificity 78.5%), BNP > 129 pg/ml (sensitivity - 80.0%, specificity - 91%) and AUC value of ADR test > 60 U.

Conclusions: The independent predictors of adverse outcomes in patients with UA and AH after stenting of the coronary arteries are the baseline levels of PVI 149%, myeloperoxidase > 348 pmol/L, platelet count of MPV > 9.8 fl, ADR test value > 68 U, and for patients with UA and without AH: baseline levels of CRP > 6.8 g/l, BNP > 129 pg/ml and ADR-test AUC value > 60 U.

CARDIOTOXICITY IN PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER UNDERGOING ANTHRACYCLINE CHEMOTHERAPY DEPENDING ON BLOOD PRESSURE LEVEL

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Objective: to study the risk of cardiotoxicity in patients with triple negative breast cancer with arterial hypertension (AH) during anthracycline chemotherapy.

Design and method: 70 women [48.6 ± 13.3 yrs] with breast cancer were enrolled. In all patients office blood pressure (BP) was thrice measured. Echocardiography, including 2D STE, was performed before and after 8 courses of antitumor therapy. Left ventricular ejection fraction (LVEF) measured with the biplane Simpson's method and global longitudinal strain (GLS) [normal GLS -22.1 ± 1.8 for women] were analyzed.

Patients depending on blood pressure level were divided into 2 groups: group 1 - with AH ($n = 18$) and group 2 - without AH ($n = 52$).

Results: The average level of office BP in group 1 was $130.8 \pm 2.3 / 79.5 \pm 2.7$ mm Hg. After chemotherapy target BP level was maintained in 10 patients. There was a significant LVEF reduction after chemotherapy (from $68.9 \pm 5.8\%$ to $63.7 \pm 6.7\%$, $p < 0.05$). Initially in group 1 GLS was lower than normal range ($-19.1 \pm 2.8\%$, $p < 0.05$), after chemotherapy further GLS decrease was recorded (from $-19.1 \pm 2.8\%$ to $-16.4 \pm 3.8\%$ [$p < 0.05$]).

There was a further progression of AH (mean systolic BP (sBP) 162.2 ± 11.2 mmHg, mean diastolic BP (dBP) -98.3 ± 4.9 mmHg) in 8 patients (44.4%) in spite of antihypertensive therapy during chemotherapy. After chemotherapy reduction in LVEF was observed (from $65.9 \pm 3.4\%$ to $62.0 \pm 2.0\%$ (n.s.)). GLS before chemotherapy was below the normal values ($-18.0 \pm 1.5\%$), after chemotherapy GLS values were $15.6 \pm 1.3\%$ (n.s.).

Also there was an increase in BP in 7 patients (13.4%) without initial AH during chemotherapy (mean sBP -148.3 ± 5.8 mmHg, mean dBP -94.1 ± 3.7 mmHg). Before and after chemotherapy the LVEF was $68.9 \pm 1.7\%$ and $67.9 \pm 1.5\%$, consequently. There were practically no changes in initially normal GLS before ($21.8 \pm 0.4\%$) and after chemotherapy GLS ($21.4 \pm 0.5\%$, (n.s.)).

Conclusions: Patients with AH already have a subclinical impairment in cardiac function, which makes them more vulnerable to cardiotoxic effects of chemotherapy.

HEMODYNAMIC MODULATORS (VOLEMIA, INOTROPY, CHRONOTROPY AND VASOACTIVITY) AND HEMODYNAMIC STATUS IN TREATMENT-NAÏVE, DEBUTING HYPERTENSIVE PATIENTS

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Objective: No single antihypertensive class has been shown to be superior to the rest of drugs, especially in treating debuting hypertension (HTN). Nevertheless, hemodynamic factors involved in HTN may vary significantly. Aim of this study is to describe the hemodynamic components of debuting HTN according to thoracic bioimpedance analysis (impedance cardiography).

Design and method: Cross-sectional, observational study in 64 consecutive, treatment-naïve hypertensive patients referred to a Hypertension Unit for study. Standard clinical and laboratory examinations were performed, including ABPM and echocardiography. Impedance cardiography by the HOTMAN® System was used for noninvasive assessment of hemodynamic modulators and evaluation of the hemodynamic status of the patients.

Results: Mean age was 50.0 years in 39 (60.9%) men and 25 (39.1%) women. Office systolic and diastolic BP averaged 144/86 mmHg, 24-h-ABPM was 137/90 mmHg. 41 patients (64.1%) were diagnosed as normodynamic, 14 (21.9%) as hyperdynamic and 9 (14.1%) as hypodynamic. 13 patients (20.3%) were strictly normal, while up to 5 different hemodynamic states were found in the rest. Intravascular hypervolemia was present in 59 patients (92.2%), in 21 patients (32.2%) as the only abnormality, followed by 22 (34.4%) with vasoconstriction, 20 (31.3%) with hyperinotropy and 18 (28.1%) with hypoinotropy. Eleven combinations of hemodynamic modulators were found, being the most common hypervolemia either combined with hyperchronotropy in 13 patients (20.3%), or with vasoconstriction or with hypochronotropy and hypoinotropy each in 6 patients (9.4%).

Conclusions: Our data suggest that abnormal hemodynamic modulators play an important role in incident hypertension. We found a strong association between intravascular hypervolemia and elevated blood pressure in debuting hypertensives, while abnormalities in peripheral vascular tone if any, played only a secondary role and always in combination with hypervolemia. Future longitudinal outcome studies are required to test the potential clinical benefits of guiding pharmacological treatment by measurement of hemodynamic modulators.

EARLY MARKERS OF CARDIOTOXICITY IN PATIENTS WITH BREAST CANCER WITH OR WITHOUT ARTERIAL HYPERTENSION

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Objective: to evaluate the development of cardiotoxicity in patients with triple negative breast cancer with or without arterial hypertension (AH) during anthracycline chemotherapy

Design and method: 70 women [mean age 48.6 ± 13.3 yrs] with triple negative breast cancer were enrolled. Echocardiography, including 2D Speckle Tracking Imaging, was performed before and after 8 weeks of chemotherapy with doxorubicin, cisplatin, paclitaxel. Left ventricular ejection fraction (LVEF) (the biplane Simpson's method) and global longitudinal strain (GLS) [mean normal GLS of -22.1 ± 1.8] were analyzed. Patients were divided into 2 gr.: gr. 1 - with AH (n = 18) and gr. 2 - without AH (n = 52).

Results: Before chemotherapy in gr. 1 GLS was lower than the normal value ($-19.1 \pm 2.8\%$ vs $-22.1 \pm 1.8\%$) ($p < 0.05$) and lower than in the gr. 2 [$-19.1 \pm 2.8\%$ vs $-20.0 \pm 2.8\%$ (n.s.)]. After chemotherapy in all patients decrease of GLS was observed (from $-20.0 \pm 2.8\%$ to $-18.5 \pm 2.9\%$) ($p < 0.05$) and in both grs: in gr. 1 from $-19.1 \pm 2.8\%$ to $-16.4 \pm 3.8\%$ ($p < 0.05$), gr. 2 from $-20.0 \pm 2.8\%$ to $-19.2 \pm 2.4\%$ ($p < 0.05$), however LVEF decreased, but remained within normal values.

Conclusions: Initially GLS was lower than the normal value in patients with AH and breast cancer. Patients with AH and breast cancer, receiving anthracycline chemotherapy constitute the risk group of cardiotoxicity. Thus, patients with AH and breast cancer must be observed by a cardiologist and an oncologist.

PROGNOSTIC VALUE OF OFFICE BLOOD PRESSURE MEASUREMENT AND HYPERTENSION DIAGNOSIS IN ATRIAL FIBRILLATION: SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: In the presence of atrial fibrillation (AF) cuff-based blood pressure measurement is uncertain. Thus, AF patients have been systematically excluded from hypertension outcome trials. A meta-analysis of prospective outcome trials in AF patients on oral anticoagulants was performed, aiming to evaluate the prognostic significance of office blood pressure (OBP) measurements and hypertension diagnosis.

Design and method: A systematic PubMed search was performed as follows: (('atrial fibrillation') AND ('blood pressure' OR hypertension)) AND anticoagula*) AND (stroke OR embolism OR thromboembolism OR outcome OR 'cardiovascular events'). Articles were also identified from reference lists of relevant papers and hand search. Prospective studies with at least 50% of AF patients on oral anticoagulant therapy were included.

Results: The meta-analysis included 8 studies (n = 73,930) in which 53% (1 study) to 100% (5 studies) of participants received anticoagulants. There was considerable heterogeneity in the OBP methodology, which was not standardized in most studies. Four studies reported on the prognostic value of baseline OBP and/or history of hypertension diagnosis, 2 on the average OBP control during follow-up, and 2 on both baseline and follow-up OBP control. Meta-analysis of 6 studies (5 studies used baseline OBP/hypertension diagnosis; 69,018 subjects; 130,943 person-years) showed elevated OBP and/or hypertension diagnosis to predict stroke or systemic embolism (hazard ratio [HR] 1.28; 95% confidence intervals [CI] 1.12, 1.45). Meta-analysis of 7 studies (n = 69,983) showed elevated OBP and/or hypertension diagnosis not to predict major haemorrhage (HR 1.11; CI 0.98, 1.25). Meta-analysis of 3 studies (n = 29,477) showed that follow-up OBP control strongly predicted stroke or systemic embolism (HR 1.79; CI 1.38, 2.32) (z-score -2.3, $p < 0.05$ versus HR of 6 studies), but not major haemorrhage (HR 1.13, CI 0.95, 1.35). OBP and/or hypertension diagnosis did not predict all-cause mortality (7 studies; n = 66,524; HR 1.07; CI 0.91, 1.26).

Conclusions: Outcome studies suggest that in AF patients, OBP and hypertension diagnosis predict stroke or systemic embolism, but not major haemorrhage or all-cause mortality. Follow-up OBP control appears to have stronger predictive ability than baseline OBP and/or hypertension diagnosis.

PREVALENCE OF ARTERIAL HYPERTENSION IN PATIENTS WITH ATRIAL FIBRILLATION: ONE CENTER EXPERIENCE

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Objective: To determine the prevalence of hypertension in patients suffering from atrial fibrillation (AF), to assess echocardiographic parameters in patients with AF with or without hypertension, and to assess the current status of the use of anticoagulation for the treatment of AF.

Design and method: The study included 167 patients with AF: 116 men (69.46%) and 51 women (30.54%) who were hospitalized at our University Hospital between 2014. and 2016 year. Out of 167 patients with AF, 133 (79.6%) had hypertension (group AFHT), while 34 (20.4%) had not (group AF). In all pts echocardiography study was performed and size of left atrium (LA), ejection fraction (LVEF) and systolic pulmonary artery pressure (sPAP) were determined.

Results: The most common type of atrial fibrillation AFHT group was paroxysmal (37.5%), while in the AF group was permanent (40.2%). Size of LA was higher in AFHT group than in AF group (48.3 ± 6.84 vs 47.4 ± 10.82 mm, ns), as well as LVEF 49.5% vs 48.8% (ns). Patients with new diagnosed AF and hypertension had statistically higher values of LVEF than patients with first diagnosed AF without hypertension (53.0 ± 14.6 vs 39.2 ± 10.5 ; $P < 0.042$). Value of sPAP was higher (ns) in the subgroup of pts with first diagnosed and pts with persistent AF in AFHT than in AF group. At the admission, only 98 (58.7%) pts had used oral anticoagulant therapy, while 127 (76.1%) pts was on OAT at discharge.

Conclusions: Our study showed high prevalence of arterial hypertension in patients with atrial fibrillation. In pts with AF, size of LA, LVEF and sPAP are higher in pts with than without hypertension. In spite of high prevalence of AF, use of OAT is still low.

CORRELATION BETWEEN GRADE OF HYPERTENSION AND EXTENSION OF CORONARY ARTERY DISEASE IN HYPERTENSIVE PATIENTS – CROSS-SECTIONAL STUDY FROM CENTRAL ROMANIA

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Objective: The prevalence of coronary artery disease (CAD) is more susceptible to develop in hypertensive patients with multiple associated cardiovascular risk (c-v) factors. We hypothesized that the number and severity of coronary lesions is directly related to hypertension grade and concomitant presence of different c-v risk factors.

Design and method: Between September 2015 to February 2016, 283 hypertensive patients (mean age 63 ± 9.039 y.o.) performed invasive evaluation of coronary arterial tree. Clinical indications were: ischemic heart disease, cardiomyopathies, valvular heart disease and rhythm and conduction disturbances. An observational, cross-sectional study was conducted; clinical and imaging results were computed.

Hypertensive patients were stratified to 3 grades according to 2013 ESH/ESC guidelines for the management of arterial hypertension (HT). Patients were divided according to the number of coronary arteries involved: single, double, triple vessel CAD.

Results: With regard to hypertension grades correlated with CAD, in our study 3.1%(9) pts were included in grade 1 HT, 53.0% (150) grade 2 HT and 19.08% (54) patients were diagnosed with HT grade 3. No significant CAD was described in 70 pts (24.73%) presenting grades 1, 2 and 3 HT.

Out of 190 male and 93 female hypertensive patients, 61.13% (173 pts) had significant CAD (>50% reference vessel diameter reduction). Single vessel disease was present in 88.8% of grade 1 hypertensive patients, and triple vessel disease was identified in 29.3% of patients presenting hypertension grade 2 compared to 24.0% in grade 3 hypertensive patients.

Correlation between grade of HT and severity of CAD (number of affected vessels) was studied using chi-square test, demonstrating a very strong statistically correlation ($p < 0.0001$).

Conclusions: Not optimally treated high grades of hypertension will increase the number of patients requiring different procedures of myocardial revascularization. Extended research on risk factors predisposing to coronary artery disease and their synergism, among them high blood pressure, is necessary in order to reduce the global burden of cardiovascular disease.

EVALUATION OF PLATELET-PLASMA HAEMOSTASIS IN PATIENTS WITH UNSTABLE ANGINA AND STENTING OF THE CORONARY ARTERIES IN THE PRESENCE OF HYPERTENSION

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Objective: To evaluate the activity of platelet and plasma hemostasis in 143 patients (pts) with unstable angina (UA) and stenting of the coronary arteries against the background of arterial hypertension (AH).

Design and method: 143 pts were examine, coronary artery stenting was performed on 3.6 ± 1.2 days after admission. 1 Group 63 (44%) pts without AH, in the 2nd Group 80 (56%) pts with AH initially, at discharge, at 6 and 12 months of observation was performed coagulation, aggregation tests; levels of troponin I, C-reactive protein, myeloperoxidase. Pharmacogenetic testing was carried out by real-time polymerase chain reaction with the BioRad CFX96TM Real-Time PCR Detection Systems.

Results: Pts in both Groups were characterized by activation of platelet-plasma haemostasis upon admission, however, in pts with UA with AH (G2) the values were significantly higher: platelet volume (MPV) (9.8fl vs 9.1fl , $p = 0.003$), FVR (158% vs. 130% , $p = 0.041$), MPO (348 pmol/L vs. 296 pmol/L , $p = 0.001$), platelet aggregation level with an AUC (122-U) test against the 106U (TRAP test) $p = 0.02$ and the AUC of the ADR test (68 U versus 52 U , $p = 0.02$). By the 6th and 12th months of monitoring, significant differences were recorded only between pts G1 and G2, who did not achieve stable target BP values. It should be noted that the pts of both Groups are comparable in polymorphism of the CY-P2C19 * 2 gene with the AA and GA variant genotype and the carrier of the A allele, which is associated with high residual platelet reactivity in response to clopidogrel 75 mg and unfavorable outcomes (carriage of the allele in T1-y8 (12.7% pts, in G2 - in 11 (13.8%) of the pts). During the year of follow-up, repeated cardiovascular complications developed in 31 pts (21.7%), 10 (15.9%) G1, and 21 (26.3%) G2 ($p = 0.048$).

Conclusions: The presence of AH in pts with UA aggravates platelet hyperaggregation and activates plasma and platelet hemostasis, increase in the number of pts with reduced sensitivity to clopidogrel and an increase cardiovascular events.

TELMISARTAN, A DUAL ARB/PARTIAL PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA AGONIST, PROTECTS MYOCARDIUM FROM ISCHAEMIC REPERFUSION INJURY IN EXPERIMENTAL DIABETES

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Objective: Apart from its angiotensin receptor blocker (ARB) activity, telmisartan is also a partial agonist of peroxisome proliferator-activated receptor gamma. Therefore, we assessed whether telmisartan treatment attenuates myocardial ischaemia/reperfusion (I/R) injury in diabetic rats through peroxisome proliferator-activated receptor gamma pathway.

Design and method: Diabetic rats were randomized to receive vehicle (sham and I/R), telmisartan (10 mg/kg/day , orally), peroxisome proliferator-activated receptor gamma antagonist GW9662 (1 mg/kg/day , intraperitoneally) or both for 14 days. On 15th day, excluding sham group, left anterior descending coronary artery occlusion was performed for 45 min followed by 1 h of reperfusion. Haemodynamic, biochemical, histopathological, ultrastructural, immunohistochemical (Bax and Bcl-2 protein), TUNEL positivity, infarct size and western blot studies were performed.

Results: Telmisartan treatment significantly improved cardiac function by normalizing mean arterial pressure, left ventricular pressure ($\pm\text{LVdP/dt(max)}$), a marker of myocardial contraction and relaxation), by decreasing left ventricular end-diastolic pressure (a marker of preload, 3.7 ± 0.41 vs. 7.3 ± 0.89 , $p < 0.001$) and percent infarct area (37.52 ± 5.83 vs. 46.27 ± 3.20 , $p < 0.01$) as compared to diabetic I/R group. Interestingly, GW9662 worsens the I/R injury (percent infarct area, 54.38 ± 6.48 vs. 46.27 ± 3.20 , $p < 0.01$), whereas telmisartan with GW9662 (percent infarct area, 41.16 ± 8.23 vs. 46.27 ± 3.20 , $p < 0.05$) showed lesser significant results as compared to telmisartan alone. Additionally, telmisartan significantly ameliorates activities of endogenous antioxidants, creatine kinase-MB isoenzyme, lactate dehydrogenase and prevented the increase of tumour necrosis factor-alpha and malondialdehyde in myocardium. Furthermore, telmisartan also decreased Bax expression ($4.45 \pm 1.24\%$ vs. $10.25 \pm 0.96\%$, $p < 0.01$), number of TUNEL-positive cells inflammation, myonecrosis and increased Bcl-2 expression. Telmisartan protective effects were partially attenuated by a co-administration with GW9662. Western blot analysis showed that telmisartan treatment enhanced peroxisome proliferator-activated receptor gamma expression, whereas GW9662 decreased it in myocardium.

Conclusions: In addition to the class effect of ARBs, Telmisartan has a beneficial effect in I/R injury in diabetic rats in part because of activation of peroxisome proliferator-activated receptor gamma.

RELATIVELY IMPAIRED CORTISOL SUPPRESSION BY DEXAMETHASONE IS ASSOCIATED WITH LEFT VENTRICULAR MASS AND GEOMETRIC CHANGES IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Objective: Both subclinical hypercortisolism and overt Cushing syndrome are associated with cardiovascular events and changes in left ventricular (LV) geometry. However, few data are available on the relationship between cortisol production and LV mass and geometry in essential hypertensive (EH) patients.

Design and method: In 103 EH subjects (age 50 ± 14 y, 58 males, 33 never treated with antihypertensive drugs), we evaluated clinical characteristics, renal function, plasma levels of glucose, insulin, and lipids, the circadian levels of plasma cortisol (8 AM, 5 PM, and 11 PM) with the area under the curve (C-AUC), 24-h urinary cortisol excretion, and the response of plasma cortisol to an overnight suppression test with 1 mg of dexamethasone (DMT). Echocardiography was performed in all patients with a standard technique.

Results: LV hypertrophy (LVH) according to current criteria was detected in 34 of 103 EH patients. Patients with LVH were significantly older, had longer duration of hypertension, and greater BMI, systolic blood pressure, plasma triglycerides, and post-DMT plasma cortisol level ($P = 0.004$) than patients without LVH. No differences were detected in circadian plasma cortisol profile nor urinary cortisol excretion between with and without LVH. Eccentric LVH was present in 13 EH patients who showed greater post-DMT plasma cortisol levels than patients with other types of LV geometry. In a logistic regression model, LVH was associated independently with BMI ($\text{OR } 1.20$, $P = 0.022$) and post-DMT plasma cortisol ($\text{OR } 1.06$, $P = 0.045$). LV mass index (LVMI) was significantly and directly related to age ($r = 0.329$, $P = 0.001$), duration of hypertension ($r = 0.243$, $P = 0.015$), BMI ($r = 0.317$, $P = 0.001$), systolic blood pressure ($r = 0.397$, $P < 0.001$), plasma glucose ($r = 0.215$, $P = 0.031$) and triglycerides ($r = 0.323$, $P = 0.001$), HOMA-index ($r = 0.226$, $P = 0.029$), and post-DST plasma cortisol ($r = 0.349$, $P = 0.002$), whereas a borderline significant relationship was found with C-AUC ($r = 0.201$, $P = 0.053$). In multivariate regression models, LVMI was independently associated post-DMT cortisol ($B = 0.245$, $P = 0.026$) and C-AUC ($B = 0.233$, $P = 0.018$).

Conclusions: Subtle changes in the regulation of plasma cortisol secretion contribute to cardiac hypertrophy and LV geometric changes in patients with EH.

CORRELATION OF ARTERIAL STIFFNESS AND 25(OH) VITAMIN D LEVEL IN POSTMENOPAUSAL WOMEN WITH CONTROLLED UNCOMPLICATED HYPERTENSION

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Objective: was to assess the association between carotid – femoral pulse wave velocity (PWV) and serum 25(OH) vitamin D level in postmenopausal women with controlled uncomplicated hypertension (UH).

Design and method: In 28 women 69.2 ± 0.85 years old with mild-moderate controlled UH and 25 healthy ones matched for age (65.6 ± 1.58 years), length of menopause (17.4 ± 1.05 years vs 15.0 ± 1.64 years), body mass index (28.3 ± 0.76 kg/m² vs 27.7 ± 0.8 kg/m²), brachial systolic blood pressure - BP (126.2 ± 2.53 mmHg vs 120.0 ± 2.54 mmHg, all $p > 0.05$), pulse wave analysis with SphygmoCor and measurements of serum 25(OH) vitamin D, total calcium and parathyroid hormone (PTH) levels by electrochemical method were performed.

Results: Women with UH compared with healthy ones had similar central systolic BP (119.4 ± 2.37 mmHg vs 114.3 ± 2.44 mmHg, $p > 0.05$), higher augmentation index normalized for heart rate of 75 beats per min ($29.3 \pm 1.51\%$ vs $20.0 \pm 2.0\%$, $p < 0.001$), augmentation pressure (12.9 ± 0.98 mmHg vs 8.4 ± 0.83 mmHg, $p < 0.001$) and femoral PWV (11.4 ± 0.51 m/s vs 9.2 ± 0.50 m/s, $p < 0.01$). The level of 25(OH) vitamin D in patients with UH was lower than in healthy ones (23.1 ± 1.3 ng/ml vs 29.1 ± 1.5 ng/ml, $p < 0.01$). The deficiency of 25(OH) D (< 20 ng/ml) was detected in 12 (42.9%) and 4 (12%) women correspondingly ($p < 0.04$), its insufficiency ($20-30$ ng/ml) – in 10 (35.7%) vs 3 (16%, $p < 0.05$) and normal level – in 6 (21.4%) vs 18 (72%, $p < 0.01$). Total calcium level in UH patients was 1.26 ± 0.02 mmol/l and in healthy women – 1.3 ± 0.02 mmol/l ($p > 0.05$) and PTH level correspondingly 65.6 ± 5.55 pg/ml vs 38.4 ± 1.35 pg/ml ($p < 0.001$). Secondary hyperparathyroidism (PTH > 65.0 pg/ml) was diagnosed in 14 (50%) women with UH. In UH patients the negative correlation was revealed between PWV and 25(OH)D ($r = -0.39$, $p < 0.05$) and positive correlation – between PWV and PTH ($r = 0.53$, $p < 0.01$) levels.

Conclusions: The correlation of elevated carotid – femoral PWV with lower serum 25(OH) vitamin D and elevated PTH levels may indicate the role of vitamin D deficiency mediated secondary hyperparathyroidism in pathogenesis of arterial stiffness in postmenopausal woman with UH.

MYOCARDIAL STIFFNESS AND LEFT VENTRICULAR HYPERTROPHY IN THE MIDDLE-AGED HYPERTENSIVE PATIENTS

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Objective: to investigate left ventricular (LV) and left atrial (LA) stiffness parameters in middle-aged patients with grade 1–2 essential arterial hypertension (EAH) without concomitant cardiovascular diseases according to the presence of LV hypertrophy (LVH).

Design and method: Case-control study. We examined 127 naive patients with uncomplicated grade 1–2 EAH and divided them into two groups according to the LV mass index (LVMI). The first one is included 96 hypertensive patients (HP) with LVH (mean LVMI 125.8 ± 2.1 g/m², mean age 52.6 ± 0.7 years; mean office blood pressure (BP) $151.9 \pm 1.5/93.8 \pm 1.1$ mm Hg). The second group consisted of 31 patients without LVH (mean LVMI 89.7 ± 2.1 g/m², mean age 51.3 ± 1.0 years; mean office BP $138.7 \pm 2.1/83.5 \pm 1.9$ mm Hg). 44 healthy individuals (mean age 51.5 ± 1.0 years; mean office BP $120.1 \pm 2.0/80.5 \pm 1.0$ mm Hg) represented the control group. All the patients underwent 24-hours ambulatory BP monitoring. Comprehensive transthoracic echocardiography using Vivid 7 Dimension system (GE) was also performed. LV end-diastolic stiffness, LV end-systolic elastance, LV diastolic elastance, LA stiffness index, LA expansion index and tissue Doppler-derived (TDD) LA strain were calculated. 2-D speckle tracking echocardiography data were acquired for determination of LV myocardial global longitudinal peak strain (LV GLPS).

Results: TDD LA strain was significantly higher in HP without LVH ($60.01 \pm 4.77\%$) compared to HP with LVH ($49.77 \pm 1.49\%$; $p < 0.05$). LV GLPS was significantly lower in absolute value in HP with LVH ($-16.9 \pm 0.3\%$) and HP without LVH ($-17.5 \pm 0.6\%$) compared to controls ($-19.9 \pm 0.4\%$; $p < 0.001$ and $p < 0.01$, respectively). No significant differences between studied groups were obtained in other myocardial stiffness parameters. LV GLPS showed a weak but significant associations with office diastolic BP ($r = 0.354$; $p < 0.01$), 24 h systolic BP ($r = 0.291$; $p < 0.05$), 24 h pulse pressure ($r = 0.296$; $p < 0.05$), and average night-time systolic and diastolic BP ($r = 0.343$; $p < 0.01$ and $r = 0.262$; $p < 0.05$, respectively).

Conclusions: the present study reveals that disturbances in myocardial stiffness parameters occur early, before the development of echocardiographic signs of LVH. They are earlier markers of target organ damage even in middle-aged untreated patients with grade 1–2 uncomplicated EAH.

ATRIAL FIBRILLATION AND ARTERIAL HYPERTENSION. VARIANCE OF SERUM URIC ACID LEVELS IN BOTH DISEASES

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Objective: Atrial fibrillation and arterial hypertension share common risk factors such as obesity, diabetes mellitus, alcohol consumption etc. There is evidence however that the aforementioned risk factors are associated with serum uric acid (SUA) levels. We sought to assess the relation of SUA levels with arterial blood pressure (BP) levels and the incidence of atrial fibrillation

Design and method: We prospectively enrolled 568 hypertensive patients (mean age 63 ± 10 years) presented for evaluation in the Hypertension clinic. All patients underwent 24-hour holter monitoring for the detection of atrial fibrillation (AF). Patients with documented AF in 24 hour recordings or patients with a history of AF were defined as AF patients. In all subjects routine blood chemistry, including SUA determination, echocardiographic examination, office and 24 h ambulatory blood pressure (BP) monitoring were obtained. In all patients data regarding lifestyle habits (smoking, alcohol consumption and exercise) were recorded.

Results: From 568 hypertensive patients, 77 patients (13%) had atrial fibrillation. Mean average 24 hour systolic blood pressure (SBP) was 132 ± 15 mmHg, mean 24 hours average diastolic blood pressure (DBP) was 77 ± 10 mmHg. Spearman analysis showed that SUA levels were significantly and positively associated with the average 24 hours systolic blood pressure levels ($r_s = 0.092$, $p < 0.05$ for SBP) but not with diastolic BP levels ($r_s = 0.06$, $p > 0.05$). Serum uric acid levels in patients with atrial fibrillation were statistically significantly higher than those without ($Z = -5.3$, $p < 0.001$). In addition, SUA levels were highly correlated with all the major risk factors predisposing for the development of arterial hypertension or AF. Specifically SUA levels were significantly higher in males (Mann-Whitney U = 25158.500, $p < 0.01$), in elder patients ($r_s = 0.117$, $p < 0.01$), in patients with increased body mass index ($r_s = 0.337$, $p < 0.01$), with diabetes (Mann-Whitney U = 25445.500, $p < 0.05$).

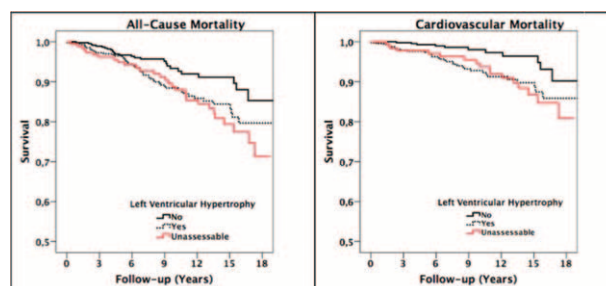
Conclusions: Increased SUA levels were significantly associated with the incidence of atrial fibrillation and systolic BP levels as well as with the majority of the risk factors predisposing for the development of both diseases.

DETERMINANTS AND PROGNOSTIC VALUE OF UNASSESSABLE LEFT VENTRICULAR MASS INDEX IN HYPERTENSIVE PATIENTS

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Objective: Left ventricular hypertrophy (LVH) assessed by transthoracic echocardiography, a subclinical target organ damages, detect a subgroup of high-risk patients. However echocardiography presents several limits, among which results unavailability in more than 10% of hypertensive subjects for technical reasons. The aim of the present study was to determine variables that can explain unassessable left ventricular mass index (LVMI) and to explore the prognostic value of this subgroup of patients.

Design and method: 1104 hypertensive patients having an echocardiography were included. LVMI was calculated with the formula of Devereux and further indexation was performed to height to the allometric power of 2.7 with the following LVH criterion: TTE LVMI_{2.7} > 51 g/m^{2.7} in both sexes. LVMI was assessable in 921 patients. After a median follow-up of 8.5 [5.4–13.3] years, 110 deaths occurred, 62 of which were from cardiovascular cause.



Results: LVMI was unassessable in 183 patients and assessable in 921 patients included 468 patients with LVH. Independent determinant of unassessable LVMI were age, gender and BMI. After a median follow-up of 8.5 [5.4–13.3] years, 110 deaths occurred, 62 of which were from cardiovascular cause. Kaplan-Meier curves demonstrated that patients with unassessable LVMI had the worst outcome for all-cause and cardiovascular mortality ($p = 0.015$ and $p = 0.006$, respectively, see Figure). After adjustment for age, gender and BMI, patients with unassessable LVMI had quite similar increase risk for all-cause and cardiovascular mortality (1.92(1.13–3.29) and 2.72(1.25–5.93), respectively) than those with LVH (1.71(1.06–2.75) and

2.70(1.33–5.45), respectively) using patients without LVH for the reference subgroup. A further adjustment for cardiovascular risk factors, previous cardiovascular events and antihypertensive treatment demonstrated a similar trend.

Conclusions: Unavailability of LVMI for technical reasons must be considered as a subclinical target organ damages in hypertensive patients if we considered the increase risk observed in our cohort.

ATRIAL FIBRILLATION DETECTION DURING AUTOMATED BLOOD PRESSURE MEASUREMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: In 2013 the UK National Institute for Health and Care Excellence (NICE) recommended opportunistic atrial fibrillation (AF) screening during routine office blood pressure (BP) measurement using the oscillometric Microlife Afib BP monitor with specific AF detection algorithm in primary care in the elderly. This study evaluated the current evidence on the diagnostic accuracy of this technology in detecting AF during automated BP measurement.

Design and method: A systematic PubMed search was conducted using the keywords “atrial fibrillation”, “blood pressure”, “detection”, “screening”.

Results: Initial search retrieved 258 articles of which 13 were relevant. Eleven articles evaluated the diagnostic accuracy of BP monitors during office measurements, and 2 during home BP measurements. Electrocardiography was used as reference method in all studies. A meta-analysis of 11 studies with adequate data ($n = 10,972$; AF prevalence $17 \pm 12\%$; 4 studies required at least 2 of 3 AF positive readings for AF diagnosis) showed pooled sensitivity, specificity and accuracy as follows: 95% (95% C.I. 92–98%), 94% (92–96) and 94% (93–96), respectively. With increasing AF prevalence across studies, meta-regression analysis showed a trend towards higher sensitivity and lower specificity.

Conclusions: The available evidence suggests that AF detection during automated BP measurement using the Microlife Afib device has high diagnostic accuracy, which is influenced by the AF prevalence. These data support the 2013 UK NICE recommendation for AF screening using automated BP measurement with specific AF detecting algorithm in the elderly.

CLINICAL DETERMINANTS OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS/ANGIOTENSIN RECEPTOR BLOCKERS USE IN AN EARLY PHASE AFTER ACUTE HEART FAILURE HOSPITALIZATION

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Objective: To investigate which clinical determinants predict the use of angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) in an early phase after acute heart failure (AHF) hospitalization.

Table 1. Univariate and multivariate predictors of ACEi/ARB use after AHF hospitalization

Variable	Univariate analysis for ACEi/ARB use at discharge		Multivariate stepwise analysis for ACEi/ARB use					
	OR	95% CI	At discharge	After 1 month	OR	95% CI	OR	95% CI
SBP increase per 1 mmHg	1.01*	1.01;1.02	1.01*	1.01;1.02	1.01*	1.01;1.02	1.01*	1.00;1.02
SBP (mmHg) <140* vs ≥140	1.94*	1.34;2.79	1.46*	1.03;2.09	1.50*	1.05;2.13	1.72*	1.21;2.46
Creatinine (μmol/l) <130* vs ≥130	0.54*	0.37;0.79	0.71	0.48;1.03	0.77	0.52;1.13	0.67	0.45;1.00
History of hypertension	2.23*	1.35;3.66	2.53*	1.56;4.10	1.83*	1.09;3.04	2.04*	1.20;3.48
Diabetes	0.53*	0.38;0.74	1.30	0.88;1.93	0.92	2.00;2.06	1.43	0.97;2.12
Chronic kidney disease	1.56*	1.08;2.25	0.73	0.51;1.05	0.53*	0.37;0.75	0.49*	0.34;0.70
Coronary heart disease	0.78	0.56;1.08						
Gender (male)	1.27	0.85;1.89						
Age per 1 year	1.01	0.99;1.02						
BNP per 1 ng/l	1.00	1.00;1.00						
Potassium per 0.1 mmol/l	1.15	0.85;1.57						

* $p < 0.05$; a – referent

Design and method: A prospective two-centre observational cohort study enrolled 1433 dyspnoeic patients consecutively admitted to an emergency department. AHF was the cause of acute dyspnoea in 635 patients (44.3%). The mean age was 69.7 ± 12.1 ; 42% were female. Medication follow up data for 574 and 567 AHF patients were available 1 and 3 months after discharge, respectively.

Predictors for ACEi/ARB use were identified by an univariate analysis and multivariate stepwise analysis.

Results: The mean systolic blood pressure (SBP) of AHF ($n = 635$) patients was 139.5 ± 27.8 ; 59% had a SBP > 140 mmHg. ACEi/ARB were prescribed in 59.7%, 47.9% and 46.9% of patients at discharge as well as 1 and 3 months after discharge, respectively. SBP of 140 mmHg was identified as a threshold to receive ACEi/ARB at discharge using ROC analysis (area under the curve 0.595). Univariate and independent predictors of ACEi/ARB use are presented in Table 1.

Conclusions: Less than half of patients received ACEi/ARB 1 and 3 months after discharge for AHF. SBP, history of hypertension and chronic kidney disease were identified as independent predictors of treatment with ACEi/ARB in an early phase after AHF hospitalization.

LEVEL OF ARTERIAL BLOOD PRESSURE DENOTES DIFFERENT BIOMARKER PROFILE IN ACUTE HEART FAILURE PATIENTS

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Objective: We aimed to investigate whether blood biomarker profile varies in patients with different baseline blood pressure at admission for acute heart failure.

Design and method: A prospective, multi-centric, observational cohort study enrolled consecutive patients with acute dyspnea from March, 2015 till December, 2017. The exclusion criterion was a suspected acute coronary syndrome. Data of 697 study patients with adjudicated diagnosis of acute heart failure (AHF) were included in the analysis. Blood biomarkers tested at admission included: cardiac and kidney markers, electrolytes, and glucose. Analysis of variance (ANOVA) was used to interpret the differences among group means. For variables that were marginally skewed, a nonparametric Kruskal-Wallis test was performed. Data were analysed using SPSS v23 statistical package.

Results: 405 (58.1%) patients were male and 292 (41.9%) female. Systolic and diastolic blood pressure, mean arterial pressure, and pulse pressure were divided into quartiles for analysis (Table 1). Kruskal-Wallis test demonstrated that the distribution of blood concentration of BNP, hs-Troponin I, urea, sodium, creatinine, and glucose differed significantly among 1st and 2nd, 1st and 3rd, 1st and 4th percentile groups of systolic BP, diastolic BP, MAP, and PP (Table 1). Patients with the lowest BP had distinctively elevated congestion, myocardial and kidney injury markers.

Percentile groups	1 (Mean, N-185)	2 (Mean, N-168)	3 (Mean, N-165)	4 (Mean, N-179)	Blood biomarkers
Systolic BP, mmHg:	104.75 ^{***}	590.40 [*]	680.00	518.60 [*]	BNP (pg/mL) (median)
25 – 120.00	238.52 [*]	57.05	60.48	42.97 [*]	Troponin I (ng/L)
.50 – 137.00	13.47 [*]	10.75	9.80	9.03 [*]	Urea (mmol/L)
.75 – 158.00	137.56 ^{**}	139.39 [*]	138.59	138.88 [*]	Sodium (mmol/L)
	131.77 ^{***}	110.63 [*]	114.00 [*]	114.30 [*]	Creatinine (mmol/L)
	6.73 [*]	6.64	7.21	7.56 [*]	Glucose (mmol/L)
Percentile groups	1 (Mean, N-192)	2 (Mean, N-218)	3 (Mean, N-94)	4 (Mean, N-193)	Blood biomarkers
Diastolic BP, mmHg:	906.10 [*]	462.30 [*]	861.15	668.85	BNP (pg/mL) (median)
25 – 70.00	238.52	57.05	60.48	42.97	Troponin I (ng/L)
.50 – 80.00	13.47 ^{**}	10.75	9.80 [*]	9.03 [*]	Urea (mmol/L)
.75 – 90.00	137.56	139.39	138.59	139.95	Sodium (mmol/L)
	131.77 ^{**}	110.63 [*]	114.00	114.30 [*]	Creatinine (mmol/L)
	6.73	6.64	7.21	7.56	Glucose (mmol/L)
Percentile groups	1 (Mean, N-184)	2 (Mean, N-160)	3 (Mean, N-175)	4 (Mean, N-178)	Blood biomarkers
Mean arterial pressure, mmHg:	930.25 [*]	575.50	710.00	531.00 [*]	BNP (pg/mL) (median)
25 – 88.16	238.19 ^{**}	46.45 [*]	62.80	44.58 [*]	Troponin I (ng/L)
.50 – 98.33	14.38 ^{***}	10.24 [*]	9.39 [*]	9.27 [*]	Urea (mmol/L)
.75 – 110.33	137.51 ^{**}	139.01	139.35 [*]	137.50 [*]	Sodium (mmol/L)
	133.93 ^{***}	110.08 [*]	111.76 [*]	115.24 [*]	Creatinine (mmol/L)
	6.78 [*]	6.76	7.20	7.47 [*]	Glucose (mmol/L)
Percentile groups	1 (Mean, N-189)	2 (Mean, N-177)	3 (Mean, N-143)	4 (Mean, N-188)	Blood biomarkers
Pulse pressure, mmHg:	1037.00 ^{**}	789.00	579.45 [*]	511.30 [*]	BNP (pg/mL) (median)
25 – 42.00	233.43 [*]	59.26	65.76	46.12 [*]	Troponin I (ng/L)
.50 – 55.00	12.74 [*]	10.78	9.30 [*]	10.00	Urea (mmol/L)
.75 – 70.00	137.51 ^{***}	138.75 [*]	139.94 [*]	139.60 [*]	Sodium (mmol/L)
	127.65 ^{**}	114.38 [*]	109.19 [*]	118.15	Creatinine (mmol/L)
	7.02	6.67	7.18	7.36	Glucose (mmol/L)

Table 1. Differences of the blood concentration of BNP, Urea, Sodium, Creatinine, and Glucose among percentile groups of Systolic BP, Diastolic BP, MAP, and PP. *1 vs. 2, *1 vs. 3, *1 vs. 4; $p < 0.05$

Conclusions: Patients with different level of admission systolic, diastolic BP, MAP, and PP are characterized by distinct biomarker profiles.

INTERRELATIONSHIP BETWEEN CHANGES OF E/E' AT REST AND AFTER EXERCISE AND NT-PRO-BNP IN MILD HYPERTENSION PATIENTS WITH STRUCTURAL CHANGES AND DYSPNOEA

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Objective: The aim was to compare the frequency of NT-pro-BNP elevation in phenotypes of mild arterial hypertension (AH) pts with left heart structural changes and heart failure (HF) symptoms based on E/E' > at rest, E/E' > 13 only after exercise and E/E' < 13 both at rest and exercise.

Design and method: Materials and methods. We consequently enrolled 84 hemodynamic stable patients with mild AH and left ventricular myocardial index LVMI > 115 g/m² (for male) and > 95 g/m² (for female), left atrial volume index LAVI > 34 ml/m², and divided them on three groups. Group A included patient with average E/e' > 13 at rest. Group B with E/e' at rest < 13 and Group C patients with E/e' < 13 both at rest and after exercise. In all pts serum NT-pro-BNP levels (ELISA) were obtained.

Results: Results. Group A included 48 pts (57,1%), Group B – 22 (26,1%) and Group C – 14 (16,6%) they didn't differ in age (60,1 ± 1,4 vs 61,2 ± 1,7 and 62,1 ± 1,4 years), gender (29 (60,4%) vs 15 (68,18%) vs 8 (57,14%) males) and diabetes incidence (25,0% vs 19,0% vs 15,0%) and body mass index (BMI) (30,22 ± 5,24 vs 31,3 ± 5,80 vs 28,65 ± 3,59; all p > 0,05). NT-pro-BNP data are demonstrated in the table.

	GrA (n=48) (M±m)	GrB (n=22) (M±m)	GrC (n=14) (M±m)
NT-pro-BNP	1046,6±819	206,29±102,8**	84,65±62,6***
NT-pro-BNP > 125 pg/ml	48 (100%)	15 (68,2%)*	5 (35,7%)*

*p<0,01, **p<0,001 compared to group A; ***p<0,01 compared to group B

Conclusions: In mild hypertension pts with left heart structural changes and HF symptoms only E/E' elevation at rest phenotype was associated with NT-pro-BNP elevation in 100% of cases. Heterogeneity of E/E' > 13 only at exercise E/E' both at rest and exercise phenotypes as regards of NT-pro-BNP elevation (in 68,2% and 35,7%) demonstrates the need of heart failure with preserved ejection fraction (HFpEF) criteria specification.

PARAMETERS OF ELASTIC PROPERTIES, ECHOCARDIOGRAPHIC RANGES, INFLAMMATION AND LEVEL OF URIC ACID IN PATIENTS WITH CORONARY HEART DISEASE COMBINED WITH LIVER PATHOLOGY

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Objective: To compare the relationship parameters of elastic properties, echocardiographic ranges, inflammation and level of uric acid in patients with coronary heart disease (CHD) combined with liver pathology.

Design and method: Studied 59 men (group A) with CHD combined with hepatic steatosis, the group B- 17 patients with CHD without hepatic steatosis. The study group was divided into 3 subgroups according to BMI (subgroup 1 - patients who are overweight, 2- obesity 1 degree, 3- obesity grade 2. Evaluated Peterson's elastic modulus (Ep), Young's elastic modulus (Es), echocardiographic ranges, C-reactive protein (CRP), and level of uric acid.

Results: Ep and Es in a group A (412,3 ± 142 kPa, 990,6 ± 227 kPa) was lower than in a group B (574,5 ± 158 kPa, 1358 ± 243 kPa p < 0,001). Ep and Es was lower in the subgroup 1 (370,1 ± 158 kPa, 846 ± 160 kPa) and in subgroup 2 (375 ± 175 kPa, 1041 ± 301 kPa) than in subgroup 3 (522 ± 125 kPa, 1106 ± 281 kPa) (p < 0,05). Echocardiographic parameters: diastolic left ventricular (LV) internal dimension, systolic LV internal dimension, LV end-diastolic volume, LV end-systolic volume, LV mass were larger in a group A compared with a group B (5,26 ± 0,37 mm and 4,8 ± 0,1 mm, p = 0,02; 3,47 ± 0,3 mm and 3,08 ± 0,3 mm, p = 0,01; 135,23 ± 23,5 mL and 110,1 ± 6,24 mL, p = 0,03; 50,47 ± 10,85 mL and 38,2 ± 9,2 mL, p = 0,03; 295,1 ± 73,57 g and 184,3 ± 31,6 g p = 0,02). In group A identified the highest levels of uric acid (402 ± 81 mkmol/l) than in the group B (328 ± 12 mkmol/l, p < 0,03). The level of CRP was higher in group A (4,8 ± 1,4 mg/l) than in group B (2,4 ± 1,2 mg/l, p < 0,05). There was correlation between the Ep and LV end-systolic volume (r = 0,93; p < 0,05),

ejection fraction (r = -0,89; p < 0,05), carotid plaques (r = 0,67; p < 0,05) in a subgroup 2. The myocardial mass index in a group A associated with level of CRP (r = 0,68; p < 0,05) and level of uric acid (r = 0,56; p < 0,05), however in a group B such connection was not observed.

Conclusions: Patients with CHD and liver steatosis showed significant differences in the structural and functional properties of the myocardium with more pronounced disorders of elastic properties of the vascular wall and no correlation with obesity.

PULSE-COR REGISTRY: VENTRICLE-ARTERIAL INTERACTIONS AND ITS ASSOCIATION WITH LV DIASTOLIC FUNCTION

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Objective: The pathogenesis of LV diastolic failure development remains unknown. The aim to maintain this registry was to evaluate ventricle-arterial interactions with the help of pulse wave contour analysis (PWA), pulse wave velocity (PWV) analysis and echocardiographic parameters along with evaluation additional factors.

Design and method: We included 553 patients with AH who were hospitalized in the Symptomatic hypertension department NSC Institute of cardiology n.a. acad. M.D. Strazhesko. Final analysis included 320 patients, that underwent all necessary diagnostic procedures. PWA and PWV analysis were performed using SphygmoCor device (AtCor, Australia) with determination of central SBP (cSBP), augmentation index (Aix) and normalized Aix (Aix@75), carotid-femoral PWV (cfPWV). Also we measured CAVI and ankle-brachial index (ABI) with the mean of VaSera 1500 (Fukuda Denshi, Japan). Ultrasound diagnostics included vascular ultrasound with intima-media thickness (IMT) measurement. Echocardiography was performed according ASE standardized protocol, LV diastolic function was evaluated according to ASE 2016 guidelines. Ventricle-arterial coupling (VAC) was evaluated using formula, described in literature.

Results: Mean SBP/DBP was 154,5 ± 1,5/92,8 ± 0,9 mmHg. VAC was significantly associated with woman sex (r = 0,276; p < 0,05), office SBP (r = 0,351; p < 0,05), E/A (r = 0,215; p < 0,001), IVRT (r = -0,127; p < 0,05), Dt (-0,131; p < 0,05), LV ejection fraction (EF) (r = 0,9; p < 0,05), LVMMI (r = -0,195; p < 0,01), mitral annulus motion (s') (r = 0,272; p < 0,001), left ventricle wall stress (LVWS) (r = -0,169; p < 0,01), CAVI (r = 0,561; p < 0,01). E/A was significantly associated with age (r = -0,373; p < 0,001), cSBP (r = -0,308; p < 0,01), IMT (r = -0,297; p < 0,05), EF (r = 0,170; p < 0,001), s' (r = 0,253; p < 0,001), ABI (r = 0,253; p < 0,05), cfPWV (r = -0,0374; p < 0,05), Aix@75 (r = -0,360; p < 0,05). E/e' was correlated with BMI (r = 0,291; p < 0,05), office SBP (r = 0,208; p < 0,05), E/A (r = 0,340; p < 0,001), IVRT (r = 0,291; p < 0,001), Dt (r = 0,248; p < 0,001), EF (r = -0,109; p < 0,05), LVMMI (r = 0,303; p < 0,001), s' (r = -0,263; p < 0,05), ABI (r = 0,258; p < 0,05).

Conclusions: Our findings demonstrates that low arterial elasticity is really involved in LV diastolic dysfunction formation. Moreover, CAVI was the only parameter significantly associated with VAC. That is why CAVI may not only diagnose arterial stiffening but also may demonstrate how it increases LV load.

THE IMPACT OF HYPERTENSION ON QT DISPERSION AND ECHOCARDIOGRAPHIC PARAMETERS IN PATIENTS AFTER MYOCARDIAL INFARCTION

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Objective: The aim of this study was to investigate the effect of hypertension on QT dispersion and echocardiographic parameters in patients after myocardial infarction.

Design and method: The study included 133 patients after myocardial infarction (average age 58.8 years), of which 87 were with hypertension, and 46 were without arterial hypertension. There were no significant differences in age and gender between the two groups of patients. In all subjects exercise stress test on a treadmill according to the Bruce protocol and echocardiographic examination were performed and from standard ECG corrected QT dispersion (QTdc) and QTd was calculated.

Results: Patients after myocardial infarction with hypertension had significantly higher values of QTd (65,2 ± 26,4 vs 52,7 ± 25,2 ms; p < 0,01) and QTdc (72,9 ± 31,8 vs 58,6 ± 28,4 ms; p < 0,005) compared to those without arterial hypertension. Also, patients after myocardial infarction with hypertension

had significantly higher values of the thickness of the interventricular septum (13.4 ± 1.8 vs 10.1 ± 1.0 mm; $p < 0.001$), left ventricle posterior wall thickness (10.9 ± 1.8 vs 9.8 ± 0.7 mm; $p < 0.001$) and left atrium diameter (40.9 ± 6.6 vs 38.5 ± 5.8 mm; $p < 0.02$) compared to those without hypertension. Patients after myocardial infarction with arterial hypertension have lower values of the left ventricular end-diastolic diameter (54.1 ± 6.3 vs 55.8 ± 5.4 mm; p-NS), and left ventricular end-systolic diameter (36.8 ± 7.1 vs 38.8 ± 6.5 mm; p-NS) and higher values of left ventricular ejection fraction (52.6 ± 13.5 vs 50.8 ± 12.5 %;

p-NS), compared to those without hypertension, but the differences were not statistically significant.

Conclusions: The study demonstrated that patients after myocardial infarction with hypertension have significantly higher values of QT dispersion parameters, thickness of the left ventricle walls and left atrium diameter in comparison to those without hypertension.

POSTER SESSION

POSTERS' SESSION PS05:

LIFESTYLE, HYPERTENSION MANAGEMENT

IMPROVING THERAPEUTIC COMPLIANCE OF DABIGATRAN IN PREVENTING STROKE IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION: DRUG INTAKE REMINDER STRATEGY

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Objective: To assess the efficacy of a mixed intervention, educational and reminder calendar of the intake, as a strategy to improve therapeutic compliance with dabigatran in patients with non-valvular atrial fibrillation (NVAf).

Design and method: Prospective, longitudinal, multicenter study, carried out in 110 specialized healthcare centers in Spain. 726 patients treated with dabigatran prescribed for stroke prevention were included.

A cluster randomization was performed based on two groups: 1) Control Group (CG) as usual clinical practice and Intervention Group (IG) with a mixed strategy: a) Healthcare education and b) Use of a reminder calendar for taking the anticoagulant medication. Three visits took place: baseline and follow up at 6 and 12 months. Compliance was measured using electronic monitors (Medication Event Monitoring System - MEMS). Average compliance percentage (%); Average CP and daily compliance (%); Daily CP was calculated. A patient was considered complier when CP was 80–100%.

Results: Six hundred twenty-five patients ended the study. There were 315 evaluable subjects in the IG and 310 in the CG, with a mean age of $73,52 \pm 8,3$ years and $73,32 \pm 8,56$ respectively. Daily CP was 91,97 % at 6 months and 91,05 % after 12 months in the IG and 82,26 % and 82,63 % in the CG. Average compliance was 90,79 % and 89,20 % in the IG and 64,51 % and 63,22 % in the CG at 6 and 12 months respectively. Significant differences were observed in the Daily CP and Average CP with higher percentages in IG. In the non-compliers group, the number of concomitant drugs, baseline and 6 months SBP values, 6 and 12 months DBP values, baseline, 6 and 12 month weight, and total cholesterol and LDL cholesterol at baseline, 6 and 12 months were significantly higher.

The number needed to treat (NNT) at the end of the intervention was 3,84 patients to prevent 1 non-compliance.

Conclusions: A mixed intervention with educational and reminder calendar of drug intake, has been proven to be effective as a strategy to improve therapeutic compliance with dabigatran in patients with NVAf. The percentage of compliance with dabigatran was high

LINKS BETWEEN BLOOD PRESSURE AND LIFE-STYLE FACTORS REPORTED VIA A MOBILE PHONE-BASED SELF-MANAGEMENT SUPPORT SYSTEM

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Objective: To explore relationships between patients' self-monitoring of blood pressure and their concurrent self-reports of medication intake, wellbeing stress, physical activity and symptoms.

Design and method: This was a prospective study exploring the eight-week effectiveness of a mobile phone based self-management support system for patients with hypertension. 50 patients undergoing treatment for hypertension, from four primary health care centers situated in urban and suburban communities in Sweden, self-reported through the system once daily during eight weeks.

Scientific data:

Associations between systolic and diastolic blood pressure and 10 self-report lifestyle-related variables.

Results: The single strongest association was found between medication intake and systolic blood pressure, where failure to take medications was associated with an estimated 7.44 mmHg higher systolic blood pressure. To a lesser degree,

medication intake was also associated with diastolic blood pressure. Wellbeing and stress were consistently associated with systolic blood pressure and diastolic blood pressure, whereas physical activity was associated with only systolic blood pressure. None of the symptoms dizziness, headache, restlessness, fatigue or palpitations were significantly associated with blood pressure.

Conclusions: Blood pressure was associated with patients' blood pressure management behaviors, eg drug intake and experiences of wellbeing and stress. No association was found between blood pressure and side effects. Enabling persons with hypertension to monitor and track their BP in relation to medication intake, symptoms and life-style variables may be a fruitful way to help them gain first-hand understanding of the importance of adherence and persistence to treatment recommendations.

A COMPARATIVE STUDY BETWEEN EUROPEAN GUIDELINES AND AMERICAN GUIDELINES USING FUZZY SYSTEMS FOR THE CLASSIFICATION OF BLOOD PRESSURE

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Objective: The main objective is using fuzzy classifiers to provide accuracy in the handling of information, which will help to be more accurate when classifying the blood pressure level of a patient. Classifiers are based on the parameters provided by the guidelines, and make the comparison given by the European and the American guide and observe the behavior that each of them can take at the time of making a diagnosis.

Systolic	Diastolic	European guidelines	European Fuzzy classifier	American Guidelines	American Fuzzy Classifier
151	89	ISH 1	ISH 1	Stage 2	Stage 2
143	96	Grade 1	Grade 1 Hypertension	Stage 2	Stage 2
134	61	High_Normal	Normal	Stage 1	Stage 1
121	78	Normal	Normal	Elevated	Elevated
108	64	Optimal	Optimal	Normal	Normal
162	86	ISH 2	ISH 2	Stage 2	Stage 2
130	86	High_Normal	High Normal	Stage 1	Stage 1
116	73	Optimal	Optimal	Normal	Normal
118	57	Optimal	Optimal	Normal	Normal
158	80	ISH 1	ISH 1	Stage 2	Stage 2
160	94	Grade 2	ISH 2	Stage 2	Stage 2
124	82	Normal	Normal	Stage 1	Stage 1
104	63	Optimal	Optimal	Normal	Normal
121	70	Normal	Normal	Elevated	Elevated
152	106	Grade 2	Grade 2 Hypertension	Stage 2	Stage 2
133	101	Grade 2	High Normal	Stage 2	Stage 2
128	61	Normal	Optimal	Elevated	Elevated
113	69	Optimal	Optimal	Normal	Normal
154	95	Grade 1	Grade 1 Hypertension	Stage 2	Stage 2
159	76	ISH 1	ISH 1	Stage 2	Stage 2
108	68	Optimal	Optimal	Normal	Normal
126	64	Normal	Normal	Elevated	Elevated
161	103	Grade 2	Grade 2 Hypertension	Stage 2	Stage 2
130	77	High_Normal	High Normal	Stage 1	Stage 1
96	61	Optimal	Optimal	Normal	Normal
143	94	Grade 1	Grade 1 Hypertension	Stage 2	Stage 2
117	60	Optimal	Optimal	Normal	Normal
126	68	Normal	Normal	Elevated	Elevated
149	100	ISH_2	ISH 2	Stage 2	Stage 2
140	81	ISH 1	ISH 1	Stage 2	Stage 2
114	74	Optimal	Optimal	Normal	Normal
151	87	ISH 1	ISH 1	Stage 2	Stage 2
121	75	Normal	Normal	Elevated	Elevated
130	93	Grade 1	Grade 1 Hypertension	Stage 2	Stage 2
115	75	Optimal	Optimal	Normal	Normal
124	74	Normal	Normal	Elevated	Elevated

Design and method: Based on this study we want to identify the way in which a patient is diagnosed using two different guidelines of blood pressure levels, the first is the European guidelines and the second it is the American guides, the latter mentioned was recently updated and it is important to see the impact that each of them can have on society. Currently there is a database with 200 patients, each patient has an average 45 measurements, these 24-hour screenings have been obtained in collaboration with a cardiologist, and this information is then processed

with neural networks to obtain the tendency, which enters in fuzzy classifier, which gives us the blood pressure level depending on the base guideline.

Results: The following result was obtained based on the parameters and levels given by each of the guidelines and using fuzzy classifiers respectively for each, which have a correct classification accuracy rate of 100% for the 30 patients processed and classified. For the European guidelines the classification of patients with hypertension is 43.3% with a standard deviation of 2.71 and using the new American guidelines is 56.6% with a standard deviation of 2.71 using the same patients.

Conclusions: The performed study reports a higher rate of hypertensive people, which based on European guidelines are within normal to high normal ranges, but based on the new American guidelines it was observed that some patients directly enter the stage 1 or stage 2 hypertensive classes, which generates an impact on their daily life, in which they need to change their lifestyle to avoid a cardiovascular event.

ASSOCIATION OF DIETARY SODIUM INTAKE AND 24H URINE SODIUM EXCRETION WITH ENDOTHELIAL DYSFUNCTION AND URINARY ALBUMIN EXCRETION IN EARLY-STAGE HYPERTENSIVE INDIVIDUALS

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Objective: Monitoring of dietary sodium intake is essential in hypertension and efforts have been made to find the least troublesome method to accurately estimate sodium consumption. Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide, which is implicated in abnormal pressure-natriuresis. Increased urinary albumin excretion (UAE) has been associated with sodium intake, possibly through alteration of intrarenal hemodynamics. We investigated which method of measuring sodium intake, including dietary and urinary assessment, correlates better with endothelial dysfunction and UAE and may be a better indicator of vascular damage in newly-diagnosed, never-treated hypertensive patients.

Design and method: Untreated individuals free from cardiovascular comorbidities were eligible to participate, whose 24 h systolic/diastolic blood pressure exceeded 130 and/or 80 mmHg based on their ambulatory blood pressure recording (MobilOGraph). Asymmetric dimethylarginine (ADMA) was measured in serum samples using commercially available competitive enzyme-linked immunosorbent assay (ELISA) kit. UAE was measured in 24 h urine samples. Dietary sodium intake was estimated with a) a 24-hour diet recall that corresponded to the same day as the 24-hour urine collection, b) a salt score questionnaire based on a 0–10 scale, with higher values indicating higher salt intake, and c) urinary sodium excretion in 24-hour urine sample.

Results: A total of 50 hypertensive patients, 28 males and 22 females, with a mean age of 47.0 ± 10.9 years and mean 24-hour ambulatory systolic/diastolic blood pressure $135.2 \pm 10.0/88.5 \pm 9.1$ mmHg, were included. Urinary albumin excretion was $6.1 (4.3–10.5)$ mg/24 h and ADMA levels were 0.99 ± 0.42 mmol/l. Urinary sodium excretion was $83.3 (48.4–146.5)$ mmol/24 h, estimated dietary sodium intake was $79.2 (36.7–130.4)$ mmol/24 h, and salt score was scaled at 4.9 ± 1.5 . Urinary sodium excretion was the only sodium indicator that positively and strongly correlated with both urinary albumin excretion ($r = 0.347$, $p = 0.043$) and ADMA levels ($r = 0.389$, $p = 0.025$).

Conclusions: In a population of untreated, relatively young, early-stage hypertensive individuals, urinary sodium excretion, yet not other dietary measures of sodium, may reflect microvascular damage. These results support the widely perceived premise that 24-hour urine collection is more accurate, although more cumbersome to perform, than other dietary sodium assessments, in terms of pathophysiology and clinical significance.

ASSESSMENT OF ADHERENCE TO ANTIHYPERTENSIVE DRUGS IN PATIENTS WITH RESISTANT HYPERTENSION RECEIVING OPTIMAL TREATMENT

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Objective: Estimate the proportion of nonadherence to antihypertensive drugs in patients with resistant hypertension despite a maximal treatment

Design and method: The study was prospective and observational. We screened all consecutive patients managed in our tertiary center for resistant hypertension between January 2014 and September 2017. Were included only those who already done an ambulatory blood pressure measure to eliminate a white coat effect and an exhaustive etiological work up to exclude a secondary cause. Hypertension

was considered resistant if the ambulatory measure was over or equal to 135/85 mmHg during the awakening period or to 130/80 mmHg during the 24 hours, despite 4 antihypertensive medications combining a renin-angiotensin system inhibitor, amlodipine, a thiazide (or indapamide) and spironolactone, at optimal doses. Treatment compliance was assessed by the eight-item Morisky Medication Adherence Scale (MMAS-8).

Results: 386 patients were enrolled, with a mean age of 57.4 ± 11.3 years, and 48.3% of men. The mean office blood pressure was $178 \pm 20.4 / 101 \pm 15.5$ mmHg and the 24 hours ambulatory blood pressure was $164 \pm 17.6 / 97 \pm 15.2$ mmHg. The proportions of fully adherence, partially nonadherence and completely nonadherence were 27.9%, 47.6% and 24.5% respectively. Fully adherent, partially nonadherent and completely nonadherent patients differed significantly in terms of proportions of women (25%, 48% and 72%), number of daily drugs, reflecting comorbidities (5.9; 6.1 and 9.8 respectively) and education level (the proportions of patients who do not achieve a secondary school were 10.1%, 28.3% and 53.2% respectively).

Conclusions: More than two out of three patients with resistant hypertension optimally treated and without white coat effect were partially or completely non-adherent to treatment in our study. Assessment of the adherence to antihypertensive treatment in these high cardiovascular risk patients should be systematic and possibly by more objective methods.

EFFECT OF RENAL DENERVATION ON CARDIAC FUNCTION AND APOPTOSIS-RELATED GENES' EXPRESSION IN HEART FAILURE DOGS

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Objective: To observe the effects of RDN on cardiac function and apoptosis-related genes' expression in MI-HF dogs.

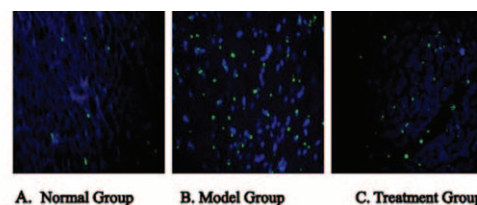


Figure1. cardiomyocyte tunel apoptosis result (x400)

Table 1. myocardial tissue Bcl-2, Bax, Caspase-3, GRP78 mRNA expression ($\bar{x} \pm s$)

	Bcl-2	Bax	Caspase3	GRP78
Normal (n=6)	0.34±0.06	0.30±0.05	0.16±0.04	0.28±0.42
Model (n=5)	0.19±0.02*	0.71±0.09*	0.40±0.06*	0.77±1.01*
Treatment (n=5)	0.26±0.06*#	0.47±0.06*#	0.25±0.05*#	0.39±0.61*#

*compared with Normal Group, $P < 0.05$; #compared with Model Group, $P < 0.05$

Table 2. myocardial tissue Bcl-2, Bax, Caspase-3 and GRP78 protein expression ($\bar{x} \pm s$)

	Bcl-2	Bax	Caspase-3	GRP78
Normal (n=6)	1.30±0.08	0.38±0.06	0.30±0.06	0.45±0.05
Model (n=5)	0.81±0.09*	0.99±0.10*	0.49±0.06*	0.89±0.09*
Treatment (n=5)	1.19±0.08*#	0.66±0.17*#	0.38±0.06*#	0.55±0.04*#

*compared with Normal Group, $P < 0.05$; #compared with Model Group, $P < 0.05$

Design and method: Eighteen healthy mongrel dogs were randomly divided into normal group (n = 6), model group (n = 6) and treatment group (n = 6). MI-HF was established in model group and treatment group by anhydrous alcohol embolization. After heart failure model was established, dogs in the treatment group and model group proceeded bilateral renal artery ablation and bilateral renal arteriography, respectively. The cardiac function parameters were measured; the serum NT-ProBNP level was detected by ELISA; the degree of myocardial fibrosis was observed through masson staining; TUNEL method was used to observe cardiomyocyte apoptosis and calculate the apoptosis index (AI). Relative expression of Bcl-2, Bax, Caspase-3 and GRP78 were detected using RT-PCR and WB. Renal artery HE staining and serum creatinine were conducted to access the efficacy and safety of RDN.

Results: No statistical differences between the baseline weight, HR, LVEDD, LVESD, LVEF, LVEDP and LVSP in all dogs. Before ablation, NT-ProBNP level increased in HF dogs (treatment group and model group) compared with normal dogs, while no difference between treatment group and model group. 4 weeks after ablation, compared with model group the NT-ProBNP values reduced in treatment group. NT-ProBNP level were higher in HF dogs. 4 weeks after ablation, compared with normal group the Bax, Caspase-3, GRP78 mRNA and protein level in myocardial tissue have increased, Bcl-2 mRNA and protein expression decreased and cardiomyocyte apoptosis index increased in heart failure HF dogs (model group and treatment group) with statistical significance. Compared with model group, the level of Bax, Caspase-3, GRP78 decreased, Bcl-2 mRNA and protein expression increased, myocardial apoptosis index decreased in RDN treatment dogs with statistical significance. 4 weeks after ablation, HE staining showed that the sympathetic nerve distribution decreased significantly after RDN operation.

Conclusions: RDN could improve cardiac function in MI-HF dogs, and we speculate that its mechanism may be related to the raise of Bcl-2 gene expression and lower of Bax, Caspase-3, GRP78 expression level by RDN.

IMPORTANCE OF THE DIRECTLY OBSERVED TREATMENT INTAKE ON THE APPROACH OF PATIENTS WITH RESISTANT HYPERTENSION

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Objective: The diagnosis of resistant hypertension (HRes) and the efficacy of renal denervation ensure proper compliance with the therapy. We intend to assess the usefulness of directly observed treatment intake (OTI) in the control of adherence to anti-hypertensive medication in patients with HTAres.

BP mm Hg (n=46)	Casual	24 h	Daytime	Nighttime	% Nighttime BP fall
Before OTI	169/96 (16/20)	148/80 (13/13)	153/84 (14/15)	136/70 (17/1)	11.3 (9.3)
After OTI	156/89 (20/13)*	131/74 (13/9)*	134/77 (14/10)*	121/65 (19/10)*	9.3 (9.4)

Design and method: We studied 46 patients with HRes (BP > 150/90 mm Hg under with at least 3 different classes of drugs in optimal doses) in outpatient hypertension clinic. Four were previously submitted to renal denervation. 24-h ambulatory BP (ABP) was evaluated before the procedure. In OTI patients took all medications in the morning for 5 days under the supervision of a technician and performing on the fifth day a second ABP.

Results: Out of the 46 patients 76% were female, ageing 63 ± 11 years and BMI 30 ± 5 Kg/m². The average of antihypertensive agents was 4.5 ± 1.2 /day. After OTI casual, daytime and nighttime BP decreased significantly (Table). After OTI, 16 patients (34.8%) reported adverse drug reactions not reported before, and 54.3% normalized ABP (24 h < 130/80 mm Hg). Also 4 patients who persisted with HRes after renal denervation were shown to be BP controlled after OTI.

Conclusions: In an organized clinic, OTI can be performed, thereby becoming a valuable tool to identify the non-compliance to therapy as a cause of HRes and to identify false non-responders to techniques such as renal denervation due to loss of drug adherence.

PATIENT-ORIENTED ASSESSMENT OF BLOOD PRESSURE TELEMONITORING AND REMOTE COUNSELING IN HYPERTENSIVE PATIENTS: A PILOT PROJECT

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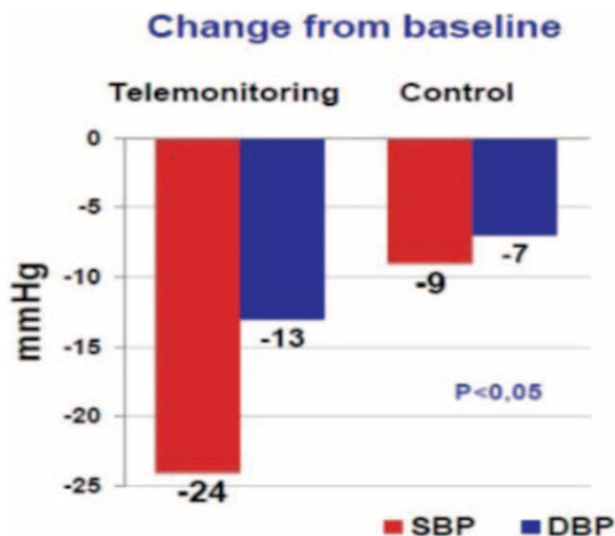
Objective: To evaluate patient-oriented endpoints and antihypertensive effectiveness of blood pressure (BP) telemonitoring and distant counseling (TMDC) in uncontrolled hypertension (HTN).

Design and method: Patients with uncontrolled HTN were assigned to TMDC group (110 patients; 74 males, mean age 51.2 ± 17.0 years) or to age, sex and BP level-matched control group (80 patients; 63 males, mean age 50.8 ± 15.9 years). Both groups had baseline and 3-months follow-up clinic visits with blood pressure measurement and evaluation of patient-reported outcomes by Hospital Anxiety and Depression Scale («HADS») and «SF-36». At baseline visit control group patients received standard recommendations. TMDC patients were educated with detailed

technical instructions on BP self-monitoring and trained for the use of website and mobile application. Remote consultations were allowed at any time by demand during a 3-month program, the frequency and reasons were also registered.

Results: After the 3-month period the decrease in office systolic (SBP) and diastolic (DBP) BP levels was significantly higher in TMDC group compared to the controls: -22 ± 12.4 versus -8.6 ± 22.4 mmHg for SBP ($p = 0.005$) and -13.6 ± 10.8 versus -7 ± 11.3 mmHg for DBP ($p = 0.02$). Target office BP level (< 140/90 mmHg) was achieved in 82 patients (75%) and 16 patients (20%), respectively ($c^2 = 20.8$; $p < 0.01$). During 3-month program every patient in TMDC group required at least 1 remote consultation (from 1 to 8, mean $n = 4$) for different reasons which in 36 cases (33%) lead to change in antihypertensive therapy. At 3-month visit TMDC group demonstrated reduction in anxiety and depression according to HADS compared to baseline data (-1.2 and -1.8 score, respectively, $p < 0.05$) and improvement in physical life quality ($+9 \pm 3.3$ points SF-36, $p = 0.04$). In control group patient-reported outcomes remained unchanged.

Conclusions: Results demonstrated that 3-month telemonitoring program in patients with uncontrolled HTN provides additional antihypertensive effect and improving of patient-reported outcomes. These results can be explained by better patients-doctor interaction and improvement of patient compliance.



ASSOCIATION BETWEEN SALT INTAKE AND URIC ACID, AND ITS INTERACTION ON THE INCIDENCE OF PREHYPERTENSION AMONG CHINESE YOUNG ADULTS

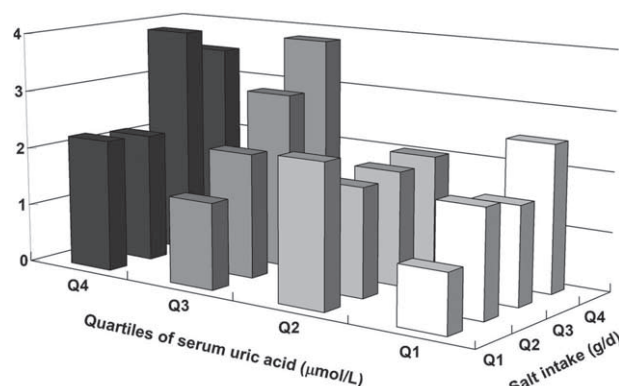
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Objective: High uric acid (UA) level and high salt intake are reportedly associated with cardiovascular disease. This study investigated the association between UA and daily salt intake, as well as its interaction on the risk of prehypertension.

Design and method: A total of 1869 participants without hypertension were recruited from a previously established cohort in Shaanxi Province, China. The participants were classified as normotensive or prehypertensive on the basis of their blood pressure. Salt intake was estimated from early-morning urine specimens using an equation validated for this study population.

Results: Increasing quartiles of salt intake were associated with high urinary UA/creatinine levels in prehypertensive participants (from quartile 1 to quartile 4: 0.12, 0.17, 0.24, and 0.33, P for trend < 0.001). Estimated salt intake positively correlated with urinary UA/creatinine excretions in the prehypertensive group ($r = 0.496$; $P < 0.001$). In addition, the prehypertensive group had higher levels of salt intake and serum UA than the normotensive group [salt intake: 13.22 ± 3.52 vs. 12.35 ± 3.42 g/day, $P < 0.001$; serum UA: 290.0 (233.6–340.6) vs. 255.6 (211.6–305.0) mmol/L, $P < 0.001$]. The multivariate-adjusted odds ratios (95% confidence interval) for prehypertension compared with normotension were 1.68 (1.27–2.22) for salt intake and 1.71 (1.21–2.42) for serum UA. Increasing salt intake and serum UA were associated with higher risk of prehypertension. Compared

with the lowest quartiles, the highest salt intake and serum UA quartiles entailed 3.48 times greater risk of prehypertension.



Conclusions: Salt intake is associated with urinary UA excretion in prehypertensive participants. High levels of salt intake and serum UA simultaneously are associated with a higher risk of prehypertension.

VENTRICULAR ARRHYTHMIAS IN YOUNG ATHLETES: ARE THERE ANY POSSIBLE PREDICTORS?

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Objective: Long-term outcomes of frequent and/or complex ventricular arrhythmias in apparently healthy athletes are still controversial. Ventricular ectopy in young athletes often originates from the right ventricle. Arrhythmias can be a clinical expression of an initial cardiovascular disease that may not be easily detected in the growing age.

Design and method: The present study was designed to investigate the right ventricle morphology and function through echocardiography in young athletes with ventricular arrhythmias originating from right ventricle. 265 young athletes were recruited, aged 9 to 18 years, 158 male and 107 females. 97 of them presented frequent and/or complex ventricular arrhythmias at baseline EKG which did not disappear nor decrease during exercise test (group A) while 168 of them had no arrhythmias (group B). All athletes underwent echocardiogram focused on right ventricle, according to the American Society of Echocardiography's guidelines. A multivariate logistic regression analysis was performed to identify possible adjusted predictors of arrhythmias. The coefficients obtained were used to develop a scoring system to calculate the risk of arrhythmia.

Results: No sex differences were found. All echocardiographic parameters were between the normal range though the athletes with arrhythmias were older, heavier and taller. Group A presented different right ventricle systolic function indexes, namely a lower TAPSE, a higher MPI index and more positive values of strain; moreover, they had lower right ventricle longitudinal dimensions and higher end diastolic area (both absolute and indexed for subject's height). The likelihood of arrhythmic increase with age, with the decrease in systolic function parameters and with a glossier aspect of right ventricle. This score seems reliable in predicting the development of frequent and complex extrasystolia in young athletes (65% sensitivity, 86% specificity).

Conclusions: Athletes with a score value of 250 or more, should be more closely followed with EKG Holter and accurate echocardiographic study of right ventricle to detect early signs of cardiac disease.

MRI BASED DETECTION OF RENAL ARTERY ABNORMALITIES RELATED TO RENAL DENERVATION BY CATHETER BASED RADIO-FREQUENCY ABLATION IN DRUG RESISTANT HYPERTENSIVE PATIENTS

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Objective: Endovascular renal denervation (RDN) using catheter-based radio-frequency (RF) ablation has emerged as a potential treatment option for drug re-

sistant hypertension. Its efficacy is currently under debate. We aimed to evaluate the capability of contrast enhanced MRI to assess the effects of RDN on the renal arterial wall in patients presenting with drug resistant hypertension.

Design and method: Patients were included prospectively following IRB approval and written informed consent. Renal arteries were imaged using a 2D T1-w TSE sequence pre- and post-administration of a Gadolinium based contrast agent, before (D0), 2 days (D2) and 6 months (M6) after RDN. Mean enhancement of the wall (mENH) and mean wall thickness (mWT) were compared across time using an ANOVA with repeated measures and post-hoc paired t-test.

Results: Follow-up was completed for 23 patients (median age, 57 years; 16 men). mENH at D2 ($96.3 \pm 36.0\%$) was significantly higher than at D0 ($61.1 \pm 26.3\%$, $p < 0.001$) and M6 ($66.1 \pm 22.7\%$, $p < 0.001$). Similarly, mWT was significantly higher at D2 (3.1 ± 0.4 mm) than at D0 (2.7 ± 0.4 mm, $p < 0.001$) and M6 (2.9 ± 0.5 mm, $p = 0.002$).

Conclusions: MRI demonstrated abnormalities of the arterial wall two days after RDN that had resolved at 6 months.

THE LONG-TERM EFFECTIVENESS OF A SMARTPHONE APPLICATION TO REDUCE SEDENTARY TIME IN PRIMARY CARE. EVIDENT II STUDY

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Objective: The objective of this study is to evaluate the long-term effectiveness of adding an app to standardized counselling in order to reduce sedentary time

Design and method: Multicenter clinical trial with 12 month-follow up, including 833, recruited by random sampling in six primary care centers (415vs418). Interventions: Counseling on healthy and active lifestyle was given to both groups by a nurse. The intervention group (IG) received additional training in the use of an app that was designed to promote active lifestyle and healthy nutrition over a 3-month period. Measures: Sedentary time by Marshall sitting questionnaire and Physical Activity by 7-day Physical Activity Recall (PAR) questionnaire.

Results: Mean age was 51y. (SD12) in the IG and 52.3(SD12.0) in the group of only counseling (CG); women predominated in both groups (60.0% and 64.1%). In the baseline assessment, 114(27.5%) were active in IG and 118(28.2%) in CG ($p = 0.807$). The total sedentary hours per week (h/w) were 42.2 ± 17.8 in IG 41.4 ± 17.9 in CG ($p = 0.506$). There were also no difference in the hours of transport, work or watching television.

At 3 months there was a decrease in the sedentary time in both groups, IG: 0.37 h/w (95%CI:-1.75to1.01) and CG: 0.77 h/w (95%CI:-2.13to0.59), without intragroup or intergroup difference. Only a significant decrease of time was observed in watching television in IG: -1.18 (95%CI:-2.21to-0.14); $p = 0.026$, but not in CG: -0.36 (CI95%:-1.35to0.62), $p = 0.466$. Difference was not reached when comparing the changes between both groups ($p = 0.613$).

At 12 months, there was a small increase in sedentary lifestyles in IG: 1.03 (95%CI:-0.52to2.58); $p = 0.191$ and in CG: 1.85 (95%CI:0.41to3.30) $p = 0.012$, although it only reached statistical significance in the second, but not when comparing both groups ($p = 0.445$). There was also an increase in time watching TV in the CG: 1.84 h/w (95%CI 0.66to3.02) $p = 0.002$, but not in IG. The comparison of the change between both groups did not reach statistical significance ($p = 0.061$).

Conclusions: The intervention based on applications for Smartphone to promote healthy and active lifestyle decreased sedentary time, especially in leisure time in IG and increased in the control group with respect to the baseline, but without reaching the significance when comparing the changes between both groups.

DIFFERENCES OF EATING HABITS CAUSING HIGH SALT INTAKE OBSERVED IN SHIMANE COHRE STUDY

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Objective: To prevent hypertension, it is important to promote the reduction of salt intake, however, its practice is not easy. One of the reasons for the difficulty is that it will be ineffective unless differences in dietary habits in each region are considered. We conducted estimation of salt intake and eating habits for 2 consecutive years.

Design and method: We conducted the survey in 2 areas, one in the middle mountainous area (Town A) and another in isolated island area (Town B) at Shimane prefecture in Japan. We collected spot urine and acquired clinical data such

as blood pressure at the annual medical examination. The amount of daily salt intake was estimated from spot urine using Tanaka's method. In addition, dietary habits were surveyed.

Results: At Town A, there was no statistical difference in the average daily salt intake in 2014 and 2015, those were 9.67 g and 9.70 g, respectively. Likewise, the average of salt intake of both years showed no difference at Town B. Analysis of relationship between eating habits and salt intake showed that causative eating habits for high salt intake were different between at Town A and B. At town A, the number of times of eating pickles showed high correlation with the amount of salt intake. However, at Town B, there was no correlation between those. Instead, the number of taking miso-soup highly correlated with the amount of salt intake at Town B. However, this trend was not observed in Town A.

Conclusions: Although the geographical distance between Town A and B were less than 100 km, eating habits which contribute to high salt intake were different. In Town A, there is a habit to eat pickles at the tea time, suggesting that eating pickles were the most causable habit for high salt intake. However, the number of times to eat pickles per day does not differ between Town A and B. It is suggested that the amount of eaten pickles or salt content may differ. Our study suggested that even in the same regional area, the difference in eating habits should be considered.

IMPACT OF SOCIOECONOMIC FACTORS ON DAILY URINARY SODIUM AND POTASSIUM EXCRETION IN CHINESE FIRST GENERATION MIGRANTS IN ITALY

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Objective: Evidence are indicating that opportunities for appropriate treatment of risk factors are unequal at population level and ethnic minorities tend to have a higher risk for stroke than the host population. Although the reduction of sodium intake is a recognized main strategy for the prevention and control of hypertension, information regarding the effective receipt of this advice by ethnic minority groups in Europe is lacking. Study aims were to assess the level of salt and potassium consumption in first-generation Chinese migrants in Italy and to explore possible associations with blood pressure and hypertension.

Design and method: Population-based, cross-sectional study. Participants were 235 first-generation Chinese migrants aged 16–59 years. Subjects provided answers to a questionnaire and anthropometry and blood pressure was recorded. They were asked to perform a 24-hour urinary collection and the relationships of 24-hour urinary sodium and potassium with blood pressure (BP) values, hypertension diagnosis (BP > 140/90 mmHg or antihypertensive drug use) and hypertension awareness was investigated with logistic regression analysis.

Results: Mean (SD) daily sodium excretion was 143.6 ± 52.4 and 127.7 ± 48.9 mmol/day in men and women respectively ($p < 0.01$), corresponding to a dietary salt intake of 9.3 ± 3.4 and 8.3 ± 3.2 g/day respectively. Mean daily potassium excretions by gender were 33.2 ± 16.7 and 32.8 ± 14.5 mmol/day respectively (ns). Daily sodium

excretion (quartiles) was positively related with hypertension diagnosis and BP values at adjusted logistic regression analyses, being not influenced by hypertension awareness or by time spent in Italy. Importantly, high education level (secondary school, college or more vs illiterate or primary school) was associated with lower daily sodium (adjusted OR 0.989; CI95% 0.981 to 0.998) and increased potassium excretion (adjusted OR 1.037; 1.007 to 1.067). Hypertension awareness was not associated with any positive behaviours or educational factors either in the general cohort or in the hypertensive group.

Conclusions: Salt intake in Chinese first generation migrant workers aware of their hypertension status and frequently treated with hypertensive drugs is higher than recommended and in line with high salt intake in Italy. Potassium consumption remains low.

USEFULNESS OF TWO-DIMENSIONAL ECHO STRAIN IN EVALUATION OF CARDIAC FUNCTION IN ELITE ATHLETES

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Objective: Cardiovascular adaptation to sport training is influenced by many factors, including the intensity and the kind of sport practiced. The “Morganroth hypothesis” asserted that a static exercise characterized by a pressure load and dynamic (isotonic) exercise which involves a volume load to the heart lead to different myocardial adaptation patterns. More recent studies revisited this hypothesis, showing that left ventricular (LV) remodelling observed in both resistance and endurance trained athletes, presented similar aspects. Although morphological modifications secondary to exercise have been largely studied, less is known on myocardial systolic function in LV remodeling patterns in different elite athletes. Two-dimensional strain analysis allows a complete study of the contractile function in different myocardial regions of interest in both ventricles. In this study we aim to underline possible differences in contractile myocardial function with strain analysis in two groups of elite athletes, trained with different loads and playing different sports (football and cyclism)

Design and method: We enrolled 47 male athletes: 23 football players and 24 cyclists, belonging to same football or cyclism team (mean age in both groups 18 ± 3 years old). The athletes were evaluated with echocardiography at the beginning of the sports season. We assessed LV contractile function using speckle-tracking echocardiographic global longitudinal strain (GLS) and global circumferential strain (GCS). We also analysed right ventricular function by strain echocardiography

Results: Cyclists showed a significantly augmented indexed LV mass and TAPSE. No significant differences were found in GLS data between the two groups (-23.4 ± 0.02 in football players and -24.1 ± 0.02 in cyclists), whereas a significantly higher GCS was found in cyclists compared to football players (-31.2 ± 0.04 and -27.2 ± 0.05 respectively, $p < 0.005$). The cyclist group showed a significant increase in right ventricular strain compared to football players (-26.3 ± 0.04 and -23.2 ± 0.04 , respectively, $p < 0.05$)

Conclusions: Our preliminary data suggest that a dynamic exercise, which involves a volume load, like cyclism, leads to a sensible increase in systolic function in elite athletes especially in right ventricle contractility.

POSTER SESSION

POSTERS' SESSION PS06:

BLOOD PRESSURE MEASUREMENT AND VARIABILITY

INFLUENCE OF HYPERURICEMIA ON ELASTIC PROPERTIES OF ARTERIES IN PATIENTS WITH ARTERIAL HYPERTENSION

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Objective: Increased level of uric acid (UA) is not well studied.

Design and method: 110 patients were examined, including 68 individuals with AH and 42 — with normal level of BP. The following studies were performed: measurements of height and weight, body mass index, office systolic (SBP) and diastolic blood pressure (DBP), heart rate, ambulatory blood pressure monitoring, non-invasive determination of central SBP and pulse wave velocity in the arteries of elastic and muscular types (PWVe and PWVm), biochemical blood test with definition of UA level.

Results: Patients with AH and controls were similar in age. UA level was increased in 55 % of patients with hypertension. 17 % of persons with normal blood pressure had elevated UA levels. Individuals with hypertension were divided into 2 subgroups — with elevated levels of UA, the second one — with its normal level. In both subgroups, patients were of the same age and, predominantly, with excess body weight or obesity, there were more men in both subgroups. Patients did not differ significantly. In the subgroup of individuals with hypertension and hyperuricemia, PWVe was significantly higher — by 1.6 m/s ($p = 0.044$) than in the subgroup of patients with hypertension and normouricemia. But the value of PWVm was equal in both subgroups. There was a significant correlation between UA level and a history of transient ischemic attack or stroke, retinopathy, arrhythmia, as well as with the 24-h SBP and DBP. Also, we found reliable correlations with central arterial pressure ($R = 0.293$; $P = 0.007$), ejection duration ($R = 0.49$; $P < 0.001$), subendocardial viability ratio ($R = 0.47$; $P < 0.001$), augmentation pressure ($R = 0.53$; $P < 0.001$) and standardized augmentation index ($R = 0.24$; $P = 0.016$), as well as with PWVe ($R = 0.47$; $P < 0.001$). Reliable correlation with the level of UA was observed also for a number of echocardiographic and biochemical parameters.

Conclusions: There was an association of UA concentration with rigidity of arteries and central blood pressure and with augmentation index and may be an additional risk factor.

INTER-ARM BLOOD PRESSURE DIFFERENCE: THE PREVALENCE AND CHARACTERISTICS IN KOREAN GENERAL POPULATION

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Objective: An increased inter-arm systolic blood pressure difference (IBPD) is an easily determined physical examination finding and a significant IBPD has recently been associated with worse cardiovascular outcome. But the prevalence of IBPD in Asian population is unknown and the relationship between IBPD and blood pressure (BP) variability is not yet determined. This study was performed to describe the prevalence and clinical characteristics of the patients with increased IBPD and to examine the association between IBPD and BP variability.

Design and method: A representative population (aged 20–65 years) was selected by list-assisted random-digit dialing method from a city with a population of one million. The BP of two arms was simultaneously measured using validated automatic BP measurement devices for 3 times and ambulatory blood pressure monitoring (ABPM) was performed in all included subjects. An increased IBPD was defined as > 10 mmHg using the average of 3 BP differences obtained simultaneously in both arms.

Results: Five hundreds of subjects were included in this study, and 13 subjects were excluded because of inadequate ABPM measurements. Mean age was 46.9 ± 9.4 years and 309 participants were female (63.4%). Overall systolic BP and diastolic BP were 118.5 ± 13.4 mmHg and 75.1 ± 10.3 mmHg and mean systolic IBPD was 5.7 ± 4.0 mmHg. Of 487 subjects, 66 subjects (13.6%) had an increased systolic

IBPD. Compared with those with normal IBPD, subjects with increased systolic IBPD showed higher clinic BP (127.2 ± 13.7 vs. 117.2 ± 12.8 mmHg in systolic BP, $P < 0.001$; 78.7 ± 11.2 vs. 74.6 ± 10.1 mmHg in diastolic BP, $P = 0.002$), higher 24-hour systolic BP (118.5 ± 12.0 vs. 115.6 ± 10.8 mmHg, $P = 0.045$) and higher 24-hour pulse pressure (42.4 ± 7.4 vs. 40.2 ± 6.5 mmHg, $P = 0.012$). The subjects with increased systolic IBPD showed higher 24-hour BP variability; increased standard deviation of daytime BPs, increased weighted standard deviation of BPs, increased coefficient of variation of daytime BPs and increased average real variability of both 24-hour BPs and daytime BPs (Table). There was no significant difference in nighttime dipping pattern of increased IBPD subjects.

Conclusions: In this community-based cohort, an increased IBPD is common and associated with an increased short-term BP variability. Bilateral BP measurements should be emphasized in routine clinical practice.

	All patients (n=487)	Systolic IABPD (+) (n=66)	Systolic IABPD (-) (n=421)	P-value
BP profiles				
24 hour SBP (mmHg)	116.0 ± 11.0	118.5 ± 12.0	115.6 ± 10.8	0.045
24 hour DBP (mmHg)	75.5 ± 10.2	76.3 ± 11.8	75.4 ± 9.9	0.491
24 hour PP (mmHg)	40.5 ± 6.7	42.4 ± 7.4	40.2 ± 6.5	0.012
Daytime SBP (mmHg)	119.3 ± 11.7	121.5 ± 12.5	118.9 ± 11.5	0.092
Daytime DBP (mmHg)	78.5 ± 10.8	78.8 ± 12.1	78.4 ± 10.5	0.800
Daytime PP (mmHg)	40.9 ± 7.5	42.9 ± 8.2	40.5 ± 7.3	0.019
Nighttime SBP (mmHg)	109.1 ± 12.2	112.0 ± 13.1	108.6 ± 12.0	0.035
Nighttime DBP (mmHg)	69.3 ± 10.7	70.8 ± 11.8	69.1 ± 10.5	0.226
Nighttime PP (mmHg)	39.8 ± 6.8	41.4 ± 7.1	39.5 ± 6.7	0.036
24 hour BP variability				
SD of 24 hour SBP (mmHg)	12.1 ± 3.2	12.7 ± 3.6	12.0 ± 3.2	0.106
SD of 24 hour DBP (mmHg)	10.2 ± 2.4	10.3 ± 2.3	10.2 ± 2.4	0.866
uSD of 24 hour SBP (mmHg)	10.3 ± 3.0	11.3 ± 3.6	10.2 ± 2.9	0.006
uSD of 24 hour DBP (mmHg)	8.7 ± 2.1	9.2 ± 2.2	8.6 ± 2.1	0.046
CV of 24 hour SBP (mmHg)	10.5 ± 2.5	10.7 ± 2.7	10.4 ± 2.5	0.338
CV of 24 hour DBP (mmHg)	11.6 ± 2.5	11.4 ± 2.3	11.6 ± 2.5	0.638
ARV of 24 hour SBP (mmHg)	9.3 ± 2.4	9.9 ± 2.9	9.2 ± 2.3	0.029
ARV of 24 hour DBP (mmHg)	8.3 ± 1.8	8.7 ± 2.0	8.2 ± 1.8	0.030
Daytime BP variability				
SD of daytime SBP (mmHg)	10.9 ± 3.9	12.2 ± 4.5	10.8 ± 3.8	0.007
SD of daytime DBP (mmHg)	9.1 ± 2.7	9.9 ± 2.9	9.0 ± 2.6	0.016
CV of daytime SBP (mmHg)	9.2 ± 3.0	10.0 ± 3.4	9.0 ± 3.0	0.019
CV of daytime DBP (mmHg)	11.7 ± 3.3	12.6 ± 3.4	11.6 ± 3.3	0.019
ARV of daytime SBP (mmHg)	9.5 ± 3.6	10.6 ± 4.4	9.3 ± 3.5	0.008
ARV of daytime DBP (mmHg)	8.4 ± 2.5	9.2 ± 2.8	8.3 ± 2.5	0.005

CORRELATION OF SERUM NGAL LEVELS, HYPERTENSION AND DIASTOLIC FUNCTION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Objective: The aim of this study was to evaluate correlation of serum level of NGAL to severity of hypertension and diastolic dysfunction in patients with ST-segment elevation myocardial infarction treated with fibrinolytic therapy.

Design and method: We included 54 consecutive ST-segment elevation myocardial infarction patients treated with fibrinolytic therapy (alteplase). The median follow-up time was 6 days (interquartile range, 5 to 7 days). Blood samples were drawn immediately after admission prior to fibrinolytic administration. The endpoints were mean systolic and diastolic pressure (continuously monitored) and mean E/A ratio as a measure of diastolic function.

Results: Patients with high NGAL (above 134.05 mg/l; 75th percentile) had significantly higher mean systolic and mean diastolic blood pressure compared to patients with low NGAL (under 134.05 mg/l; 75th percentile), $p = 0.001$ and $p = 0.003$, respectively. Patients with high NGAL (above 134.05 mg/l; 75th percentile) had significantly lower E/A ratio compared to patients with low NGAL (under 134.05 mg/l; 75th percentile), $p = 0.004$.

Conclusions: High NGAL significantly correlates with severity of hypertension and diastolic dysfunction in patients with acute STEMI.

HOW TO IMPROVE THE CALCULATION OF MEAN ARTERIAL PRESSURE AT THE BRACHIAL ARTERY LEVEL

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Objective: Mean arterial pressure (MAP) is the time-averaged pressure through the cardiac cycle and may be calculated from brachial pressure values. Previous studies proposed thumb-rules, as adding 40% of pulse pressure to diastolic BP, to calculate MAP, but this approach is not unanimously accepted. We aimed to find the best way of calculating MAP by analyzing the brachial pressure wave.

Design and method: We examined the pressure waveform obtained with brachial arterial tonometry (PulsePen, DiaTecne) in 1526 subjects from 3 cohorts (age 64.4 ± 18.2 years, 44.1% males), one from general population ($n = 490$, age 49.6 ± 12.7 years, 39.4% males), one of elderly patients ($n = 284$, age 87.6 ± 4.7 years, 25.4% males) and one of hypertensive patients ($n = 752$, age 59.2 ± 14.4 years, 54.3% males). Brachial pressure wave was calibrated with oscillometric systolic and diastolic brachial blood pressure measurement. The “real” MAP and the percentage of pulse pressure that needs to be added to diastolic blood pressure (PP%) to obtain the MAP were calculated from the time-averaged brachial pressure waveform.

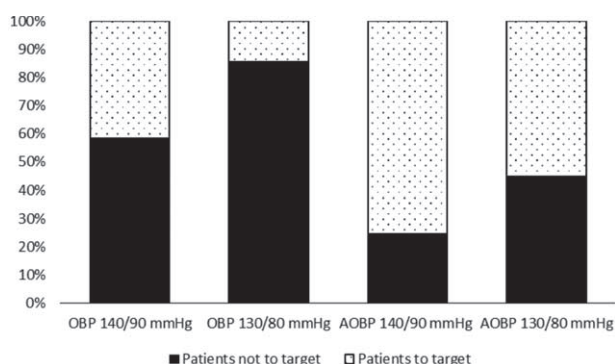
Results: The mean PP% in the pooled population was $42.2 \pm 5.5\%$ and was lower in the elderly cohort ($40.8 \pm 5.4\%$, $p < 0.0001$) than in the general population cohort ($42.8 \pm 6.0\%$) and in the hypertensives ($42.2 \pm 5.0\%$). PP% was higher in women ($42.9 \pm 5.6\%$) than in men ($41.2 \pm 5.1\%$, $p < 0.0001$), and was significantly correlated in multiple regression analysis with diastolic pressure ($b = 0.337$, $p < 0.0001$), heart rate ($b = 0.091$, $p < 0.0001$), while it was weakly related with age ($b = -0.053$, $p = 0.05$) and not related to systolic pressure. An equation to obtain an improved calculation of MAP in a single subject was derived from our data: $PP\% = 25.361 + 0.047 \times \text{heart rate} + 0.163 \times \text{Diastolic pressure} (+2.137 \text{ if female})$.

Conclusions: Our data provide an estimate of the PP% required to be added to diastolic pressure to obtain the “real” MAP, which is 42.2% (with and SD of 5.5%). PP% presents a marked inter-individual variability, which discourages the use of a unique PP% for everyone. Our results offer the possibility to improve the calculation of MAP in the single subject by applying a formula derived from the analysis of the brachial waveforms in a large population.

EFFECT OF DIFFERENT BLOOD PRESSURE TARGETS AND MEASUREMENT METHODS ON PREVALENCE OF CONTROLLED HYPERTENSION: THE IMPACT OF THE 2017 ACC/AHA BLOOD PRESSURE GUIDELINES

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Objective: Objective. The new 2017 ACC/AHA Blood Pressure Guidelines changed the definition of hypertension and its treatment targets, reducing blood pressure (BP) thresholds from 140 and/or 90 mmHg to 130 and/or 80 mmHg. The aim of the study was to compare the percentage of hypertensives to target following the new threshold and the previous ones, by using OBP and AOBP measurements.



Design and method: 118 treated non-diabetic hypertensive adults afferent to our Hypertension Unit were included in the study. All underwent an AOBP measurement with Omron HEM-907XL following the SPRINT and Myers unattended methodology, followed by a traditional OBP measurement, obtained as the mean of three readings, with a Microlife BP A150 AFIB (Microlife, Swiss) with an appropriate cuff. All patients signed an informed consent and the study was approved by local ethical committee (CEI 652). Patients were classified according to BP measurement method and different guidelines (ESH/ESC 2013/AHA 2014 or AHA 2017). Pearson's correlation coefficient was used to evaluate agreement between AOBP and OBP measurement.

Results: Mean AOBP values were significantly lower than the “traditional” ones. A mean SBP and DBP difference respectively of 12.1 ± 15.9 mmHg and 3.6 ± 9.4

mmHg was found at Bland Altman analysis. Pearson's correlation coefficients were 0.65 for SBP and 0.67 for DBP. Receiver operating characteristic (ROC) curves and the area under curve (AUC) used for evaluating the diagnostic accuracy of the thresholds identified 130/79 mmHg as the best AOBP threshold in our population compared to OBP. 60% of patients were not to target with the ESH/ESC 2013/AHA 2014 vs 86% with AHA2017 by using OBP, while only 25% and 44% remained uncontrolled respectively with ESH/ESC 2013/AHA2014 and AHA2017 by using AOBP.

Conclusions: Our data confirm that the new BP thresholds will dramatically increase the number of hypertensives not to target, but only when the “traditional” OBP measurement is used. In conclusion, these new guidelines will lead to important modifications in hypertension management, starting from BP measurement, even if a general adoption of AOBP may raise practical and economical concerns.

MASS SCREENING FOR HYPERTENSION IS FEASIBLE IN RURAL INDIA

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Objective: To evaluate if it is a feasible to screen for hypertension, and to estimate the prevalence of hypertension in rural India. To evaluate economical feasibility of mass screening for hypertension.

Design and method: An active door to door and opportunistic screening of adults for hypertension was done in villages in rural India. Blood pressure (BP) was measured two to three times in sitting position using a calibrated digital apparatus. Height, weight and heart rate were recorded as well. A short questionnaire including history of prior hypertension, diabetes, cardiovascular diseases and importantly any prior BP measurement was completed. The screening was performed by accredited Social Health Activists (ASHA), social health leaders, doctors and paramedics after a short training in measuring BP. All the expenses for the screening were calculated.



Results: During one month, a total of 61,839 adults were screened for hypertension. Complete data set was available in 43,647 individuals (Men/Women: 46%/54%). Seven percent refused to get BP checked. 84% individuals (Men/Women: 86%/82%) got their BP checked for the first time in life although 31% of them was older than 50 years. Among the 3,744 individuals older than 70 years,

15% got their BP checked for the first time in their life. Among the 124 individuals older than 90 years, 101 individuals had never got their BP checked before although 39% had hypertension ($\geq 140/90$ mmHg). Overall the prevalence of hypertension was 29.3%. Hypertension was known in 4.4% of the individuals. In a random subgroup of 4613 individuals, 6% had diabetes which was known by half of the individuals. The expenses for this screening was only 0.07 USD per individual screening.

Conclusions: In rural India, the prevalence of hypertension is high, but often unrecognized and untreated because of lack of screening although only very few individuals refuse screening. It is also economically feasible and possible to mass screen people for hypertension.

UNATTENDED VS ATTENDED BP MEASUREMENT: MEAN VALUES AND DETERMINANTS OF THE DIFFERENCE

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Objective: The results of the SPRINT study have called attention on the possible differences between blood pressure (BP) values obtained by health-care professionals in the office, during the visit ("attended BP") as compared to those obtained in the office leaving the patient alone ("automated office BP" or "unattended BP"). Only few studies have compared the two techniques and none of them implemented the approach for unattended BP measurement used in SPRINT by the use of completely automated device for both attended and unattended BP and by the measurement of 3 values after 5 minutes of rest.

Design and method: In 261 consecutive outpatients attending the outpatient clinic at an ESH Excellence Centre, BP values were measured by the physician with an automated oscillometric device (Omron HEM 9000Ai, mean of 3 measurements), after 5 minutes of rest. After the measurement of BP by the physician, the patient was left alone in the room, and the device was programmed to automatically perform 3 BP measurements after 5 minutes.

Results: Mean age was 61 ± 16 yrs, 60% F, BMI 26.1 ± 4.2 , 88 % with a previous diagnosis of hypertension (64 % treated). Unattended systolic BP (SBP) and diastolic BP (DBP) were both lower as compared to attended SBP (130.1 ± 15.7 vs 138.6 ± 17.2 mmHg) and DBP (77.1 ± 11.7 vs 78.9 ± 12.2 mmHg). The differences (Delta) between the values obtained using the two techniques were 8.5 ± 7.9 mmHg for SBP and 1.8 ± 5.6 mmHg for DBP. Delta SBP was directly correlated with age ($r = 0.235$ $p < 0.001$) and with attended BP values ($r = 0.407$ $p < 0.0001$); Delta SBP was significantly lower in males than in females. At multivariate analysis Delta SBP remained independently correlated with age and attended SBP. Delta DBP was directly correlated with attended DBP ($r = 0.322$ $p < 0.001$) and was lower in males.

Conclusions: Our findings indicate that "unattended BP" measurement provides values significantly lower as compared to measurements obtained in the presence of the physician. Interestingly, the difference between the values obtained by the two approaches is not constant for all patients, being significantly affected by age, gender and BP values

MUSCULAR ARTERIAL TONE IS A DETERMINANT OF PERIPHERAL MUSCULAR ARTERY STIFFNESS

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Objective: Due the practical weaknesses of cuff based methods for arterial blood pressure (BP) measurement, efforts are made to establish non-invasive and continuous PB measurement by using alternative methods. One of them is based on the determination of the pulse transit time and pulse wave velocity (PWV), respectively. Arterial BP and PWV correlate, which opens the possibility of the determination of arterial BP by measuring the pulse transit time (PTT). Recent validation studies revealed usefulness of this method in clinical practice. The accuracy of this method depends on the transfer function (model) between arterial BP and PWV. Since PWV is mainly determined by the arterial elasticity (stiffness), knowledge about the contribution of different components and to the arterial stiffness as well as their modulation is important. We hypothesize that the vascular smooth muscle (VSM) tone significantly determines arterial stiffness in muscular arteries and thus may contribute to the PWV-BP relation.

Design and method: We used the pressurized artery method and investigated the influence of inherent and pharmacologically modified VSM tone on measures of arterial stiffness. We first characterized passive and active components of arterial stiffness by calculating pressure-diameter-relation, stress-strain-relation, and

the stiffness parameter beta in vessels with spontaneous tone and in vessel after calcium depletion. Further, the effect of norepinephrine in different concentrations on the measures of stiffness was investigated.

Results: Vessels with spontaneous myogenic tone showed left shifted pressure-diameter- and stress-strain-relations compared to passive vessels, expressing an increased vascular stiffness. Norepinephrine in higher concentration further shifted these curves to the left and consequently increased vessel stiffness. The stiffness parameter beta was also increased.

Conclusions: The data suggest that the myogenic tone and the action of norepinephrine increases arterial stiffness in muscular arteries of rats. This effect may contribute the PWV in muscular arterioles and thus influences to the PWV-BP relation.

ASSOCIATION OF SHORT-TERM VARIABILITY INDICES WITH COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS IN CHRONIC KIDNEY DISEASE PATIENTS

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Objective: Several studies have demonstrated that increased blood pressure (BP) variability is associated with target-organ damage development in hypertensive patients. However, the impact of short-term BP variability indices on target-organ damage in chronic kidney disease patients (CKD) is unclear. Aim of the study was to evaluate the association between ambulatory BP variability indices and common carotid artery intima-media thickness (CCA-IMT) in chronic kidney disease patients.

Design and method: A total of 83 CKD patients, referred for evaluation at the Hypertension Unit of our department, underwent 24-h ambulatory blood pressure (BP) monitoring and CCA-IMT ultrasonographic measurements. Short-term BP variability was expressed by standard deviation (SD), time rate of BP variation (TR), average real variability (ARV) and coefficient of variation (CV) of systolic and diastolic BP for both 24-h, daytime and nighttime intervals. Statistical analysis was performed by means of bivariate correlations, simple and multiple linear regression analysis.

Results: The study population consisted of 65 men (78%) and 18 women (22%). All diastolic BP variability indices did not correlated significantly with CCA-IMT. In contrast, 24-h systolic SD ($r = 0.429$, $p < 0.001$), TR ($r = 0.576$, $p < 0.001$), ARV ($r = 0.537$, $p < 0.001$) and CV ($r = 0.309$, $p = 0.004$) significantly correlated with CCA-IMT. The multivariate analysis revealed (ARV was excluded due to collinearity reasons) that 24-h systolic TR of BP variation was the only variable that was significantly and independently associated with CCA-IMT ($B = 0.702$, 95%CI $0.377-1.027$, $p < 0.001$). The association remained significant after adjustment for baseline characteristics and risk factors.

Conclusions: Systolic ambulatory BP variability indices such as SD, TR, ARV and CV are associated with CCA-IMT in CKD patients. The systolic TR of BP variation is better associated with CCA-IMT than the other indices in CKD patients.

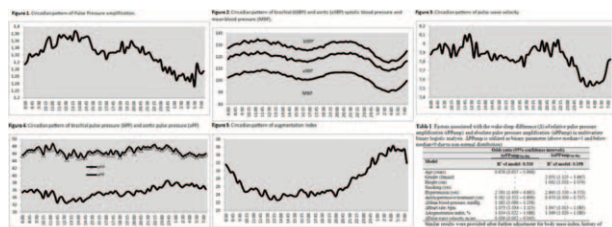
PULSE PRESSURE AMPLIFICATION DIPPING PATTERN DURING SLEEP TIME: THE SAFAR STUDY

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Objective: The difference in pulse pressure (PP) between peripheral arteries and the aorta, called pulse pressure amplification (PPamp), is a well-described physiological phenomenon which is independently associated with cardiovascular events. Recent studies suggest that it exhibits circadian variability. Our aim was to evaluate the 24 hour profile of peripheral and central hemodynamics and detect the factors associated with the circadian variability of PPamp.

Design and method: In 497 consecutive subjects (aged 54 years, 56.7% male, 79.7% hypertensives) we assessed the circadian pattern of peripheral and central arterial hemodynamics by 24-hour evaluation of brachial and aortic blood pressure (BP), augmentation index (AI) and pulse wave velocity (PWV) using a validated brachial-cuff based oscillometric device (Mobil-O-Graph).

Results: All parameters exhibited a circadian variation. Sleep dipping (decrease) pattern was observed for PPamp (Figure 1), brachial and aortic systolic BP, mean BP (Figure 2) and PWV (Figure 3), whereas a rising pattern (higher sleep than wake values) was observed for brachial PP, aortic PP (Figure 4) and AI (Figure 5). The factors independently associated with the less sleep-dipping in PPamp were: older age, lower height, the use of antihypertensive medication, sleep decrease in arterial stiffness (PWV); whereas female gender, the presence of hypertension, sleep increase of pressure wave reflections (AI), sleep decrease in heart rate and mean BP were associated with a greater sleep-dipping in PPamp (Table 1).



Conclusions: These data provide further pathophysiological understanding of the mechanisms leading to PPamp dipping. Several implications regarding the clinical use of the aortic and brachial BP, especially during sleep time, are raised that should be addressed in future research.

FACTORS ASSOCIATED WITH AN INCREASED SYSTOLIC BLOOD PRESSURE VISIT- TO-VISIT VARIABILITY IN A TERTIARY HEALTH CARE CENTER

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Objective: Identify factors associated with an increased systolic blood pressure visit to visit variability in a “real-life” setting.

Design and method: The study was observational, and retrospective. We included 2436 hypertensive outpatients, followed at our tertiary health care center, who had at least 8 visits with blood pressure readings. Epidemiological, clinical and therapeutic data were extracted and analyzed. Systolic blood pressure visit to visit variability was defined as the standard deviation around the mean systolic blood pressure of the 8 recordings.

Results: The mean age of the population was 63.7 ± 10.9 years, and 55.7% of the patients were men. The proportions of diabetes, smoking, dyslipidemia and history of major cardiovascular events were 32.4%, 28.6%, 39.9% and 22.6% respectively. The mean blood pressure was $157.2 \pm 11.7 / 90.8 \pm 8.3$ mmHg. The proportions of patients receiving one, two, three or more antihypertensive drugs at time of inclusion were 19.6%, 59.4% and 21% respectively. We found that age, systolic blood pressure, left ventricular hypertrophy, low eGFR, use of diuretics and use of beta-blockers were significantly associated with an increased systolic blood pressure variability. In a multiple regression analysis, the remaining independent factors were: age ($p = 0.001$), low eGFR ($p = 0.003$), use of diuretics ($p = 0.0001$) and treatment with beta-blockers ($p = 0.0001$).

Conclusions: Among factors affecting blood pressure visit to visit variability in our hypertension unit, the most deleterious are related to the type of drug prescribed, suggesting that limiting the use of these medications, at least in the first step, could result in a risk reduction of cardiovascular events linked to blood pressure visit to visit variability.

IS 30 MINUTES INTERVAL ENOUGH FOR ANALYZING? AMBULATORY BLOOD PRESSURE MONITORING?

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Objective: The National Institute for Health and Clinical Excellence (NICE) undertook detailed analysis for ambulatory blood pressure monitoring (ABPM) and showed that the use of ABPM is the most cost-effective method of confirming a diagnosis of hypertension. ABPM device should be set to record with the measurement frequency set at 15 – 30 minute intervals. In some papers the frequency was recommended at 10 – 15 minute intervals. The aim of this study is to see if there is a significant difference if the measurement frequency set at 15 or 30 minute intervals.

Design And Method: Our clinic took part in the International Ambulatory Blood Pressure Registry: Telemonitoring of Hypertension and Cardiovascular

Risk Project (ARTEMIS). We have analysed 425 subjects from the ARTEMIS study. Validated Meditech ABPM05 devices were used to record for a duration of 24 hours with the measurement frequency set at 15 minute intervals. Analyses were done by using Levene Test of Homogeneity of Variances as a part of Analysis of Variance in order to see if there is a significant difference between the measurement frequency set at 15 or 30 minutes intervals.

Scientific data: The resulting p-value of Levene's test in 92% subjects was higher than 0.05. The obtained differences in sample variances are not significant.

Results and conclusions: We didn't find a significant difference between 15 and 30 minute interval analyses of ABPM. In 34 subject we missed information regarding blood pressure and pulse during some events. Dipper status findings were different in 25 subjects. In most subjects the measurement frequency of ABPM device set at 30 minute intervals provides proper analysis of blood pressure and pulse during 24 hours.

UNOBSERVED OFFICE BLOOD PRESSURE MEASUREMENTS ARE NOT PROBABLY NECESSARY IN ALL PATIENTS VISITING AN OUTPATIENT CARDIOLOGY CLINIC

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Objective: The incidence of white coat hypertension is approximately 15–20%. Unobserved automatic office blood pressure measurement (AOBP), i.e. SPRINT trial-like BP measurement, has given new evidence regarding treatment goals in the recent American arterial hypertension guidelines. However, this kind of BP measurement is time-consuming while it needs extra available space in medical office which makes it difficult to implement in clinical practice. We aimed to study any differences regarding BP parameters between baseline semi-AOBP and subsequent conventional BP measurements in patients visiting a medical office.

Design and method: We performed semi-AOBP (Microlife, Watch BP) followed by conventional BP measurements in 114 patients (mean age 63 ± 15 years, 46 males, 47% hypertensives) visiting an outpatient cardiology clinic for follow-up appointments. Briefly, patients were advised to take two unobserved semi-automated BP measurements (preBP), at 5' after rest and at 3' after the first measurement and then they changed office and examined by the physician. Conventional BP was measured using a mercury sphygmomanometer at least after 5' of patient's rest (office BP). BP was characterized as normal or controlled if SBP < 140 mmHg and DBP < 90 mmHg.

Results: We found that office BP compared with preBP measurements were increased in: a. the whole population [SBP ($p < 0.001$) and DBP ($p = 0.02$)], b. the women [SBP ($p < 0.001$) and DBP ($p = 0.01$)], c. both the hypertensives [SBP ($p = 0.004$) and DBP ($p < 0.001$)] and non-hypertensives [SBP ($p = 0.04$)], d. patients with SBP > 140 mmHg and DBP > 90 mmHg [SBP and DBP ($p < 0.001$)], e. in diabetic patients there was a trend towards higher office SBP ($p = 0.07$). No differences were found in men as well as in those patients with normal ($n = 36$) or controlled BP ($n = 18$). In the whole population, we took in consideration regarding changing treatment plan, the preBP measurements in only 29(25%) patients (mostly hypertensives) in whom the latter were normal or controlled while office BP was uncontrolled.

Conclusions: Unobserved BP measurements might be useful for decision making in clinical practice in hypertensive patients with apparently uncontrolled office BP and especially women. Those results probably narrow the need for SPRINT trial-like measurements and raise doubts regarding new BP treatment goals.

RECTANGULAR CUFFS OVERESTIMATE BLOOD PRESSURE IN OBESE PEOPLE WITH VERY LARGE ARMS

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Objective: Rectangular cuffs and bladders are currently used for blood pressure (BP) measurement at the upper arm. However, large arms always have a tronco-conical shape. Aim of this study was to ascertain whether rectangular and tronco-conical cuffs provide different readings in obese subjects with very large arms.

Design and method: In 33 subjects with morbid obesity (BMI, 45 ± 5.0 Kg/m², 16 men) aged 51 ± 12 years, with arm mid-circumference ranging from 42 to 55 cm, and 33 subjects of control with standard arm circumference (range, 22–31 cm) the upper-arm frustum slant angle was measured. Two different rectangular and two different tronco-conical bladders of appropriate size and shape were constructed, on the basis of previous anthropometric measures obtained in our laboratory. In each subject, BP was measured in triplicate by two observers using the two cuffs in a random order. In addition, in the obese participants, the pres-

sure under the two cuffs was measured at five pressure levels (60, 90, 120, 150 and 180 mmHg) using a paper-thin pressure sensor attached to the central point of the cuffs.

Results: In all obese participants the upper arm shape was tronco-conical with slant angles ranging from 80.4 to 87.6° (mean 84.1 ± 1.4°). Systolic BP (SBP) and diastolic BP (DBP) differences between the troncoconical and the rectangular cuff were -4.8 ± 4.0 and -3.0 ± 4.3 mmHg, respectively, whereas they were negligible in the controls (SBP, $p < 0.001$ and DBP, $p = 0.01$). In the subjects of the top SBP quintile (SBP > 150 mmHg), the between-cuff SBP difference was -9.1 ± 5.1 mmHg. Arm slant angle was an independent predictor of the between-cuff SBP discrepancy ($p = 0.003$). Measurement with the pressure sensor showed a higher pressure under the rectangular compared to the conical cuff at any pressure level. The mean difference was -10.2 ± 5.2 mmHg and the difference progressively increased with increasing level of pressure applied to the cuffs.

Conclusions: In obese people, the upper arm has a pronounced tronco-conical shape and rectangular cuffs may overestimate BP. Tronco-conical cuffs should be used for BP measurement in subjects with very large arms.

DIURNAL RHYTHM OF CENTRAL HEMODYNAMICS DURING TWENTY-FOUR-HOUR AMBULATORY MONITORING

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Objective: 24-hour ABPM is a better method for diagnosing hypertension and predicting BP-related complications than office-based measurements. In addition increasing amount of evidences supports that central (aortic) BP is stronger predictor of cardiovascular risk than the conventional brachial BP. Dipping status of subjects can be easily assessed according to night-to-day brachial BP ratio provided by ABPM. However there is no data in the literature whether the diurnal rhythm of central aortic systolic blood pressure (CASP) follows the same pattern as the brachial one (BrSP). The aim of our study was to compare the 24-hour pattern of peripheral and central blood pressure in the same individuals.

Design and method: 24-hour monitoring of aortic and brachial blood pressure was performed with Arteriograph24, a newly developed upper-arm cuff oscillometric device in 55 hypertensive and normotensive subjects, 36 males and 19 females. The 24-hour systolic pressure amplification, the difference of brachial and aortic systolic pressures measured simultaneously was calculated. Augmentation index (AIx) which is one of the main determinants of central blood pressure was also assessed.

Results: The nocturnal fall of CSP was significantly lower than the peripheral pressure fall in 47 subjects of 55. 24-hour systolic pressure amplification was significantly lower during the night than during the day. In contrast to the nighttime decrease of central-to-peripheral systolic pressure Augmentation index was increased during the night.

Conclusions: Central hemodynamic parameters (AIx, cSBP) also have diurnal rhythm but in contrast to peripheral BP the circadian variation of central BP is not necessarily parallel with the corresponding peripheral values. Theoretically elevated peripheral vascular resistance (which is represented by the augmentation index) during nighttime helps to maintain the appropriate central systolic pressure which is mandatory for the perfusion of the brain, heart and kidneys.

ASSESSMENT OF SUBCLINICAL TARGET ORGAN DAMAGE BY COMPONENTS OF BLOOD PRESSURE: COMPARISON OF CENTRAL AND PERIPHERAL ARTERIAL PRESSURE

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Objective: Central aortic pressure (cAP) has stronger association with markers of vascular function and compared to peripheral arterial pressure (pAP), particularly in groups with elevated cardiovascular risk. However, the potential clinical use of blood pressure (BP) components of cAP and pAP as markers of target organ damage (TOD) has not been well established. The Aim of this study was to assess the association of pulsatile components of cAP and pAP with markers of TOD and to seek any differences related to age.

Design and method: From noninvasive waveform recordings, indices of cAP and pAP (pulse pressure [aPP, pPP], augmentation index. AIx) were assessed in relation with TOD in 770 hospital inpatients (age 60.0 ± 10.0 years, 473 males) with primary hypertension (brachial BP > 140/90 mmHg). TOD was quantified by arterial stiffness (carotid-femoral pulse wave velocity [cfPWV]), carotid intima-media thickness (IMT), urine albumin-to-creatinine ratio (ACR). Subclinical

TOD was defined as carotid IMT > 0.9 mm, urine ACR > 3.5 mg/mmol (females) and > 2.5 mg/mmol (males) and/or cfPWV > 12 m/s.

Results: Females showed greater cPP (mmHg) (50 ± 13) compared to males (40 ± 13) ($p < 0.01$) for similar pPP (mmHg) (62 ± 15, 60 ± 16 respectively). For the whole cohort, cPP and pPP were correlated with cfPWV ($r = 0.41$ vs. $r = 0.40$; $p < 0.01$), ACR ($r = 0.24$ vs. $r = 0.27$; $p < 0.01$) and carotid IMT ($r = 0.14$ vs. $r = 0.15$; $p < 0.01$). Each SD increase in pPP and cPP was associated with respective Odds Ratios (of 2.7, 2.9 (cfPWV), 1.2, 1.4 (ACR), 1.46, 1.53 (IMT). For males > 60 years, each SD increase in AIx corrected for heart rate was associated with 1.5 times increase in risk of cfPWV > 12 m/s. When corrected for confounding variables, cPP had higher predictive power for TOD for age > 60 years compared to pPP.

Conclusions: Both pPP and cPP were associated with TOD in a hypertensive population. However, compared to pPP, cPP provides independent and additional information associated with TOD elderly hypertensive subjects (> 60 years). Additional hemodynamic indices of cAP as potential biomarkers of subclinical TOD require validation by further prospective studies.

STRATEGY OF DISTANCE ACTIVE CONTROL IS ASSOCIATED WITH MORE PRONOUNCED ACHIEVEMENT OF TARGET BLOOD PRESSURE AND REDUCED EMERGENCY CALLS

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Objective: The aim of the study was to evaluate the influence of the distance control of blood pressure on the efficacy of treatment, frequency of emergency calls in patients with arterial hypertension (AH) in Voronezh out-patient clinic.

Design and method: 249 patients with AH (31% men, age 59 ± 6.1 years, AH duration 12 ± 4.2 years, smokers 7%, obesity 31%) were openly randomized in 2 groups. In the intervention group patients (n = 127) were under active distance physicians' control and in the control group patients (n = 122) received routine standard care. Patients in the intervention group reported the physician the results of home blood pressure monitoring (HBPM) by phone or e-mail daily (weekly in patients with target BP) and antihypertensive therapy was changed accordingly. Achievement of target BP level and number of emergency calls were assessed in 12 months.

Results: In the intervention group BP decreased from 158.2 ± 15.4 to 142.1 ± 13.7 mmHg, proportion of patients with target BP increased from 32 to 82% ($p < 0.001$). In the control group BP decreased from 157.9 ± 16.1 to 154.8 ± 12.7 mmHg, proportion of patients with target BP increased from 33 to 50% ($p < 0.01$). The number of emergency ambulance calls with hypertensive crises was significantly less in the intervention group (108 vs 186, $p < 0.01$).

Conclusions: The active distance control with modification of antihypertensive therapy based on HBPM compared with routine practice significantly increased the proportion of patients with target BP and decreased the amount of the emergency ambulance calls.

THE ACCURACY OF CENTRAL BLOOD PRESSURE OBTAINED BY OSCILLOMETRIC NONINVASIVE METHOD IN CHILDREN

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Objective: Analyzing central (aortic) blood pressure waveform obtained by an invasive method is the gold standard for the pulse wave analysis. In adult, central systolic blood pressure (cSBP) is thought to relate more closely to target organ damage than peripheral systolic blood pressure, and cSBP can now be reliably assessed non-invasively with a number of devices. However, noninvasive estimates of central blood pressure have not been validated in children. The purpose of this study is to clarify the reliability of a central blood pressure obtained by oscillometric noninvasive method in children.

Design and method: This study enrolled 10 patients (1 men and 9 women) who underwent a cardiac catheterization. The mean age was 9.9 ± 5.8 years (range 3 to 18 years). For each individual, we compared estimates of cSBP obtained from oscillometric noninvasive method (Mobil-O-Graph) with that measured directly by a catheter in the aortic root.

Results: Comparison of the cSBP values measured by the two methods showed a linear correlation ($r = 0.72$). The mean cSBP obtained from invasive method (catheter) was 92.5 ± 7.8 mmHg, and mean cSBP obtained from noninvasive method (Mobil-O-Graph) was 88.5 ± 11.2 mmHg. Bland-Altman analyses showed that the mean differences (95% confidence interval) between two measurements was 2.1 ± 0.75 (1.35–2.85) mmHg.

Conclusions: Oscillometric noninvasive estimation of cSBP with the Mobil-O-Graph is as effective as using the catheter. Because of the small sample size, result need to be interpreted with caution and further investigation is required.

THE DIAGNOSTIC THRESHOLD OF 2017 ACC/AHA HYPERTENSION GUIDELINES INCREASES WHITE-COAT HYPERTENSION

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Objective: We compared the diagnostic office blood pressure (OBP) threshold of 2017 American College of Cardiology and the American Heart Association hypertension (ACC/AHA) guidelines ($\geq 130/80$ mmHg) to that of European Society of Hypertension (ESH) guidelines ($\geq 140/90$ mmHg) using ABP based diagnosis of each guidelines as a reference.

Design and method: Among individuals ($n = 319$) who had high blood pressure (BP, $> 140/90$ mmHg) measured by physicians at the outpatient clinic and did not take antihypertensive drugs, 263 patients (mean age, 51.6 ± 9.6 years; 125 men) with valid 24-hour ABP measurements were analyzed. Research grade OBP was measured three times for each occasion during three-days visit with attendance of study nurses using a validated oscillometric device (WatchBP Home, Colson, Belgium) after 5 minutes of seated rest and at 1-minute intervals.

Results: The prevalence of hypertension by OBP was increased to 93.9 % ($n = 247$) based on 130/80 mmHg from 65.4 % ($n = 172$) based on 140/90 mmHg. The mean difference of systolic and diastolic BP between OBP and daytime ABP were 3.9 ± 11.0 mmHg and -0.4 ± 8.6 mmHg, respectively. When diagnosis of hypertension was based on daytime ABP diagnostic threshold of each guidelines, the sensitivity, specificity, positive and negative predictive value of ESH guidelines were 78.4, 71.0, 88.4 and 53.8 %. Those of ACC/AHA guidelines were 98.2, 28.6, 87.8, and 75.0 %. The diagnostic agreement (kappa) of ESH and ACC/AHA guidelines between OBP and daytime ABP were 0.448 and 0.357, respectively. The prevalence of white-coat hypertension based on daytime ABP in normotensive individuals was 29.0% (20/69) by ESH guidelines and 71.4% (30/42) by AHA guidelines ($p = 0.001$). Among 86 individuals with systolic OBP 130 – 139 mmHg, 37 (43.0 %) had white-coat hypertension. Among 86 individuals with diastolic OBP 80 – 89 mmHg, 18 (20.9%) had white-coat hypertension.

Conclusions: The diagnostic threshold of OBP and ABP by new ACC/AHA guidelines shows poor diagnostic agreement and increases the frequency of white-coat hypertension, which may lead to over-treatment of hypertension.

CUFF-LESS BLOOD PRESSURE MEASUREMENT USING THE PULSE TRANSIT TIME - A COMPARISON TO CUFF-BASED OSCILLOMETRIC 24 HOUR BLOOD PRESSURE MEASUREMENT IN CHILDREN

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Objective: Ambulatory blood pressure monitoring (ABPM) is recommended as mandatory for diagnosis of hypertension in children and adolescents. However, utility of cuff-based ABPM in children has several important limitations, e.g. fail recordings due to high motoric activity or arousal reactions followed by blood pressure (BP) fluctuations during sleep. SOMNOtouch[®] NIBP (SOMNOmedics GmbH) is an ESH validated cuff-less BP monitor, based on pulse transit time (PTT) measurement. It provides a beat-to-beat, non-invasive and non-reactive measurement of BP determined by the time interval between R- spike of the ECG and peripheral recorded pulse wave and a one-point calibration with a cuff device. Previous studies in adults showed a good agreement of both methods. The aim of this study was to compare the reliability of the PTT method versus conventional ABPM in children over 24 hours.

Design and method: Systolic (SBP) and diastolic (DBP) blood pressure were measured in 27 children (6 females, mean age 10.7 ± 2.6 years, 152.7 ± 15.6 cm, 48.7 ± 17.4 kg) using an oscillometric ABPM (Mobil-O-Graph PWA, I.E.M.). Measurement intervals were 30 min during daytime (6–22 h) and 60 min during night-time (22–6 h). Simultaneously, BP was recorded based on PTT (SOMNOtouchTM NIBP) on the contralateral arm. In addition, a 3-channel ECG, motoric activity, body position, finger plethysmogram, oxygen saturation and cuff pressure curve were recorded. All fail recordings of cuff measurements influenced by arrhythmia, activity, arousals during sleep and artefacts in cuff in/deflation were excluded from analysis (approximately 25%).

Results: Preliminary results (228 BP values) revealed a linear correlation of SBP and DBP ($r = 0.8$ for SBP, $r = 0.7$ for DBP). Limits of agreement in Bland-Altman

plot were $+22$ and -17 mmHg, with a mean difference of 2.2 mmHg, for SBP, resp. $+22$ and -12 mmHg, with a mean difference 4.9 mmHg, for DBP.

Conclusions: Our preliminary results imply that PTT and ABPM-based BP values are closely correlated in children during a 24-hour measurement in case invalid recordings were excluded. Despite high activity of children, the PTT method provides considerably more BP values than the cuff-based method.

HEALTH PROFESSIONALS AND BLOOD PRESSURE MEASUREMENT: SCOPING REVIEW AND PROTOCOL FOR KNOWLEDGE, PERCEPTION AND PRACTICE

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Objective: Blood pressure measurement (BPM) is a fundamental aspect of hypertension management. Guidelines regarding BPM methods namely home (HBPM), ambulatory (ABPM), office (OBPM) and automated (AOBP) are strongly recommended and supported by Hypertension Canada guidelines. Since health professionals (HP) play an important role in BPM and hypertension management a clearer picture of the knowledge, perception and practices of HP is needed. A scoping review was conducted to identify all studies assessing knowledge, perception and practices of HP with regard to all BPM methods.

Design and method: Keywords were identified and extraction was completed using the CINAHL and MEDLINE databases. A total of 74 potentially relevant studies were identified for scoping review.

Results: Of the 74 studies identified, 16 studies focused on HBPM, 7 studies focused on ABPM, 5 studies focused on AOBP, 46 studies focused on OBPM. Majority of studies enrolled physicians, whereas few studies enrolled nurses. The results presented focused on knowledge, perception and practices. As for knowledge, studies on HBPM (5), AOBP (1) OBPM (17) demonstrated lack of agreement among HP with regard to BPM techniques. No Canadian study assessed the knowledge of HP with regard to BPM techniques. As for perception, majority of studies on HBPM (7), ABPM (3), AOBP (1), OBPM (3) showed positive perceptions towards the usefulness of BPM methods in clinical practice. As for practice, the majority of studies on ABPM (4), AOBP (4), OBPM (21) showed unsatisfactory practices among HP with regard to BPM techniques. Lack of knowledge, less positive perceptions and unsatisfactory practices were observed in studies performed in USA, Canada, UK, Europe, and Asia.

Conclusions: Knowledge, perception and good practices are essential components of accurate BPM. The present scoping review therefore suggests the need to identify the gap between recommended guidelines and actual knowledge, perception and practices in primary care. A proposed protocol will include descriptive survey with an online questionnaire. Items in the questionnaire will distinctly focus on knowledge, perception and practices of HP with regard to BPM methods. This questionnaire will be developed in accordance with the guidelines.

NURSE-OBP: A NURSING STANDARDISED METHOD FOR MEASURING BLOOD PRESSURE

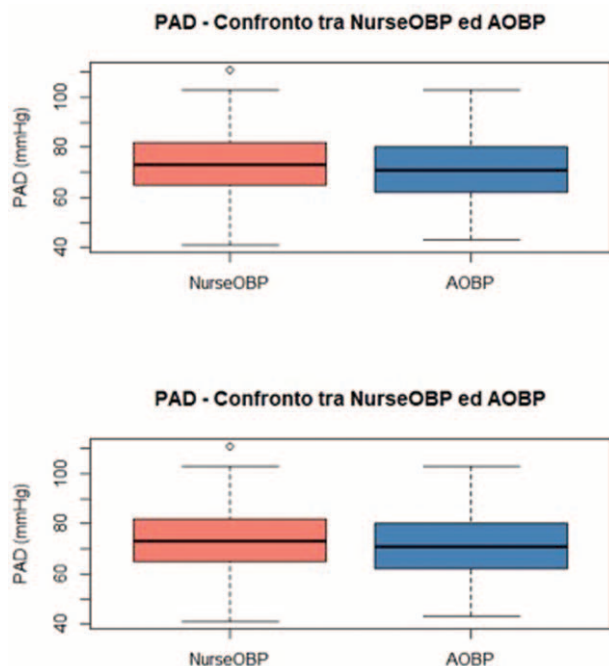
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Objective: Objective. The role of the nurse in both diagnostic and therapeutic management of hypertensive patient is becoming more and more important; nevertheless until now there is not a nursing standardised method of blood pressure (BP) measurement. The aim of this study was to standardise a nursing method for measuring blood pressure (Nurse-OBP) and to compare it with the Ambulatory Office Blood Pressure.

Design and method: Design and Method. 118 treated non-diabetic hypertensive adults afferent to our Hypertension Unit were included in the study. All underwent an AOBP measurement with Omron HEM-907XL and the Nurse-OBP measurement, designed to be methodologically identical to the classical AOBP proposed by Meyers and colleagues but which takes place with the nurse staying in the same patient's room during the BP measurement. All subjects were randomized into two groups, different according to the order in which the two method of measurement were performed to avoid eventual reduction of white coat effect mostly deriving from changes in patient behaviour, and finally, during the medical examination all underwent a traditional OBP measurement. All patients signed an informed consent and the study was approved by local ethical committee (CEI 652). Pearson's correlation coefficient was used to evaluate agreement between AOBP and Nurse-OBP measurements

Results: Results. Mean Nurse-OBP values ($132 \pm 19.4/73.3 \pm 12.9$) were significantly lower than OBP ones ($141.3 \pm 18.8/84.7 \pm 10.7$). When AOBP and Nurse-OBP were compared, no statistically significant differences between the two methods were found. The Bland - Altman analysis showed how the presence of the nurse could cause a minimum rise of BP values, (mean SBP and DBP difference respectively of 3.57 ± 12.23 mmHg and 2.25 ± 7.26 mmHg), but clinically non significant; therefore the two modalities, AOBP and Nurse-OBP, can be considered as comparable. Furthermore no differences in terms of Nurse-OBP values were found when the two groups were compared.

Conclusions: Conclusions. Our study proposes a standardised nursing method for measuring BP absolutely comparable to AOBP technique, that could have practical implications mostly when it is not possible to have a dedicated room where performing AOBP.



AN ABNORMAL BETWEEN-ARM BLOOD PRESSURE DIFFERENCE IS ASSOCIATED WITH CARDIOVASCULAR RISK FACTORS AND DISEASE: A COMMUNITY STUDY

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Objective: Hypertension guidelines recommend to measure blood pressure (BP) at both arms, at least in one occasion, since an abnormal between-arm BP difference is associated with an increased risk of vascular abnormalities and of cardiovascular (CV) disease. In the present community study we tested whether an automatic oscillometric BP monitor allowing simultaneous both arm BP measurement might be effective for screening of subjects with potential vascular disease.

Design and method: 220 consecutive subjects from an unselected sample of individuals of a small Italian community were screened using an automatic electronic BP monitor (MicroLife WatchBP Office). Seated BP was measured in triplicate at 1 min interval, using cuffs of the appropriate size for the subject's upper arm. Demographic and clinical data were collected prior to any BP measurement. An abnormal between-arm BP difference was defined as systolic (S) BP was > 20 mmHg and/or diastolic (D) BP > 10 mmHg.

Results: In 9 of 220 subjects (4.1%) an abnormal between-arm BP difference was found, with lower BPs measured in the non-dominant arm ($147 \pm 28 / 78 \pm 9$ vs. $154 \pm 15 / 92 \pm 11$ mmHg dominant, $p < 0.01$). In an univariate analysis, subjects with a significant between-arm BP difference were significantly older (71 ± 8 vs. 57 ± 15 years, $p < 0.01$), had a greater body mass index or BMI (32 ± 7 vs. 25 ± 4 kg/m², $p < 0.001$), higher BP levels ($154 \pm 15 / 92 \pm 11$ vs. $134 \pm 18 / 80 \pm 10$ mmHg, $p < 0.01$) and were more likely to report obesity (56 vs. 13%, $p < 0.01$), a history of hypertension (67 vs. 35%, $p < 0.05$) or of cardiovascular disease (33 vs. 10%, $p < 0.05$) than subjects with non-significant difference. In a multivariate analysis, a higher BMI and SBP were significantly associated with a

larger risk of a between-arm difference [odds ratio (95% confidence interval) for BMI: 1.29 (1.11, 1.51), $p = 0.001$; for SBP: 1.06 (1.01, 1.10), $p = 0.012$].

Conclusions: A significant between-arm BP difference is associated with a larger prevalence of CV risk factors (in particular obesity and hypertension), and CV disease. Thus, our study confirms that simultaneous both arm BP measurement must always be accomplished in all subjects at risk for CV disease.

EFFECTS OF 5-STEP COST-EFFECTIVE TREATMENT ALGORITHM ON AWARENESS, TREATMENT AND CONTROL OF HYPERTENSION IN RESOURCE-CONSTRICTED NORTHWEST CHINA OVER THE PAST 17 YEARS

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Objective: Prevalence of hypertension in Xinjiang, Northwest China is approximately 30–54.6% in population aged 30 years and older, and ranks at the national forefront due to its geographical remoteness, unhealthy eating habits, and physical inactivity, whereas treatment and control rates are too low for several reasons, which encompass a relatively backward economy (GDP ranking 25th among 31 provinces in China by 2014), extremely premature medical conditions (lower educational level (illiteracy rate: about 19%, far higher than 4% of national level in 2004) and the existence of multi-ethnic background and thus communication barrier, which make it difficult to implement campaigns against hypertension. Therefore, our center has focused on training and education of local medical staff and population and has generalized easy-to-comprehend 5-step evidence-based cost-effective ant-hypertensive treatment algorithm in three counties (Hefeng, Fuhai and Fukang) of Xinjiang since 1998 after completing a baseline survey.

Design and method: Between 1998 and 2015, training and educational programs in four language were conducted to local medical staff and population. Meanwhile, seven independent population-based cross-sectional surveys were performed in these three counties to assess the changes in awareness, treatment and control of hypertension.

Results: 6144 (n = 1551 in 1998–2000, n = 2331 in 2007–2008 and n = 2262 in 2015) adults aged 30 years or older were enrolled for the survey. Awareness, treatment and control rates of hypertension were 34.8%, 11.1% and 0.2% in 1998–2000, 52.3%, 24.7% and 2.9% in 2007–2008 and 52.8%, 30.9% and 10.1% in 2015. Mean SBP was 144.4 mmHg in 1998–2000 and 127.7 mmHg in 2015 and mean DBP was 89.6 mmHg in 1998–2000 and 76.4 mmHg in 2015.

Conclusions: Over the past 17 years, awareness, treatment and control of hypertension showed substantial improvements. Particularly control rate increased 50%, although still lower than the most parts of the world and China (13–15%). We consider generalization of easy-to-comprehend 5-step evidence-based cost-effective ant-hypertensive treatment algorithm has been effective in population-based management of hypertension in resource-constricted area, whereas secular trends must also be kept in mind.

BLOOD PRESSURE AND HEMODYNAMIC PARAMETERS AFTER ACUTE AEROBIC, RESISTANCE AND COMBINED EXERCISES IN RESISTANT HYPERTENSIVE SUBJECTS

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Objective: Evaluate the acute effects of aerobic, resistance and combined exercise on blood pressure (BP) and hemodynamic parameters in resistant (RH) and non-resistant (non-RH) hypertensive subjects

Design and method: This interventional, randomized, single-blind, crossover study was conducted with 20 patients (RH = 10, non-RH = 10) from the Resistant Hypertension Clinic at UNICAMP- Brazil. All subjects were submitted to a previous adaptation of physical activity to determine the load to be implemented in resistant exercise session. Subjects were randomized to perform 45 minutes of: a) Aerobic exercise (AE): activity on a treadmill (70% of maximum heart rate obtained from ergometric test); b) resistance exercise (RE): 4 series of 12 repetitions of each exercises at moderate intensity (Borg scale); and c) combined exercise (CE): AE (25 minutes) + RE (20 minutes). Clinical and hemodynamic parameters were assessed before and after each exercise session.

Results: We found no difference between RH and non-RH subjects after each exercise, except for a reduction in aortic pulse pressure (41 ± 13 vs. 37 ± 9 mmHg, $p = 0.04$) after CE in non-RH subjects and Augmentation Index after AE (31 ± 11 vs. 22 ± 9 %, $p = 0.02$) in RHTN patients. Daytime 24 hour ambulatory diastolic

pressure (76 ± 8 vs. 74 ± 8 mmHg, $p < 0,001$) and nighttime pulse pressure (58 ± 11 vs. 43 ± 8 mmHg, $p = 0,03$) decreased in RH subjects after CE. When we compared the type of exercise in RH subjects, we found a higher reduction on systolic (AE -7 ± 26 vs. RE $+8 \pm 25$ vs. CE -15 ± 21 mmHg, $p < 0,001$), diastolic (AE -5 ± 14 vs. RE $+2 \pm 15$ vs. CE -8 ± 10 mmHg, $p = 0,04$) and mean blood pressure levels (AE -4 ± 17 vs. RE $+7 \pm 17$ vs. CE -8 ± 13 mmHg, $p = 0,002$) after CE

Conclusions: The hemodynamic parameters after one session of AE, RE and CE were similar between RH and non-RH subjects. However, when compared the different types of exercises, we observed that EC was more effective in reducing blood pressure in RH patients.

RELATIONSHIP BETWEEN BLOOD PRESSURE VARIABILITY IN WORKPLACE AND PSYCHOLOGICAL STATE IN HYPERTENSIVE PATIENTS

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Objective: The aim of our study was to determine relationship between blood pressure variability (BPV) in workplace (BPVw), daytime (BPVd), nighttime (BPVn) periods and psychological state in hypertensive patients without serious concomitant diseases.

Design and method: We analyzed ambulatory blood pressure monitoring (ABPM) data recorded from 189 hypertensive patients without serious concomitant diseases. The washout period was 1 week. The monitor (Spacelabs 90207) was applied between 10.00 - 10.30 A.M. We defined daytime period as 8–22, nighttime period as 0–6, workplace period as 11–19 hours. After ABPM session each patient completed the psychological questionnaire “Minnesota Multiphasic Personality Inventory” (MMPI). We analyzed the following scale scores: L – lie scale, F – aggravation scale, K – correction scale, Hs(1) - hypochondria, D(2) - depression, Hy(3) - hysteria, Pd(4) - psychopathy, Pa(6) - rigidity of affect, Pt(7) - psychasthenia, Sc(8) - schizothemia, Ma(9) - hypomania. Spearman Partial Correlation Coefficient was used for correlation analysis. The analysis model was adjusted for age, sex and duration of hypertension.

Results: The initial daytime period systolic BP was $142,3 \pm 11,3$, diastolic BP - $91,4 \pm 7,1$ mm Hg. We found correlations ($p < .05$) between: 1) Pa(6) scale score and BPVd, BPVw; 2) L scale scores and BPVd, BPVw. Thus, increase of L, Pa(6) scale score (psychological immaturity, aggressiveness, leadership traits e. t. c.) was associated with BPV increase. We revealed inverse correlations ($p < .05$) between: 1) Ma(9) scale score and BPVd, BPVw; 2) Hs(1) scale scores and BPVd; 3) Pt(7) scale scores and BPVw. Thus, increase of Hs(1), Pt(7) scale scores (asthenia behavioral type, otherwise, social conform, compassion, leadership traits absence e. t. c.) and Ma(9) scale scores (cheerfulness level) was associated with BPVd and BPVw decrease.

Conclusions: Social disadaptation (aggression, leadership traits, psychological immaturity e. t. c.) was related with higher BPV. High social conform, compassion (asthenia behavioral type) and cheerfulness is associated with decreased possibility of conflict situations and lower BPVd and BPVw.

WAVE REFLECTION IS INVERSELY ASSOCIATED WITH THE DEVELOPMENT OF MYOCARDIAL HYPERTROPHY AMONG HYPERTENSIVE SUBJECTS

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Objective: Wave reflection forms the basis of arterial input impedance and they offer valuable information on arterial stiffness. Thus, it has emerged as a strong, important marker of premature cardiovascular disease.

Objective: To evaluate the association between wave reflection coefficient and the myocardial hypertrophy among hypertensive subjects.

Design and method: Subjects with office blood pressure (BP) $> 140/90$ mmHg, without treatment attending our Hypertension Center participated in the study. Exclusion criteria were renal dysfunction, heart failure, severe arrhythmia including atrial fibrillation and evidence of secondary hypertension. A complete medical history was obtained from all participants. Office BP was measured in 3 consecutive visits (Microlife WatchBPN, Microlife, Widnau, Switzerland). Consequently, all participants underwent 24 h ambulatory blood pressure monitoring (24h-ABPM), using the Mobil-O-Graph monitor (IEM, Stolberg, Germany). Mobil-O-Graph records oscillometric brachial BP, and calculates pulse wave velocity (PWV), aortic BP, augmentation index (Aix) and wave reflection as measure of arterial stiffness. BP measurements were performed at 20-min intervals for 24 hour. Daytime and nighttime periods were defined according to the patients' diaries (awake and asleep periods). Transthoracic echocardiogram for the assessment of myocardial hypertrophy was performed in all subjects. Results are expressed as frequencies and percentages for qualitative variables and as mean values with SD for quantitative variables. Statistical analysis was performed using the Student's t-test for independent samples. A p-value of 0.05 was considered statistically significant.

Results: A total of 72 individuals, mean age 52.15 ± 11.97 years, 31 women were included in the analysis. A strong inverted association between wave reflection coefficient and myocardial hypertrophy was observed, with p values < 0.002 . Similar association were found for 24-hour, awake and asleep BP ($p = 0.002$, $p = 0.018$ and $p = 0.002$, respectively).

Conclusions: Wave reflections markedly affect the central pressure profile, further contributing to increased cardiovascular risk. Future studies should assess the role of genetic versus geographic and other environmental influences in wave reflection coefficient as an index of vascular remodeling and especially aortic stiffness.

COMPARISON OF AUTOMATED BLOOD PRESSURE MEASUREMENTS WITH CONVENTIONAL READINGS IN A MUNICIPAL OUTPATIENT CLINIC

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Objective: Conventional office blood pressure (COBP) readings are compromised by artificial increases in blood pressure (BP). Automated office blood pressure (AOBP) technique eliminates the white-coat response and sequel improves the validity of office readings. The clinical interpretation of BP readings taken in real life outside hospital clinics is not clear.

Objective: To compare community AOBP with COBP readings in a public outpatient clinic.

Design and method: Blood pressure (BP) was measured twice in the clinic with a validated oscillometric device, after a 5-min rest period in a sitting position (Microlife WatchBP Office, Microlife AG, Widnau, Switzerland). Consequently, all participants were measured with an Omron 907 XL to obtain AOBP readings. The patient was left alone to rest for 5 min after which the device was set to record BP at 1 min intervals. All three readings were used to determine the mean AOBP.

Results: A total of 81 individuals, mean age 63.14 ± 12.32 years, 45 women were included in the analysis. The mean systolic AOBP \pm SD was 133.83 ± 14.54 mmHg and the mean systolic COBP \pm SD was 146.62 ± 20.95 mmHg, $p < 0.001$. The mean systolic AOBP-COBP difference was 12.79 ± 12.11 mmHg (95% confidence interval 10.11 to 15.47, $p < 0.001$). Furthermore, the mean diastolic AOBP was 76.93 ± 11.27 mmHg and the mean diastolic COBP was 84.99 ± 12.40 mmHg, $p < 0.001$ and the mean diastolic AOBP-COBP difference was 8.06 ± 7.55 mmHg (95% confidence interval 6.39 to 9.73).

Conclusions: AOBP readings appear to yield lower BP values compared to COBP and could be recognized as a valuable tool for hypertension diagnosis in public clinics.

POSTER SESSION

POSTERS' SESSION PS07:

KIDNEY AND RAAS, ENDOCRINE HYPERTENSION

EFFECTS OF EMPAGLIFLOZIN ON SALT-SENSITIVE HYPERTENSION AND RENAL INFLAMMATION IN RAT

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Objective: Renal inflammation may have a role in salt-sensitive hypertension. Although sodium-glucose cotransporter-2 (SGLT2) inhibitors were reported to exert blood pressure lowering in type 2 diabetes mellitus, whether they have a role in non-diabetic kidney diseases is not clear. This study was undertaken to investigate whether salt-sensitive hypertension and its accompanying renal inflammation are ameliorated by SGLT2 inhibition.

Design and method: The animal model of salt-sensitive hypertension was established by salt loading in uninephrectomized rats. Male Sprague-Dawley rats were randomly divided into 3 groups: sham controls (SC, n = 4), uninephrectomized controls (UC, n = 4), and empagliflozin-treated rats (ET, n = 5). All rats were fed a rodent diet with 8% NaCl throughout the study period. Empagliflozin (20 mg/kg/d) was orally administered for 3 weeks after uninephrectomized rats were stabilized over 2 weeks. Systolic blood pressures (SBPs) were weekly measured, and kidneys were harvested for qPCR at the end of animal experiment.

Results: At baseline, SBPs were 122 ± 4 , 127 ± 1 , and 125 ± 3 mmHg in SC, UC, and ET, respectively. At the end of animal experiment, SBP in UC was higher than that in SC (167 ± 4 vs. 137 ± 6 mmHg, $P < 0.01$). However, ET had a lower SBP (146 ± 3 mmHg) compared with UC ($P < 0.05$). As expected, urinary glucose excretion was remarkable in ET (2.61 ± 0.59 mmol/d/100 g BW versus 0 in controls). Whereas natriuresis was not different between groups, urinary excretion of osmoles in ET (29.8 ± 3.6 mmol/d/100 g BW, $P < 0.01$) was higher than that in SC (20.6 ± 2.3 mmol/d/100 g BW) or UC (19.3 ± 1.4 mmol/d/100 g BW). Compared with SC, the mRNA expression level of IL-1 β ($268 \pm 91\%$, $P < 0.05$), RANTES ($167 \pm 20\%$, $P < 0.05$), and gp91phox ($300 \pm 36\%$, $P < 0.05$) were increased in UC but ameliorated in ET (IL-1 β , $159 \pm 29\%$; RANTES, $87 \pm 34\%$; gp91phox, $142 \pm 74\%$, all $P < 0.05$).

Conclusions: Empagliflozin was effective in controlling salt-sensitive hypertension induced by renal mass reduction, via glycosuria-driven osmotic diuresis rather than natriuresis. The upregulation of renal inflammation in salt-sensitive hypertension may be relieved by empagliflozin treatment.

KLOTHO SUPPLEMENTATION ATTENUATES BLOOD PRESSURE AND CYST GROWTH IN MOUSE POLYCYSTIC KIDNEY DISEASE

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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. Renal expression of klotho is diminished in chronic kidney disease. In the present study, the effects of klotho supplementation on polycystic kidney disease (PKD) model were assessed.

Design and method: Recombinant human klotho protein (10 mg/kg/day) or vehicle was administered daily by subcutaneous injection to 6 week-old PKD (DBA/2-*pcy*) mice. Blood pressure was measured by tail-cuff methods. After 2 months, mice were killed by over-dose of anesthesia and the kidneys were harvested for the analysis.

Results: Exogenous klotho protein supplementation reduced right (1.24 ± 0.10 vs. 0.84 ± 0.09 g, $p < 0.01$) and left kidney weight (1.19 ± 0.10 vs. 0.88 ± 0.06 g, $p < 0.01$), cystic area (51 ± 5 vs. $34 \pm 4\%$, $p < 0.05$), systolic blood pressure (110 ± 3 vs. 101 ± 2 mmHg, $p < 0.05$) and 8-*epi*-prostaglandin F $_{2\alpha}$ excretion (354 ± 86 vs. 100 ± 35 ng/day, $p < 0.01$) without changes in body weight.

Creatinine clearance in klotho-treated PKD mice was higher than the untreated (1.01 ± 0.08 vs. 0.51 ± 0.04 ml/min/g.kidney.wt, $p < 0.01$). Klotho supplementation reduced plasma angiotensin II levels (459 ± 76 vs. 217 ± 31 fmol/ml, $p < 0.05$) without significant changes in renal angiotensin II concentrations. Exogenous klotho protein supplementation improved renal expression of superoxide dismutase (SOD), as well as renal klotho expression itself ($p < 0.01$ for each). Klotho supplementation reduced renal expressions of fibronectin and collagen I ($p < 0.05$ for each), and diminished renal abundance of phosphorylated Akt and mTOR ($p < 0.05$ for each). Pathological examination revealed that klotho reduced fibrosis index and nuclear staining of Smad3 in PKD kidneys.

Conclusions: The present data indicate that klotho supplementation reduces blood pressure in association with ameliorating renin-angiotensin system in PKD mice. 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 cystic growth in PKD mice. Finally, the present findings suggest that klotho inhibits TGF- β signaling through Smad to attenuate fibrosis. The present data provide translational evidence to examine whether klotho supplementation is the treatment of choice for PKD patients resistant to AVP antagonist.

ASSOCIATION STUDY OF URIC ACID TRANSPORTER GLUT9 GENOTYPE WITH THE RENIN-ANGIOTENSIN SYSTEM

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Objective: Uric acid is thought to be one of risk factors for atherosclerotic disorders. The mechanisms have been thought to include endothelial dysfunction, inflammation, oxidative stress and the renin angiotensin system (RAS) activation. It is known that the RAS plays a pivotal role in the atherosclerotic disorders. However, the evidence that uric acid is involved in the activation is not sufficient. We therefore tested the hypothesis that a genetic variant of a uric acid transporter, glucose transporter 9 (GLUT9) could show significant association with prevalence of hyper-reninemic state.

Design and method: We enrolled consecutive 804 subjects who had consulted our hospitals for life style related diseases (statistic power 80%, significance level 0.05). We defined the subjects with plasma renin activity (PRA) equal with or more than 0.70 mg/ml/hr. as hyper-reninemic group as cases of the study and the subjects with PRA less than 0.70 mg/ml/hr as normo-reninemic group as controls. Genomic DNA was isolated from human leukocytes. Genotypes were assayed with genomic DNA for a C/T variant of GLUT9 (rs1014290) using real-time PCR system by TaqMan method. Association between the genetic variant and the prevalence of hyper-reninemic state was tested.

Results: They consisted of cases (51.0%) and controls (49.0%). The serum uric acid (mg/dl) with each genotype of GLUT9 were as follows: CC (127 cases) 5.04 ± 1.45 , CT (392 cases) 5.08 ± 1.49 , TT (286 cases) 5.44 ± 1.45 (CC vs CT, $p = 0.77$; CC vs TT, $p = 0.011$; CT vs TT, $p = 0.002$). The numbers of individuals with each genotype were as follows (CC, CT and TT): 52, 204 and 154 for cases and 75, 187 and 132 for controls. Accordingly, the risk for hyper-reninemic state was 1.24 (95% confidence interval; 1.02–1.52), $p = 0.033$ for allelic comparison and also $p = 0.032$ for Armitage's trend test, the T allele being the risk allele.

Conclusions: The uric acid concentration is associated with a genetic variant of transporter GLUT9 and the subjects with genetic variant of high uric acid have hyper-reninemic constitution. Thus, from a view point of Mendelian randomization theory, it is found that high uric acid state may have a significant impact on the RAS activation.

ANGIOTENSIN II TRIGGERS PODOCYTE APOPTOSIS THROUGH THE MODULATION OF CD2AP AND AMPK

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Objective: Angiotensin II (Ang II) promotes the pathogenesis and progression of renal diseases and also plays a direct role in the pathogenesis of proteinuria. CD2-associated protein (CD2AP) in podocytes serves as an adaptor protein binding to nephrin and podocin, anchoring these slit diaphragm proteins to actin fila-

ments of podocyte cytoskeleton, and sending signals inward or outward. In addition, CD2AP can facilitate the nephrin-induced PI3-K/AKT signaling, which protects podocytes from apoptosis. AMP-activated protein kinase (AMPK), as a sensor of cellular energy status, has been known to play an important role in the pathophysiology of metabolic diseases, including diabetes, and its renal complications. We investigated the role of AMPK on the changes of CD2AP and podocyte apoptosis by angiotensin II (Ang II), a major vascular injury inducer.

Design and method: Mouse podocytes were incubated in media containing various concentrations of Ang II and AMPK-related agents. The changes of CD2AP and podocyte apoptosis were observed by confocal imaging, western blotting, and TUNEL assay according to the presence of Ang II.

Results: CD2AP and AMPK α were located diffusely but predominantly in peripheral cytoplasm and co-localized with nephrin. Ang II reduced AMPK α in time and dose-sensitive manners and also decreased CD2AP stainings diffusely and induced spatial separation from concentrated nephrin, similar to those of compound C-treated condition. AICAR and metformin, AMPK activators, ameliorated the abnormal distributional changes of AMPK α and CD2AP. In western blot analysis, Ang II also reduced (Thr172) phosphorylation of AMPK α and CD2AP in time- and concentration-dependent manners, which were significantly recovered by metformin and AICAR. Ang II type 1 receptor antagonist, losartan also recovered CD2AP suppressed by Ang II. LY294002, a PI3-K inhibitor, reduced CD2AP suppressed by Ang II. Ang II increased apoptosis in time- and concentration-dependent manners, which were ameliorated by AMPK activators and siCD2AP.

Conclusions: Our findings suggest that Ang II induces the relocation and suppression of podocyte CD2AP and AMPK α via Ang II type 1 receptor and through the inhibition of PI3-K signaling, which trigger podocyte apoptosis induced by Ang II.

LOSARTAN NORMALIZES BLOOD PRESSURE AND PREVENTS RENAL DAMAGE AND INFLAMMATION INDUCED BY FRUCTOSE OVERLOAD. L-DOPA/DOPAMINE INDEX AS A NEW POTENTIAL BIOMARKER OF RENAL DAMAGE

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Objective: The renin angiotensin system (RAS) and the renal dopaminergic system (RDS) act as autocrine and paracrine systems to regulate renal sodium management and inflammation, and their alterations have been associated to hypertension and renal damage. Nearly 30–50% of hypertensive patients have insulin resistance (IR), which has a strong correlation to microalbuminuria. The aim of this study was to evaluate the effects of RAS blockade with losartan on blood pressure and renal damage in a model of IR produced by fructose overload (FO), and its association to changes in the RDS. Finally, we studied the urinary L-dopa/dopamine index as a potential biomarker of renal dysfunction.

Design and method: Male Sprague Dawley rats were divided into: Control (C, tap water), FO (10% w/v of fructose solution), Losartan (L, 30 mg/kg/day in tap water), FO+L (30 mg/kg/day in fructose solution) groups for 4, 8 and 12 weeks. Systolic blood pressure (SBP) and metabolic parameters were measured. Urinary L-dopa and dopamine, diuresis, natriuresis and microalbuminuria were determined. Renal expression of D1 receptor (D1R), pro-inflammatory markers (IL-6, TNF- α , TGF- β 1, angiotensin II [Ang II]) and Na⁺,K⁺-ATPase expression and activity were measured.

Results: Losartan prevented the increase in SBP and Na⁺,K⁺-ATPase activity and the reduction in natriuresis induced by FO from week 4 ($p < 0.05$). Increased L-dopa/dopamine index and decreased D1R expression in FO rats were prevented by losartan since week 4 ($p < 0.05$). The same pattern was observed for renal expression of Na⁺,K⁺-ATPase, IL-6, TNF- α and TGF- β 1 since week 8 ($p < 0.05$), with no changes in Ang II. FO was associated with the appearance of microalbuminuria at week 12, effect prevented by losartan ($p < 0.001$).

Conclusions: These results provide the mechanisms by which a prohypertensive and proinflammatory system, such as RAS, downregulates another antihypertensive and antiinflammatory system such as RDS, establishing a positive feedback

loop that leads to hypertension and kidney inflammation due to FO. Furthermore, we demonstrated the potential usefulness of the L-dopa/dopamine index as a biochemical marker of renal dysfunction, earlier than microalbuminuria, and as a predictor of treatment response and follow-up of hypertension and kidney damage.

HYPERBARIC OXYGEN PRECONDITIONING IMPROVES RENAL HAEMODYNAMIC AND KIDNEYFUNCTION IN SPONTANEOUSLY HYPERTENSIVE RATS WITH ISCHEMIC ACUTE KIDNEY INJURY

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Objective: Acute kidney injury associated with other risk factors, such as hypertension, causes high mortality rate. Hyperbaric oxygen preconditioning has been shown to prevent ischemia reperfusion injury in different tissues. The aim of our study was to determine the effect of hyperbaric oxygen preconditioning on renal haemodynamic and kidney function in spontaneously hypertensive rats suffered kidney ischemia-reperfusion injury.

Design and method: An experiment was performed in anesthetized, adult six-month-old male spontaneously hypertensive rats (SHR). SHR were randomly selected in three experimental groups: sham operated (SHAM; $n = 7$); AKI control group (AKI; $n = 9$); and AKI group with hyperbaric oxygen preconditioning (AKI+HBO; $n = 9$). The right kidney was removed and the renal ischemia was performed by clamping the left renal artery for 45 minutes. Treated rats were placed into experimental HBO chambers and exposed to pure oxygen, twice a day (in a 12 hour interval, 8AM and 8 PM) for two consecutive days in the following manner: 10 minutes slow compression, 2.026 bar of oxygen for 60 minutes, 10 minutes slow decompression. AKI was performed on the next morning. Mean arterial pressure (MAP) and renal blood flow (RBF) were measured and renal vascular resistance (RVR) was calculated 24 h after reperfusion. Plasma creatinine (PCr) was measured on Cobas integra 400 plus.

Results:

	SHAM	AKI	AKI+HBO
MAP mmHg	179±10	96±6***	95±7
RBF ml/min x kg	25,3±2,5	10,4±1,5***	21,1±3,3##
RVR mmHg x min x kg/ml	7,4±0,8	16,5±3,2**	9,3±2,1#
PCr μmol/l	60,4±1,8	236,8±11,5***	155,5±16,7***

** $p < 0.01$; *** $p < 0.001$ vs. SHAM; # $p < 0.05$; ## $p < 0.01$; ### $p < 0.001$ vs. AKI

Conclusions: Our results suggest that HBO treatment improves renal haemodynamic and kidney function of SHR with AKI episode. This implies that preconditioning with hyperbaric oxygen may attenuate consequences of AKI development in hypertensive subjects exposed to risky surgical procedures.

EXERCISE HEART RATE DURING TREADMILL TEST IS RELATED TO RENAL FUNCTIONAL RESERVE IN ESSENTIAL HYPERTENSIVE PATIENTS: A NOVEL LINK BETWEEN THE HEART AND THE KIDNEYS

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Objective: Renal functional reserve (RFR) refers to the capacity of the kidney to augment its level of function under the influence of certain stimuli and it constitutes a valuable diagnostic tool for recognizing high risk patients for acute kidney injury and chronic kidney disease. The aim of our study was to assess the relation of RFR with diverse clinical parameters in patients with essential hypertension and glomerular filtration rate (GFR) > 60 ml/min/1.73m².

Design and method: 15 hypertensive subjects [mean age = 57 years, body mass index = 28.5 kg/m², office systolic/diastolic blood pressure (BP) = 148/90 mmHg] were included and underwent exercise treadmill stress test, 24-hour ambulatory BP and echocardiographic examination. All subjects were fasted for 8 hours and then baseline hydration status was recorded using bioimpedance analysis. Basal GFR

was measured after hydration and stress GFR was achieved after ingestion of oral protein 1 g/kg as cooked meal. Basal and Stress GFR were determined by Creatinine Clearance = Urine Creatinine/Serum Creatinine x Urine Volume/time x 1.73/body surface area. RFR was calculated as Stress GFR – Basal GFR.

Results: Patients with a history of hypertension greater than 10 years, had lower RFR values (-14.59 ± 43.26 vs 21.35 ± 28.19 ml/min/1.73m², $p < 0.001$). There was no correlation of RFR values with respect to age, family history, smoking, dipping status and office BP. In contrast, a statistically significant positive correlation was found between RFR and maximum heart rate during treadmill test ($r = 0.880$, $p = 0.009$). Hypertensives with high RFR were also characterized by higher maximum HR during treadmill test (157 ± 22 vs 142 ± 20 bpm, $p < 0.05$).

Conclusions: RFR is related to treadmill exercise heart rate in essential hypertension, suggesting a link between the dynamic regulation of renal function and sympathetic overdrive's influence on the heart rate. These findings suggest that treadmill test may be used to identify hypertensive patients with unfavorable RFR, thus more susceptible to kidney damage.

THE ROLE OF ALDOSTERONE AND ANGIOTENSIN II IN THE REGULATION OF PARATHORMONE SECRETION

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Objective: We recently proposed the existence of a pathophysiological link between the adrenocortical Zona Glomerulosa (ZG) and the parathyroid glands. However, the role of the other components of the renin-angiotensin-aldosterone system in the regulation of parathyroid gland remains unknown. The aims of this study was therefore to investigate: 1) in vivo effects of acute inhibition of angiotensin II (Ang II) signalling on parathormone (PTH) secretion in patients with primary aldosteronism (PA) and essential hypertension; 2) in vitro effects of angiotensin II and aldosterone on PTH secretion in primary parathyroid cells.

Design and method: Referred hypertensive patients with primary aldosteronism (PA, n = 34) and primary hypertension (PH, n = 17) were prospectively investigated by assessing the acute effect of captopril (50 mg p.o.) on plasma PTH levels. Proteins expression for type 1 angiotensin receptor (AT1R) and 11-beta hydroxy steroid dehydrogenase type 2 (11HSD2) were quantified in parathyroid tissues. Cultures of parathyroid primary cells characterized in terms of specific markers (Calcium Sensing Receptor, Chromogranin A and Glial cell missing-2 homolog) were developed and PTH production in response to angiotensin II (100 nM) and aldosterone (10–3 M) was measured by ELISA kit.

Results: Captopril lowered PTH in PA (from 36.9 ± 16.0 to 31.2 ± 13.2 ng/L $p = 0.0005$) but not in PH (from 31.6 ± 9.0 ng/L to 29.7 ± 10.9 ng/L $p = 0.1024$). Parathyroid tissues express both AT1R and 11-beta hydroxy steroid dehydrogenase type 2 proteins. Parathyroid primary cells cultured up to 7 days without losing their capability to produce PTH. Secretion of PTH was increased after cells stimulation with aldosterone (10–3 M) (% secretion of PTH vs control: 240 ± 52 , $p < 0.01$) and Angiotensin II (% secretion of PTH vs control: 168 ± 15 , $p < 0.01$); this effect was abolished by canrenone (% secretion of PTH vs control: 135 ± 35) and irbesartan (% secretion of PTH vs control: 102 ± 15).

Conclusions: These results show that acute lowering of Ang II formation lowers PTH secretion in vivo. The finding that parathyroid glands express AT1R and 11HSD2, alongside that of the MR, and the response to Ang II and aldosterone stimulation of primary parathyroid cells, provide further support for an involvement of the renin-angiotensin-aldosterone system in the regulation of parathyroid function.

AT1 AND GPER-1 HETERODIMERIZATION POTENTIATES CYP11B2 GENE EXPRESSION IN ALDOSTERONE PRODUCING ADENOMA

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Objective: Aldosterone producing adenomas (APAs) exhibit increased expression levels of G protein-coupled receptors (GPCRs), including the GPCRs Angiotensin (Ang) II type 1 receptor (AT1R) and G protein-coupled estrogen receptor-1 (GPER-1), which trigger aldosterone production by binding Ang II and 17B-estradiol or aldosterone.

Since a functional crosstalk between GPCRs has been reported, we investigated if AT1R and GPER-1 crosstalk to activate CYP11B2 gene expression in APA

Design and method: APA strips and adrenocortical carcinoma cell line HAC15 were exposed to [100 nM] aldosterone alone or in presence of [100 nM] Ang II for 12 hours, and/or after pre-treatment with the selective AT1R antagonist irbesartan and/or the selective GPER-1 antagonist G36. The experimental end-point was

CYP11B2 gene expression change. HAC15 proteins were immunoprecipitated with an antibody for AT1R, and GPER-1 expression was revealed by immunoblot in immunoprecipitated proteins.

Results: In APA strips both aldosterone and Ang II increased CYP11B2 gene expression (+220% and +190%, respectively, $p < 0.01$ vs untreated); aldosterone on top of Ang II potentiated the secretagogue effect of Ang II (+400%, $p < 0.001$ vs untreated). The synergistic effect of aldosterone and Ang II was inhibited by either irbesartan or G36. Similarly, in HAC15 cells aldosterone potentiated the effect of Ang II (+800% vs Ang II alone; +1300% vs aldosterone alone), and pre-treatment with irbesartan and/or G36 blunted the synergistic effect of aldosterone plus Ang II. After immunoprecipitation for AT1R, GPER-1 protein expression was detected by immunoblot

Conclusions: Aldosterone and Ang II can increase the expression of CYP11B2 through a crosstalk between GPER-1 and AT1R receptors. In HAC15 cells AT1R and GPER-1 form heterodimers which interact to induce an autonomous aldosterone production in APAs.

CIRCADIAN HAEMODYNAMIC CHARACTERISTICS IN PATIENTS WITH PRIMARY ALDOSTERONISM

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Objective: The circadian variability of central blood pressure (BP), arterial stiffness indices, and haemodynamic parameters in primary aldosteronism (PA) patients remains to be elucidated. The present study aimed to compare circadian haemodynamic characteristics in hypertensive patients with and without PA.

Design and method: Circadian haemodynamics, including 24-hour brachial and central BP, systolic BP variability indices, central pulse wave velocity (PWV), augmentation index (AIx@75), cardiac index, and total vascular resistance (TVR) were evaluated using an oscillometric device, Mobil-O-Graph NG device (IEM, Stolberg, Germany), in 60 patients with PA (63.4 ± 13.3 years, 47% female) and 120 age- and sex-matched patients with essential hypertension. The device monitored the above parameters every 30 minutes during the daytime (6 AM to 9 PM) as well as at nighttime (9 PM to 6 AM) for 24 hours until the next day.

Results: Office systolic BP, PWV, AIx@75, and BP variability indices were similar between groups; however, 24-hour brachial (124 ± 14 vs 130 ± 11 mmHg) as well as central (112 ± 12 vs 120 ± 10 mmHg) systolic BP was higher (both $p < 0.01$), and the difference between 24-hour brachial and central systolic BP (11 ± 5 vs 9 ± 3 mmHg, $p < 0.05$), an index of pressure amplification, was smaller in PA compared to essential hypertension. In both groups, cardiac index decreased from daytime to nighttime (both $p < 0.01$), but this decrease was smaller in PA ($p < 0.05$). During daytime, TVR in PA was higher than that in essential hypertension ($p < 0.05$), and the significant increase of TVR from daytime to nighttime was lost in PA. In a multivariate stepwise regression model, PA emerged as an independent predictor of 24-hour central systolic BP as well as the difference between 24-hour brachial and central systolic BP.

Conclusions: Our results demonstrated that circadian haemodynamics in PA patients are characterized by increased central systolic BP, smaller disparity between brachial and central systolic BP, and disturbed circadian haemodynamic variation.

CARDIAC REMODELLING IN RENAL TRANSPLANTED PATIENTS: A QUESTION OF GENDER?

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Objective: Cardiovascular diseases are the most common cause of morbidity and mortality among renal transplanted patients and one of the main determinant of cardiac remodelling is hypertension. The aim of the present study was to explore clinical and echocardiographic characteristics of renal transplanted patients, and to evaluate the role of elevated blood pressure (BP) in determining cardiac organ damage.

Design and method: We examine 44 patients, 15.4 ± 8.8 years after renal transplantation, who underwent to echocardiographic examination, including speckle

tracking evaluation, and to ambulatory blood pressure monitoring (ABPM). Significant determinants of cardiac remodelling were explored with regression analysis adjusted for several clinical confounders.

Results: 86% of the study participants were hypertensives, 45% diabetics, 68% had lipid abnormalities and 47% high serum uric acid levels. Among hypertensive patients the majority (51%) were taken three pills and the most frequent treatment prescribed were B-blockers (79%). At echocardiographic evaluation 64% of the patients presented concentric hypertrophy, 27% concentric remodelling, 9% a normal morphology, none had eccentric hypertrophy. Mean longitudinal strain was $-21 \pm 4\%$ and 20% of the study participants had an impaired longitudinal function. With regard to diastolic function, 27% had a normal function, 68% a diastolic dysfunction, 5% had a pseudo-normal pattern. According to ABPM data 27.3% had diurnal hypertension and 90.9% had nocturnal hypertension; the majority of the patients were risers (53%) or non-dippers (30%), only 17% had a normal dipping pattern. In multivariate regression analysis, adjusted for several clinical and biochemical analysis, none of the ABPM parameters was a significant determinant of left ventricular mass, diastolic function or global longitudinal strain, while the main determinant was gender ($p = 0.018$ for left ventricle mass, $p = 0.033$ for GLS, $p = 0.007$ for diastolic function). Only serum calcium level presented a significant difference according to gender and was higher in females compared to males.

Conclusions: Renal transplanted patients presented an unfavourable cardiac remodelling and nocturnal hypertension, however none of ABPM indexes significantly correlated with cardiac organ damage. Gender and in particular male gender, is a significant determinant of cardiac remodelling, indicating that probably these patients should be treated more intensive.

A MASS IMAGING TECHNIQUE REVEALED A RENO-PROTECTIVE EFFECT OF THE XANTHINE OXIDASE INHIBITOR FEBUXOSTAT IN THE ISCHEMIC KIDNEY BY PROMOTING ATP RECOVERY IN THE CORTEX

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Objective: The kidney has different energy metabolism depending on the region. However, the distribution of phosphorylated adenosine (ATP, ADP and AMP) and their alteration after transient ischemia have not been known due to the technical difficulties.

Design and method: Imaging mass spectrometry (IMS) with metabolome analysis is a novel technique to quantify the small metabolites in the tissues. We performed the IMS analysis in the ischemic kidney after transient ischemia by renal artery clipping.

Results: In the normal kidney, ATP was significantly rich in both the cortex and outer medulla. After transient ischemia, ATP in the cortex degraded and the energy charge value decreased within a minute. ATP in the inner medulla did not decrease within a minute and needed 10 minutes to start decreasing. After the 10 minutes of ischemia, total adenylates decreased in the cortex, although the decrease in energy charge value was homogeneous in the kidney. During the 24 hours reperfusion after 10 minutes ischemia, restoration of total adenylates in the cortex was not sufficient. Febuxostat is a xanthine oxidase inhibitor which might promote reuse of hypoxanthine as a progenitor of adenylates and therefore might improve the restoration of total adenylates and ATP after transient ischemia. The administration of febuxostat in accordance with the reperfusion period supported the restoration of ATP level in the cortex and improved renal function which was impaired by transient ischemia.

Conclusions: In these ways, IMS revealed the region-specific alteration of phosphorylated adenosine in the ischemic kidney and the novel effect of febuxostat on the restoration of total adenylates and ATP in the cortex after transient ischemia.

JUXTAGLOMERULAR CELL TUMORS: A CASE SERIES

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Objective: Juxtaglomerular cell tumors (JCTs) are a rare but potentially curable cause of hypertension. Their diagnosis is challenging because these tumors may not be detected or mistaken for a cyst on CT-scan.

Design and method: Between 1986 and 2017, 10 patients with JCTs were retrospectively identified in our Hypertension Unit. Clinical, biological and radiological features were extracted from our clinical data warehouse.

Results: Among the 10 patients with JCT, ⁸were women, ²were men. Median age was 24.5 [15–49] years. 8 of 10 patients had grade III hypertension. Severe hypokalemia related to a marked secondary hyperaldosteronism was a constant feature. Medians of plasma renin and aldosterone concentrations were 392 [70.5–4800] mUI/L and 1490 [671–2492] pmol/L, respectively. Median plasma pro-renin concentration was 835.5 [133–6546] mUI/L. Median tumor size was 17.5 [8–33] mm. On CT-scan, JCTs were spontaneously isodense with little enhancement after contrast media injection. On MRI, JCTs were iso (7/10) or hypointense (3/10) on T1-weighted images (WI). On T2-WI, JCTs were hypointense (2/10), isointense (4/10), with 3/4 heterogeneous or heterogeneously hyperintense (4/10). Six of 10 JCTs had a thin peripheral “pseudo-capsule” (hypointense on T2-WI). Contrast enhancement was low, slightly heterogeneous and delayed. On diffusion-WI, tumors were hyperintense with a restricted apparent diffusion coefficient. Surgical resection allowed hormonal recovery in all cases and hypertension cure in all but one patient because of a mild zone of renal infarction in the tumorectomy area. After 43 [0–228] months follow-up, one patient had a recurrence of hypertension 4 years after surgery.

Conclusions: This is the largest study describing clinical, biological and radiological characteristics of JCTs, including detailed description of MRI features. In hypertensive patients with secondary hyperaldosteronism, imaging (CT or ultrasound) should be performed to analyze renal arteries and renal cortex. In case of unexplained secondary hyperaldosteronism, renal MRI should be performed if a renal lesion without cystic specific characteristics is detected. MRI should also be discussed in patients with grade III hypertension, severe secondary hyperaldosteronism and normal CT-scan, particularly in women. Non-invasive imaging technics, especially renal MRI, may improve diagnosis of JCTs.

PARATHYROID HORMONE, BUT NOT 25-HYDROXY VITAMIN D, SERUM LEVELS ASSOCIATE WITH ALDOSTERONE-TO-RENIN RATIO AND NOCTURNAL MEAN BLOOD PRESSURE VARIABILITY

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Objective: To assess the association between serum parathyroid hormone (PTH) or vitamin D serum levels with blood pressure, aldosterone-to-renin ratio, and target organ damage in a series of hypertensive patients.

Design and method: Observational cross-sectional study of hypertensive patients who undergone 24-hour ambulatory blood pressure monitoring (24-h ABPM), in whom plasma aldosterone, plasma aldosterone-to-renin ratio, PTH and 25-OH D serum levels were available. Blood pressure (BP) was measured by 24-hour ABPM. BP was assessed as average real variability. Renin-angiotensin-aldosterone axis status was assessed through plasma aldosterone levels and aldosterone-to-renin ratio. Electrocardiography, echocardiography and urine albumin-to-creatinine ratio were used to evaluate left ventricular hypertrophy and renal damage, respectively. Patients with primary hyperparathyroidism were excluded.

Results: We enrolled 170 consecutive patients (median age [IQR] -year, 52 [42–64]; 48.2%, female). In comparison with patients with normal PTH serum levels (<88 pg/ml), those with high PTH serum levels (>88 pg/ml) showed a significantly increase in plasma aldosterone-to-renin ratio [mean \pm SD] (37.8 ± 46.6 vs. 20.7 ± 27.0 ; $p = 0.032$), and nocturnal pulse pressure (56.3 ± 17.9 vs. 50.6 ± 13.1 mm Hg; $p = 0.029$). Furthermore, when compared with patients in the PTH 1st quartile, those in the 4th PTH quartile showed significantly higher nocturnal systolic BP (129.5 ± 25.6 vs. 119.9 ± 14.4 mm Hg; $p = 0.038$), plasma aldosterone (204.9 ± 128.4 vs. 153.8 ± 88.7 pg/ml; $p = 0.037$), plasma aldosterone-to-renin ratio (36.4 ± 45.8 vs. 18.9 ± 24.5 ; $p = 0.033$), and nocturnal mean BP variability (8.9 ± 4.4 vs. 7.1 ± 1.7 mm Hg; $p = 0.016$). Differences in aldosterone-to-renin ratio and nocturnal mean BP variability remained significant after adjusting by age, gender, renal function and ACE/ARB therapy in multivariate analysis. No such differences were observed in patients with vitamin D deficiency (25-OH D < 20 ng/ml), when compared with patients with normal vitamin D serum levels.

Conclusions: High PTH, but not low 25-OH D serum levels associate with increased aldosterone-to renin ratio and elevated nocturnal mean blood pressure variability. Our results might explain, in part, the lack of consistent clinical benefit of vitamin D supplementation on high blood pressure and cardiovascular risk. We suggest that serum PTH status should be considered in trials searching for cardiovascular benefits from vitamin D supplementation in patients with hypovitaminosis D.

EFFECTS OF A NOVEL INTERACTING MOLECULE WITH AT1 RECEPTOR, ATRAP, ON ANG II-INDUCED PROLIFERATIVE ACTIVITY AND OXIDATIVE STRESS IN VASCULAR SMOOTH MUSCLE CELLS

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Objective: Superoxide anions are recognized as mediators of intracellular signaling cascades and are known to participate in cardiovascular diseases such as arteriosclerosis and hypertension. Previous studies reported that the production of superoxide is modulated by many factors including Ang II - AT1 receptor signaling. One of the major sources of superoxide in the aorta is NADPH oxidase located in the smooth muscle cells. The NADPH oxidase complex in the vascular smooth muscle cells consists of p22phox, Rac1, and Nox1. Previous studies showed that the carboxy-terminal cytoplasmic domain of AT1 receptor is involved in the control of receptor internalization and in linking receptor-mediated signal transduction to the specific biological response.

Design and method: We previously cloned a novel molecule interacting with carboxy-terminal domain of AT1 receptor, which we named ATRAP (for AT1 receptor-associated protein), using the yeast two-hybrid strategy. In this study, we tested the hypothesis that vascular smooth muscle cells express ATRAP and that ATRAP modulates Ang II-induced proliferative activity and oxidative stress in vascular smooth muscle cells. We identified that the ATRAP mRNA and protein were endogenously expressed in VSMC, and found a colocalization of ATRAP and AT1 receptor in Ang II-stimulated VSMC.

Results: The results of gain-of-function studies by adenoviral gene transfer demonstrated that overexpression of ATRAP significantly inhibited Ang II-mediated increases in c-fos gene transcription, BrdU incorporation, and mRNAs expression of NADPH oxidase complex ($p < 0.05$, $n = 6$).

Conclusions: These results indicate that ATRAP significantly attenuates Ang II-mediated proliferative activity and oxidative stress in vascular smooth muscle cells, and may suggest a novel strategy to inhibit cardiovascular disease such as arteriosclerosis and hypertension.

PRIMARY ALDOSTERONISM AND PREGNANCY

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Objective: Primary aldosteronism (PA) may present in younger age and it may so complicate pregnancy if not diagnosed early. Our aim was to identify female patients in whom PA was diagnosed after pregnancy and to seek for possible complications during pregnancy.

Design and method: Retrospective analysis of female patients with PA diagnosed and treated at our Department in the period from 2000 to 2017.

Results: We found 12 patients with PA (age at diagnosis 32.4 ± 4.6 years, hypertension duration 5.4 ± 3.1 years) suffering from hypertension 2.4 ± 1.7 years before pregnancy (5 patients had hypertension diagnosed during pregnancy). Three subjects were pregnant twice before the final diagnosis of PA was made. In 8 cases, pregnancy was terminated with caesarean section (3 times due to preterm preeclampsia and twice due to significantly increased blood pressure) and in 7 cases by spontaneous delivery (twice due to term preeclampsia). Preterm delivery occurred in 5 cases – the earliest one in the sixth month of gestation (4 times due to blood pressure related complications). Subsequent diagnosis of PA [(sometimes with a long delay (12 years))] was made on the basis of significantly low potassium values (2.6 ± 0.4 mmol/l; 2 subjects suffered even from hypokalemic paralysis) and hypertension (mostly moderate), elevated plasma/serum aldosterone (57.4 ± 19.4 ng/dl) and suppressed plasma renin activity (0.33 ± 0.1 ng/ml/h) or plasma renin 3.25 ± 1 ng/l). Eleven subjects underwent laparoscopic adrenalectomy [in all cases, diagnosis of a larger cortical adenoma (16.5 ± 5.7 mm) was made] and one subject was classified with bilateral hyperplasia according adrenal venous sampling. Operation has normalized blood pressure in 8 subjects and has improved significantly blood pressure control in remaining 3 subjects. One patient became pregnant after adrenalectomy and her pregnancy went uneventful.

Conclusions: Primary aldosteronism is associated with high rate of pregnancy-related complications. The most frequent one is preeclampsia, in some cases leading to preterm delivery. The best prevention of these complications is the early diagnosis of PA, in these particular hypertensive cases the awareness of hypokalemia.

THE LOCATION SPECTRUM OF THE ORIFICE OF RIGHT ADRENAL VEIN IN PATIENTS WITH PRIMARY ALDOSTERONISM: THE EXPERIENCE BASED ON 575 CASES OF ADRENAL VENOUS BLOOD SAMPLING

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Objective: To determine the distribution characteristics of the right adrenal vein orifices to improve the success rate of right adrenal vein catheterization in adrenal vein sampling (AVS).

Design and method: 575 patients with confirmed diagnosis of primary aldosteronism and undertook successful AVS in the Hypertension Center of People's Hospital of Xinjiang, China between January 2006 and October 2013 were consecutively enrolled. A SIM-ADS V4.2 medical imaging workstation was used to determine the location of the right adrenal vein orifices. The distribution characteristics of the right adrenal vein orifices were analyzed according to the markers in the spine.

Results: 1) the orifice of the right adrenal vein was located ranging from the middle edge of Th10 to the middle edge of Th12 in 457 patients (79.5%). Only 3.5% orifices were found between the upper edge of L1 to the middle edge of L1. 2) Distributions of the right adrenal vein orifices were significantly different based on gender, height, weight, BMI, and abdominal circumference, while the age did not show significantly different in groups.

Conclusions: The middle edge of Th10 to the middle edge of Th12 should be main target area for successful right adrenal vein catheterization when performing AVS.

A COMPARISON STUDY BETWEEN MOBIL-O-GRAPH AND SPHYGMOCOR DEVICES IN ASSESSING AORTIC SYSTOLIC PRESSURE AND PULSE WAVE VELOCITY IN PERITONEAL DIALYSIS PATIENTS

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Objective: The newly-introduced Mobil-O-Graph monitor has been validated against invasive and non-invasive measurements of aortic systolic pressure (aSBP) and pulse wave velocity (PWV) in the general hypertensive population. However, the validity of Mobil-O-Graph-derived measurements among patients on peritoneal dialysis (PD) remains unclear. The aim of this study is to compare oscillometric measurements of aSBP, heart-rate adjusted augmentation index (AIx75) and PWV obtained with the Mobil-O-Graph monitor (IEM, Germany) against tonometric measurements taken with the Sphygmocor device (ArtCor, Australia) in patients receiving long-term PD.

Design and method: A comparison study of 27 consecutive PD patients using the Sphygmocor-derived aSBP, AIx75 and PWV as reference standard. After a 10-min rest in the supine position, we applied the Mobil-O-Graph and Sphygmocor devices in a randomized order. Brachial BP recordings taken with a conventional sphygmomanometer were used to calibrate the Sphygmocor device.

Results: Measurements of aSBP, AIx75 and PWV obtained with the Mobil-O-Graph device did not differ from relevant measurements taken with Sphygmocor (120.5 ± 18.2 vs 124.4 ± 19.0 mmHg, $P = 0.438$ for aSBP, 27.0 ± 12.4 vs $24.5 \pm 10.6\%$, $P = 0.428$ for AIx75 and 9.5 ± 2.1 vs 10.1 ± 3.1 m/sec, $P = 0.397$ for PWV). The slight difference in estimation of aSBP is possibly explained by the numerically higher brachial SBP values used for the calibration of Sphygmocor (131.0 ± 20.6 vs 134.5 ± 19.7 mmHg, $P = 0.525$). Mobil-O-Graph-derived parameters were strongly and significantly correlated with paired measurements taken with Sphygmocor ($r = 0.889$, $P < 0.001$ for aSBP, $r = 0.816$, $P < 0.001$ for AIx75 and $r = 0.794$, $P < 0.001$ for PWV). Bland-Altman plots showed no evidence of asymmetry and wide range of agreement between the two devices.

Conclusions: This study suggests that oscillometric measurements of aSBP, AIx75 and PWV taken under static conditions with the Mobil-O-Graph monitor are closely related to tonometric measurements taken with the widely applied Sphygmocor device among patients on PD. The use of the Mobil-O-Graph monitor may facilitate the accurate determination of arterial stiffness indexes under ambulatory conditions in this population.

THE IMPACT OF OSTEOCALCIN, OSTEOPROTEGERIN AND OSTEOPONTIN ON ARTERIAL STIFFNESS IN CHRONIC RENAL FAILURE PATIENTS ON HEMODIALYSIS

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Objective: Background/Aims: This cross-sectional study was designed to assess the relationship between vascular stiffness (VS) and bone-related proteins involved in the development of arteriosclerosis in patients on regular hemodialysis (HD).

Design and method: Methods: 68 consecutive patients in stable clinical condition who received regular HD in the FMC Dialysis Center, Pécs were included. VS parameters (carotid-femoral pulse wave velocity – PWV, aortic augmentation

index – AIX) were determined by applanation tonometry (SphygmoCor, AtCor Medical, Sidney) and the routine laboratory test were completed with measurements of osteocalcin (OC), osteopontin (OP) and osteoprotegerin (OPG) by using commercially available ELISA kits. 35 healthcare workers served as controls.

Results: Results: In patients on regular HD PWV markedly increased and there was several-fold elevation in the interrelated bone-specific proteins (OC, OP, OPG). PWV was found to be independently associated only with OC (beta: -0.25, $p < 0.029$) and age ($r = 0.411$, $p < 0.000$), but risk factors for arterial calcification had significant impact on OC (systolic blood pressure, hsCRP, BMI), OPG (age, BMI) and OP (LDL-cholesterol).

Conclusions: Conclusion: Except for OC, our results failed to document direct association of vascular lesion with OP and OPG, therefore their high circulating levels may be an epiphenomenon or they may have counter-regulatory role to attenuate the uremic calcification process.

POSTER SESSION

POSTERS' SESSION PS08:

METABOLIC DISORDERS AND SLEEP APNOEA

EFFECT OF BETA BLOCKERS ON NOCTURNAL ARRHYTHMIAS AND HEART RATE VARIABILITY IN OBSTRUCTIVE SLEEP APNOEA PATIENTS

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Objective: To explore the effects of BB on nocturnal peri-apnoeic heart rate variability (HRV) and on arrhythmias in OSA patients.

Design and method: Arrhythmias and increased cardiovascular V are highly prevalent in patients with obstructive sleep apneas (OSA), possibly resulting in fatal events, as showed by the significant increase of sudden cardiac death and arrhythmias during sleep in OSA patients. Data concerning drug effects on this phenomenon are scarce and the use of beta blockers (BB) has been limited by the concern that they might lead to bradyarrhythmias. However, recent evidence suggests that BB mostly reduce rhythm accelerations with trivial influence on decelerations.

We enrolled 166 OSA patients (78 BB-treated and 88 BB-naïve), who performed cardiorespiratory polysomnography (PSG) between 2013 and 2015. Patients on antiarrhythmic therapy were excluded.

We analysed PSG-derived ECG traces for the assessment of arrhythmias. Moreover, through an ad hoc developed software, we performed a specific analysis of HRV associated with apnoeic events. We considered HR decelerations occurring during the apnoeic phase and accelerations during the post-apnoeic phase (the first five seconds after the resumption of breathing). Statistical analysis was performed with Mann-Whitney U test.

Results: We did not find any difference between BB-treated and BB-naïve groups concerning prevalence of nocturnal arrhythmias. HRV analysis showed a reduction of HR accelerations, expressed as RR length, during post-apnoeic phase in BB group (940.7 ± 121.4 msec BB-treated vs 897.8 ± 122.5 msec BB-naïve; $P = 0.040$). Moreover, BB-treated patients showed a smaller delta between HR decelerations/accelerations and mean HR during apnoeic phase (58.5 ± 28.5 vs 74.6 ± 40.2 msec; $P = 0.010$ and 75.0 ± 42.4 vs 96.7 ± 55.5 msec; $P = 0.018$, respectively). Finally, the delta between HR accelerations and decelerations was smaller in BB-treated group (133.5 ± 63.8 vs 171.3 ± 87.7 msec; $P = 0.010$).

Conclusions: BB therapy does not worsen apnoea-induced HR decelerations nor increase the risk of bradyarrhythmias, while reducing the frequency and magnitude of apnoea-induced HR acceleration.

Therefore, our study suggests that BB are safe and possibly advantageous in OSA patients, although further studies are needed to establish if in the long term they may have a role in reducing fatal events.

ASSOCIATION OF MEASURES OF SHORT- AND LONG-TERM GLYCAEMIC VARIABILITY AND GLYCAEMIC CONTROL WITH AMBULATORY BLOOD PRESSURE PATTERN IN TYPE 1 DIABETES MELLITUS

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Objective: Long-term glycaemic variability (GV) is associated with microvascular complications in patients with type 1 diabetes mellitus (T1DM). The exact mechanism underlying this association are unclear, but might be related to effects of GV on patients' blood pressure pattern.

This study was conducted to establish whether there is a relationship between glycaemic variability, glycaemic control and blood pressure pattern in patients with T1DM.

Design and method: Using 24 h ambulatory blood pressure monitoring (ABPM) (Spacelabs Healthcare Company Headquarters, Issaquah, WA), blood pressure patterns were assessed in 68 patients with T1DM for longer than 10 years who were free from known cardiovascular disease. Continuous glucose monitoring (CGM) (DexCom G4 Platinum (San Diego, CA) Continuous Glucose Monitoring (CGM)) for 7 days was used to estimate short-term GV (mean glucose CGM and standard deviation CGM). Long-term glycaemic control and GV were computed as mean and SD of HbA1c measurements over the last 5 and 10 years, respectively.

Results: Current HbA1c and HbA1c averaged over 5 and 10 years were positively correlated with systolic and diastolic blood pressure, and were higher in hypertensive patients.

SD of HbA1c over 5 years was negatively correlated with both systolic and diastolic nocturnal dipping. Mean glucose CGM correlated positively with nocturnal diastolic blood pressure.

Conclusions: In T1DM, both poorer short- and long-term glycaemic control are associated with higher diastolic and systolic blood pressure and a higher prevalence of hypertension. Long-, but not short-term GV is associated with lack of nocturnal dipping. Minimizing glycaemic fluctuations might therefore be important in preventing complications in patients with T1DM.

CENTRAL SLEEP APNEAS AND BLOOD PRESSURE DURING ACUTE EXPOSURE TO MODERATE ALTITUDE

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Objective: The association between obstructive sleep apnea (OSA) and both acute and chronic blood pressure (BP) increase is well established but it is not clear whether similar relationship exists for central sleep apneas (CSA). CSA are common in advanced heart failure but in these patients BP is usually low due to the effects of the disease and drugs used. Exposure to elevated altitudes may induce both CSA and BP increase. Aim of this study was to investigate the relationship between the presence of CSA and BP changes in healthy subjects acutely exposed to moderate altitude (MA).

Design and method: 44 healthy volunteers (mean age 41 ± 12 y, 16 males) residing at low altitude were transported to the altitude of 2035 m asl (Sestriere, Italy). During the first and second 24-hours of exposure they underwent in a random order 24-hour ambulatory BP monitoring (AND TM-2430) and cardiorespiratory sleep study (Embletta). The investigations were performed also at sea level (SL). Analyses involved pairwise comparisons of BP and cardiorespiratory variables between SL and MA as well as unadjusted and adjusted correlations between changes in these variables.

Results: Significant increases occurred at MA in 24-hour, daytime and night-time systolic/diastolic BP (difference vs. SL $5.36 \pm 8.4/3.55 \pm 4.6$, $4.98 \pm 11.0/2.98 \pm 6.7$, $4.97 \pm 10.8/3.75 \pm 7.0$ mmHg), respectively. No changes in the size of nocturnal BP fall were observed. In parallel, the rate of CSA increased (total Apnea Hypopnea Index: 1.55 vs 4.90, $p < .0001$; central apnea index: 0.75 vs 1.30, $p = 0.0004$; Oxygen Desaturation Index 1.50 vs 7.85, $p < .0001$ for SL vs MA, respectively), while mean nocturnal oxyhemoglobin saturation decreased ($95.7 \pm 1.5\%$ vs. $91.6 \pm 1.5\%$, $p < .001$). No correlations between BP changes and indices characterizing breathing during sleep were observed either in univariate analysis (all correlation coefficients < 0.2) or after considering possible confounders (age, sex, BMI).

Conclusions: At variance with what observed with OSA, presence and severity of CSA induced in healthy lowlanders by MA exposure seems unrelated to BP increase occurring in this condition, either during day or during night-time. This may depend either on pathophysiological differences between OSA and CSA or on inadequacies of indices characterizing breathing pattern during sleep.

MITOCHONDRIAL DYSFUNCTION IN MACROPHAGES LEADS TO SYSTEMIC INSULIN RESISTANCE, WHICH CAN BE IMPROVED BY GROWTH DIFFERENTIATION FACTOR 15

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Objective: Although epidemiological studies have linked adipose inflammation with obesity, the underlying mechanisms are incomplete. It is widely accepted that the interaction between insulin target cells and pro-inflammatory cytokines from accumulated macrophages is a cause of insulin resistance. Reduced mitochondrial capacity has been confirmed in patients with type 2 diabetes, and generally disposes macrophages toward a pro-inflammatory phenotype. However, little is known about decreased mitochondrial function and its effects on secreted macrophage factors which regulate macrophage polarization.

Design and method: To find out the soluble factors of macrophages in adipose inflammation, we have sought six transcriptomes from control macrophages and macrophages that were treated with rosiglitazone. We identified a secretory factor, GDF15, which is required for increased oxidative metabolism in M2-like macrophages stimulated with IL-4 and the PPAR γ agonist, rosiglitazone.

Results: Administration of GDF15 increased the oxidative function of macrophages, leading to their polarization into an M2-like phenotype, and reversed insulin resistance in ob/ob mice and in HFD-fed mice harboring myeloid-specific deletion of Crf1.

Reintroduction of GDF15-null macrophages into HFD-fed mice in which macrophages were depleted with clodronate treatment rendered them glucose intolerant. Moreover, GDF15 deficiency prevented improvement of insulin sensitivity in mice treated with the Th2 cytokine IL-4.

Conclusions: Thus, GDF15 is an important microenvironmental factor regulating phenotypic polarization of macrophages linked to improvement of systemic insulin resistance.

REDUCING CARDIOVASCULAR RISK IN PATIENTS WITH MORBID OBESITY AFTER BARIATRIC SURGERY

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Objective: The rate of obesity is rising logarithmically, especially morbid obesity (BMI > 40 kg/m²). Obesity is commonly associated with multiple conditions imparting adverse cardiovascular risk including, hypertension, dyslipidemia and diabetes. Severe obesity is generally refractory to lifestyle modification, including diet, exercise and pharmacological treatment.

The main objective of the study is to confirm the use of bariatric surgery as a means to reduce cardiovascular risk in severely obese patients.

Design and method: We examined 164 patients with morbid obesity (BMI > 40 kg/m²), they formed two groups. The first group included 81 patients who treated with diet, physical activity and drugs. The second group included 83 patients who using bariatric surgery (gastric bypass). Patients were examined before and after 6 months of treatment. All patients underwent clinical examination, determination of anthropometric parameters, measurement office SBP and DBP, daily monitoring of blood pressure, echocardiography, exploration indicators carbohydrate and lipid metabolism, definition cardiovascular risk with using scales SCORE, PROCAM, DRS, FRAMINGHAM.

Results: It was found that after 6 months of treatment weight loss was observed in both groups. A more significant decrease in body weight was observed in patients after surgical treatment (in first group by 4.6%, in the second group by 22.8%). Weight loss in patients after surgical treatment was associated with a greater decrease in blood pressure, improvement in the daily BP profile, changes in the structural and functional characteristics of the myocardium, decrease in the number of patients with LV hypertrophy, decrease LDL cholesterol, TG, glucose level, which was accompanied by a decrease in the number of patients with glucose intolerance (by 41.2%) and with diabetes (by 75%). Weight loss was associated with reducing the number of patients at very high risk on a scale SCORE by 78%, on a scale PROCAM by 100%, on a scale FRAMINGHAM by 95.6% and on a scale DRS by 13% in patients after surgical treatment.

Conclusions: Weight loss with the use of bariatric surgery contributes to the normalization of BP, reduces LV hypertrophy, has a positive effect on the lipid, carbohydrates profile and reduces cardiovascular risk.

RISK OF DEVELOPING TYPE 2 DIABETES ACCORDING TO BLOOD PRESSURE LEVELS AND PRESENCE OR ABSENCE OF HYPERTENSIVE TREATMENT: THE SAKU STUDY

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Objective: To investigate the risk of developing type 2 diabetes according to blood pressure (BP) levels and presence or absence of hypertensive treatment.

Design and method: Methods: This 5-year cohort study comprised 3,508 Japanese adults aged 30–74 years without diabetes who had undergone a medical checkup including a 75-g oral glucose tolerance test between April 2008 and March 2009 at Saku Central Hospital. Participants receiving antihypertensive treatment were categorized into controlled hypertension (<140/90 mmHg) or uncontrolled hypertension (140/90 mmHg or higher) groups. Participants not receiving antihypertensive treatment were categorized according to the definition of the Japan Society of Hypertension: optimal BP (less than 120/80 mmHg), normal BP (120–129/80–84 mmHg), high-normal BP (130–139/85–89 mmHg), grade I hypertension (140–159/90–99 mmHg) and grade II/III hypertension (160/100 mmHg or higher). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the incidence of type 2 diabetes as defined by the 75-g oral glucose tolerance test were estimated using multivariable-adjusted Cox proportional hazard models in reference to optimal BP.

Results: During the follow-up, 295 participants developed type 2 diabetes. Those with high-normal BP, grade I hypertension, grade II/III hypertension and uncontrolled hypertension were at significantly higher risk for developing type 2 diabetes, with HRs (95% CIs) of 1.53 (1.03–2.29), 1.53 (1.02–2.32), 2.19 (1.01–4.77) and 1.81 (1.10–2.99), respectively.

Conclusions: Conclusion: Compared with those with optimal BP, individuals with BP 130/85 mmHg or higher not receiving antihypertensive treatment and uncontrolled hypertensives with BP 140/90 mmHg or higher receiving antihypertensive treatment were at a significantly higher risk for developing type 2 diabetes.

THE INFLUENCE OF PREHYPERTENSION, HYPERTENSION AND HbA1c ON THE DEVELOPMENT OF TYPE 2 DIABETES MELLITUS IN PREDIABETES: THE KOREAN GENOME AND EPIDEMIOLOGY STUDY (KOGES)

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Objective: It has been reported that elevated blood pressure (BP) was significantly associated with the increased risk for type 2 diabetes mellitus (T2DM). However, there is still limited information about the influence of BP on the risk for T2DM across the level of glycated hemoglobin (HbA1c).

Design and method: In a cohort of the Korean Genome and Epidemiology Study (KoGES), 2,830 non-diabetic Korean adults with prediabetes defined by HbA1c level of 5.7–6.4% were followed-up for 10 years. Multivariate cox proportional hazards assumption was used to assess the risk for T2DM according to the baseline BP categories (normal, prehypertension and hypertension) and HbA1c level (low: 5.7–5.9% and high: 6.0–6.4%).

Results: The risk for T2DM significantly increased proportionally to BP categories (adjusted Hazard Ratio (HR); reference in normal BP, 1.32 [1.10–1.59] in prehypertension and 1.61 [1.35–1.92] in hypertension). Subgroup analysis indicated that individuals with high HbA1c had the higher risk for T2DM than individuals with low HbA1c regardless of BP. Additionally, combined presence of hypertension and high HbA1c had the highest risk for T2DM (adjusted HR: 3.82 [3.00–4.87]). In each systolic and diastolic BP level, the risk for T2DM significantly increased from systolic BP > 130 mmHg (adjusted HRs: 1.39 [1.15–1.71]) and diastolic BP > 80 mmHg (adjusted HRs: 1.30 [1.07–1.58]).

Conclusions: BP and HbA1c may be useful tools in identifying individuals with prediabetes more potentially predisposed to T2DM. Prospective studies should be considered to examine whether controlling BP actually lowers the risk for T2DM.

ASSOCIATION OF VITAMIN D WITH THE COMPONENTS OF THE METABOLIC SYNDROME IN GENERAL POPULATION WITHOUT CARDIOVASCULAR DISEASES. EVA STUDY

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Objective: To analyze the association of vitamin D with the metabolic syndrome (MS) and its components in general population without previous cardiovascular diseases.

Design and method: Cross-sectional study of general population without cardiovascular diseases. There were included 360 subjects between 35 and 75 years old (51% female), selected by random sampling stratified by age and gender groups using the Sanitary Card base of 4 urban health centers. The MS was defined following the recommendations of the National Cholesterol Education Program III. The circumference of the waist was measured with a tape measure, blood pressure with an OMRON tensiometer model M10-IT. Plasma glucose, lipid profile and 25 hydroxyvitamin D (25OH-D) were measured in blood.

Results: Mean values: age 56.8 ± 14.9 years (with MS = 65.4 ± 12.3 years, without MS = 55.5 ± 14.8 years, $p < 0.001$); 25OH-D 17.90 ± 7.34 ng/ml (with MS = 19.73 ± 8.03 ng/ml, without MS 26.70 ± 13.34 ng/ml, $p < 0.001$), without gender differences ($p = 0.129$).

Prevalence of MS and its components: 14.3% (14.9% women, 13.7% men). Blood pressure increased 44.1% (40.0% women, 48.8% men), HDL-cholesterol under 13.4% (14.0% women, 12.7% men), triglycerides increased 14.2% (10.8% women, 18.1% men), abdominal obesity 41.9% (49.7% women, 32.7% men) and glycemia increased 14.6% (11.9% women, 17.9% men). They had values 25OH-D < 20 ng/ml 33.6% (44.2% with MS, 31.8% without MS) ($p < 0.05$), 31% in women and 36% in men ($p > 0.05$). The presence of MS components had lower OH-D values, or $p < 0.05$ in HDL cholesterol, triglycerides and glycemia.

After adjusting by age and sex, we found positive correlation of 25OH-D with HDL-cholesterol ($r = 0.261$), negative with glycemia ($r = -0.165$), waist circumference ($r = -0.163$ and triglycerides ($r = -0.261$) No correlation with systolic and diastolic blood pressure.

In the logistic regression analysis after adjusting by age and sex, the subjects with MS had an OR = 1.690 (95% CI 0.913–3.130) of having figures of 25OH-D < 20 ng/ml ($p = 0.085$).

Conclusions: Subjects with MS have lower values of 25OH-D and correlates with HDL-cholesterol, triglycerides, glycemia and waist circumference. Subjects with MS have 1.7 times more risk of having 25 OH-D < 20 ng/ml.

ESTRADIOL AND LEPTIN OVEREXPRESSION HAVE INDEPENDENT MODES OF ACTION ON DECREASED FOOD INTAKE AND BODY WEIGHT IN MALES RATS

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Objective: We recently reported that male compared with female rats are less responsive to long-term central leptin overexpression, as assessed by decreased food intake and delta body weight. Moreover, males were more susceptible to development of leptin resistance than females suggesting that either male hormones mitigate or female hormones exacerbate leptin responses or both. To address the potential role of estradiol, we examined the treatment of leptin with or without estradiol on body weight parameters in male rats.

Design and method: To this end, we centrally delivered a viral vector to over-express either leptin or green fluorescence protein (GFP) into male rats that were simultaneously treated with either estradiol (25 mg/kg; S.C., daily) or vehicle in a two x two design. We examined chronic changes in food intake (FI), BW, and body composition over 26 days.

Results: BWs in both Leptin-vehicle and GFP-Estradiol were reduced compared with GFP-vehicle but more sustained in Leptin-Estradiol reminiscent of the pattern in females. Changes in FI were unique to each treatment, with a rapid decrease in Leptin-vehicle followed by gradual renormalization typical of leptin-induced leptin resistance. In contrast, the GFP-Estradiol decrease in FI was of lower amplitude ($P < 0.001$) but sustained over the 26 days ($P < 0.003$). The Leptin-Estradiol group was mostly additive but with a delay in leptin resistance typical of the pattern observed in female rats. Decreased body fat by TD-NMR was unique to each treatment paralleling FI. Phosphorylation of STAT3 (P-STAT3) was examined at death. No exogenous leptin was administered, thus detected P-STAT3 was due to central overexpressed leptin. P-STAT3 was greater in both leptin groups compared with GFP, but there was no difference between Leptin-vehicle and Leptin-Estradiol.

Conclusions: In conclusion, these data suggest that leptin and estradiol both decrease FI and BW, with the pattern of Leptin-Estradiol reminiscent of that observed in females. Furthermore, the estradiol-induced decrease in FI & BW does not involve P-STAT3. These data suggest that estradiol may be one factor in the increased leptin response and the mitigated leptin resistance observed in female rats.

INFLUENCE OF METABOLIC SYNDROME ON RENAL FUNCTION IN PATIENTS WITH HYPERTENSION

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Objective: Metabolic syndrome (MetS) is a condition linking insulin resistance, dyslipidemia, hyperglycemia, and hypertension that increases the risk of developing diabetes, cardiovascular disease, and subsequent cardiovascular morbidity and mortality. Hypertension is the key component of the metabolic syndrome. Aim of this study to estimate the impact of MetS on renal function in patients with hypertension.

Design and method: 312 hypertensive patients without history of chronic kidney disease (CKD) or cardiovascular disease at baseline were analyzed. Participants were categorized into two groups based on the presence of MetS at baseline. Group-1, 218 patients with MetS and Group-2, 94 hypertensives without MetS. Mean age of the patients was 52.4 ± 12.4 years, male-52%. Incident CKD was defined as eGFR < 90 ml/min per 1.73 m² over 3 years. Metabolic syndrome was diagnosed according to the "Harmonized definition of the MetS".

Results: During the 3-year follow-up period, CKD developed in 27 subjects (12.5%) in the Group-1 and in 7 subjects (7.5%) in the Group-2. Compared to subjects without MetS, the odds ratio (OR; 95% confidence interval, CI) of incident CKD in those with MetS was 1.29 (1.09–1.52) after controlling for confounding factors. The risk of decline of eGFR was also higher in hypertensive patients with MetS than those without MetS (OR: 1.14, 95% CI: 1.02–1.27).

Conclusions: Metabolic syndrome is the risk factor for the development of CKD and patients with MetS should be treated more aggressive with reno-protective drugs.

EMPAGLIFLOZIN MAY ATTENUATE ADIPOSE TISSUE INFLAMMATION AND ARTERIAL STIFFNESS IN NORMOTENSIVE TYPE 2 DIABETICS

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Objective: Adipose tissue inflammation impairs arterial compliance at early stages of type 2 diabetes mellitus (T2DM). We aimed to assess the impact of empagliflozin as compared to sitagliptin on aortic stiffness and serum adiponectin (ADPN), an adipocytokine with insulin-sensitizing, anti-inflammatory and anti-atherogenic properties, in normotensive patients with T2DM.

Design and method: In this 24-week, randomized, open, parallel-group, controlled trial, 106 Caucasian normotensive T2DM subjects, inadequately controlled on metformin monotherapy (at least 1700 mg daily), were randomly assigned to receive 25 mg empagliflozin ($n = 54$) or 100 mg sitagliptin ($n = 52$) orally once daily. Arterial stiffness was assessed as carotid-femoral pulse wave velocity (PWV) measured via Complior (Artech Medical), whereas a sandwich enzyme-linked immunosorbent assay was employed for ADPN measurement. Office blood pressure (BP) was measured using a validated automated sphygmomanometer (Omron 705IT). Three measurements were taken at a 1-minute interval and were averaged for a single systolic/diastolic BP value.

Results: In the entire study population, mean age was 50.4 years, diabetes duration 6.1 years, baseline HbA1c 7.7%, fasting plasma glucose [FPG] 159 mg/dl, body mass index 30.2 ± 4.1 kg/m², systolic/diastolic BP $132.2/82.9$ mmHg, glomerular filtration rate 89.9 mL/min/1.73m², PWV 13.0 ± 2.1 m/s and ADPN 6.0 ± 1.8 mg/ml at baseline. After 24 weeks significant changes were observed in HbA1c and FPG with both empagliflozin (-0.72% and -25.3 mg/dl, respectively) and sitagliptin (-0.70% and -23.2 mg/dl, respectively; $p < 0.001$ for all comparisons, between-group differences being non-significant), whereas hypoglycemia rates were comparable (2.1% with empagliflozin and 1.9% with sitagliptin; $p = 0.494$). BP values decreased with empagliflozin (-4.9 ± 0.9 mmHg [$p < 0.05$] systolic -2.4 ± 0.4 mmHg [$p < 0.05$] diastolic), but not with sitagliptin (-1.3 ± 1.0 mmHg [$p = 0.672$] systolic -0.1 ± 0.5 mmHg [$p = 0.848$] diastolic). Body weight declined by 3.8 kg ($p < 0.001$) with empagliflozin and 0.5 kg ($p = 0.082$) with sitagliptin ($p < 0.001$ for between-group difference). PWV decreased (-3.1 ± 0.3 m/s [$p < 0.001$] with empagliflozin and -1.6 ± 0.4 m/s [$p < 0.05$] with sitagliptin) and ADPN increased (3.3 ± 0.8 [$p < 0.001$] with empagliflozin and 1.3 ± 0.3 mg/L [$p < 0.05$] with sitagliptin), the differences being greater with empagliflozin ($p < 0.01$ for both comparisons).

Conclusions: Addition of empagliflozin to metformin may attenuate adipose tissue inflammation and arterial stiffness to a greater extent than sitagliptin in normotensive patients with T2DM.

EFFECTS OF LOSARTAN AND METFORMIN ON VASCULAR PROSTANOIDS RELEASE IN RATS IN A HIGH-FAT DIET

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Objective: High-fat diet in rats is an experimental model that resembles human metabolic syndrome (MS). This multifactorial alteration is related to hypertension. Metformin (Mf, antidiabetic drug used in type 2 diabetes and MS treatment); and losartan (L, an angiotensin 1 receptor antagonist) play an important role in the regulation of vascular tone. Prostanoids (PR) are endogenous substances derived from arachidonic acid via cyclooxygenases with vasoactive effects. The aim of this study was to analyze the effects of Mf and L on prostanoids (PR) release by the mesenteric vascular bed (MVB).

Design and method: Six groups (n = 6) of male Sprague-Dawley rats were studied during 8 weeks: Control (C), standard diet (SD) and tap water (W) to drink; HF diet (HF), 50% (w/w) bovine fat added to SD and W; C + Mf (CMf), SD + 500 mg/Kg/day Mf in W; C + L (CL), SD + 30 mg/Kg/day L in W; HF + Mf (HFMf) 500 mg/Kg/day Mf in W; HF + L (HFL) 30 mg/Kg/day L in W. MVBs were removed and incubated and the released PR measured by HPLC. Adiposity index is calculated: body weight/MVB weight x 100.

Results: HF diet increased systolic BP (SBP, mmHg, HF: 145 ± 5 vs. C: 118 ± 2 , $p < 0.01$); MVB adiposity index (%), HF: 1.7 ± 0.1 vs. C: 0.9 ± 0.04 , $p < 0.01$); and the release of vasoconstrictor PR thromboxane (TX) B₂, stable metabolite of TXA₂, (ng PR/mg of tissue, HF: 117 ± 6 vs. C: 66 ± 2 , $p < 0.001$); and prostaglandin (PG) F₂alpha (ng/mg, HF: 153 ± 9 vs. C: 88 ± 3 , $p < 0.001$). In HFM and HFL groups, M and L treatment prevented the increases of SBP (HFM: 127 ± 2 , HFL: 111 ± 3 vs. HF, $p < 0.001$ and $p < 0.01$), TXB₂ release (ng PR/mg of tissue, HFM: 65 ± 12 , HFL: 66 ± 7 vs. HF, $p < 0.05$ and $p < 0.01$); and PGF₂alpha (ng PR/mg of tissue, HFM: 99 ± 13 , HFL: 90 ± 7 vs. HF, $p < 0.01$ and $p < 0.05$). Meanwhile Mf also prevented the increase of MVB adiposity index (%), HFM: 1.3 ± 0.2 vs. HF, $p < 0.05$).

Conclusions: Treatments with Mf and L could exert beneficial effects on the vascular system improving endothelial dysfunction by preventing the increase of vasoconstrictor PR in MVB. In addition, Mf prevents adiposity increase.

UTILITY OF WAIST-TO-HEIGHT RATIO AS AN INDICATOR OF CARDIO-METABOLIC RISK COMPARED WITH ROUTINELY USED ADIPOSITY INDICES

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Objective: The tools used to identify obesity, a common risk factor for hypertension and other cardio-metabolic abnormalities, are not always optimal in all populations; therefore, the utility of other instruments are constantly being assessed. This study aims to compare the utility of waist-to-height ratio (WHtR) with commonly used adiposity indices of body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) to identify cardio-metabolic diseases including hypertension in 25–74-year-old black residents in Cape Town.

Design and method: This cross-sectional study, stratified for age and gender, determined cardio-metabolic abnormalities by administered questionnaires, clinical measurements and biochemical analyses, including oral glucose tolerance tests. Correlations between BMI, WC, WHR and WHtR with cardio-metabolic components were examined. Age- and gender-adjusted logistic regression analyses determined the associations of obesity by these adiposity indices with cardio-metabolic abnormalities.

Results: The study comprised 392 men and 707 women. Age-standardised prevalence (95% confidence interval (CI)) for men and women, respectively, were: hypertension: 39.3% (95% CI: 33.4–45.2) and 39.4% (95% CI: 35.5–43.4), diabetes: 11.3% (95% CI: 8.0–14.6) and 14.7% (95% CI: 12.1–17.3). Compared with other adiposity indices, WHtR in men correlated most closely with fasting (0.360) and 2-hour (0.388) glucose levels, total cholesterol (0.267), low-density lipoprotein cholesterol (LDL-C) (0.351) and triglycerides (0.400). WHR and WC, respectively, correlated the best with systolic BP (0.310) and diastolic BP (0.287) in men. In women, WHtR correlated the best with systolic BP (0.254) and diastolic BP (0.287). Of the adiposity indices, raised WHtR was most closely related to hypertension (OR 1.61, 95% CI: 1.07–2.42), hypercholesterolaemia (OR 1.72, 95% CI: 1.04–2.83) and raised LDL-C (OR 2.46, 95% CI: 1.70–3.55), while raised WC was most strongly associated with diabetes (OR 4.27, 95% CI: 2.39–7.62),

low high-density lipoprotein cholesterol (OR 2.84, 95% CI: 1.90–4.26) and hypertriglyceridaemia (OR 3.60, 95% CI: 2.03–6.40).

Conclusions: Compared with other adiposity indices, the better correlation of WHtR with many cardio-metabolic components, particularly in men, and the stronger association of raised WHtR with hypertension, hypercholesterolaemia and raised LDL-C supports the utility of WHtR in routine assessments of adiposity in this population, which may improve the identification of cardio-metabolic risk in black South Africans.

COMBINED THERAPY WITH TELMISARTAN AND AMLODIPINE ON BLOOD PRESSURE, ECHOCARDIOGRAPHIC PARAMETERS AND MICROALBUMINURIA IN PATIENTS WITH METABOLIC SYNDROME

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Objective: Patients with hypertension (H) with metabolic syndrome (MS) have a high risk of cardiovascular events. The aim of the study was to assess the effects of combination therapy with Telmisartan (L) and Amlodipine (A) on BP, left ventricular (LV) hypertrophy, LV diastolic function, and microalbuminuria in patients with hypertension and MS.

Design and method: Sixty four patients with moderate to severe hypertension and metabolic syndrome were provided to T (80 mg) + A (5 mg) in combination once a day (31 males and 33 females). The presence of metabolic syndrome was diagnosed by "Harmonized" Metabolic Syndrome definition. Anthropometric, laboratory and instrumental measures was performed at baseline and after 12 weeks of therapy. Statistical comparisons were performed by 2 tailed Student's t test for quantitative parameters.

Results: All patients completed the study without showing intolerance or side effects to the drugs. At the end of the study therapy normalized BP (from $178.26 \pm 9.1/109.3 \pm 7.2$ mmHg to $127.8 \pm 6.2/80.2 \pm 4.8$ mmHg, $p < 0.01$) in 95.3 % of patients. LV mass index reduced from 162.0 ± 9.4 to 137.8 ± 5.0 g/m², ($p < 0.01$) in 79.7 % of patients. At the end of the study E/A ratio increased from 0.87 ± 0.04 to 1.42 ± 0.05 ($p < 0.01$) in 82.8 % of patients. IVRT has been decreased from 108.4 ± 8.5 to 77.3 ± 5.2 msec ($p < 0.01$) in 81.2% of patients. Deceleration time passed from 170.6 ± 7.2 to 134.1 ± 4.0 msec ($p < 0.05$) in 78.1% of patients. Microalbuminuria decreased from 56.6 ± 12.5 to 35.4 ± 10.6 mg/l ($p < 0.05$) in 84.3 % of patients.

Conclusions: These data suggest significant antihypertensive and nephroprotective efficacy of the combination of T 80 mg + A 5 mg. Combination therapy with T + A has been demonstrated positive effect on the echocardiographic indexes of the heart by reducing LV hypertrophy and improving LV diastolic function, and renal function by reducing albuminuria in patients with moderate to severe hypertension and metabolic syndrome.

CHEMERIN IN EXTREMELY OBESE HYPERTENSIVE AND NON-HYPERTENSIVE PATIENTS AFTER BARIATRIC SURGERY

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Objective: Extreme obesity is associated with subclinical inflammation, which is important for development of several obesity-associated complications. Increased level of chemerin protein in obesity may influence on inflammatory cascades. The objective of the study was to assess changes of chemerin levels after bariatric surgery among hypertensive and normotensive subjects.

Design and method: Study population consisted of patients with severe obesity who met the eligibility criteria and underwent bariatric surgery (sleeve gastrectomy and Roux-en-Y gastric bypass). Body mass index (BMI), ambulatory blood pressure (Spacelabs 90207), and laboratory investigations (glucose, cholesterol, leptin, adiponectin, insulin, chemerin, hsCRP) were measured before and six months after bariatric surgery. Data were analyzed in two groups: I—patients with diagnosis of hypertension and II—normotensive subjects.

Results: Data from 49 patients (mean age 41.0 ± 12.0 years, 40% men) were analyzed. Hypertensives (n = 30) were older (44.4 ± 11.4 vs 36.8 ± 11.8 years, $p = 0.02$), presented higher values of systolic blood pressure (SBP; 124.8 ± 12.2 vs 118.0 ± 8.7 mmHg, $p = 0.02$) and insulin levels (40.7 ± 15.0 vs 31.2 ± 13.9 mIU/ml, $p = 0.01$), but lower levels of adiponectin (3461 ± 1728 vs 4605 ± 2329 pg/ml, $p = 0.04$) than normotensives. However, initial values of BMI, diastolic BP and other laboratory parameters were similar in both groups. BMI diminished similarly in both groups after surgery. SBP decreased in both groups but remained

significantly higher in hypertensives. Chemerin levels decreased significantly in both groups, but hsCRP diminished only in the normotensive group. Adiponectin and insulin levels were similar in both groups after surgery.

Conclusions: Modulation of immunity after bariatric surgery changes in different way in hypertensive and non-hypertensive obese patients.

RELATIONSHIP BETWEEN OBSTRUCTIVE SLEEP APNOEA AND ERECTILE DYSFUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION

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Objective: The aim of our study was to determine the impact of obstructive sleep apnea (OSA) on erectile dysfunction (ED) in patients with arterial hypertension (AH). Currently, ED is evaluated as a predictor of cardiovascular diseases.

Design and method: We included 71 men (mean age 47,9 ± 9,2 years) with AH, receiving antihypertensive therapy (except b-blockers), OSA and ED (according to the IIEF-5 questionnaire), not suffering from coronary artery disease and diabetes mellitus. All patients underwent sleep study and 21 patients underwent intracavernous pharmacodopplerography (IPD) with alprostadil, which included an assessment of the erection degree (Er scale, from 0 to 5), penile blood flow parameters such as peak systolic velocity (PSV), end diastolic velocity (EDV) and a resistive index (RI). The results of IPD were compared with the IIEF-5 questionnaire.

Patients characteristics (n=71)

Parameters	Mean / Median
Weight, kg	99,2 [75; 127]
BMI, kg/m ²	30,8±2,8
SBP, mm Hg	147,4 [120; 180]
DBP, mm Hg	87,9 [70; 110]
AHI/h	25,4±20,8
ODI/h	22,2±20,8
PSV, cm/sec	38,6 [18,8; 62,3]
EDV, cm/sec	9,2 [4,3; 18,7]
RI	0,79 [0,52; 1,0]

Results: Statistical analysis showed no correlation between the severity of ED according to IIEF-5 and IPD ($r = .42$, $p = .07$), as well as no correlation has been shown between the severity of OSA and ED by IIEF-5 ($r = .20$, $p = .10$). 21 patients who underwent IPD had mean AHI 25,6 ± 18,1/h; mean ODI – 21,6 ± 20,8/h; mean SBP was 146,4 ± 12,1 mm Hg and mean DBP – 8,6 ± 8,7 mm Hg. We found statistically significant correlation between parameters of OSA and severity of ED, such as apnea/hypopnea index (AHI) and Er 0–5, PSV and RI ($r = -.50$, $p = .02$; $r = -.52$, $p = .02$; $r = -.67$, $p = .0009$ respectively); oxygen desaturation index (ODI) with PSV and RI ($r = -.61$, $p = .003$; $r = -.60$, $p = .003$ respectively). A statistically significant correlation between the quality of penile blood flow and the systolic blood pressure (SBP) was revealed too ($r = .49$, $p = .02$).

Conclusions: There is a significant correlation between the level of SBP, the severity of OSA and ED according to objective method of its evaluation.

PREVALENCE OF ABDOMINAL OBESITY IN RUSSIAN FEDERATION AND ITS RELATIONSHIP WITH ARTERIAL HYPERTENSION AND OTHERS COMORBIDITIES. BY THE DATA OF EPIDEMIOLOGICAL STUDY ESSE-RF

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Objective: Data from cross-sectional epidemiological study ESSE-RF (Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of Russian

Federation) of 21817 adults 25–64 y.o. stratified by age and sex from 12 regions RF (females - 13483, males - 8334). Final analysis included 20817 (average age 49 ± 11,62, females – 64,77%, males – 35,27%).

Design and method: We used the systematic stratified multistage random sampling creating by the territorial principle of method by Keesh. Abdominal obesity (AO) was defined by cut-off of > 80 cm in women and > 94 cm in men. General obesity criterion was taken like BMI > 30.0 kg/m². Data related to regions, comorbidity, socio-economic status, general health assessment, stress influence, education, pernicious habits, physical activity. Calculation was done with software STATISTICA 10.0, SPSS 14.0

Results: AO prevalence in RF was 55,02% (women – 61,83%; men – 44,0 %). The proportion BMI obesity was significantly lower in all regions (Tabl.1). The number of people with AO increased with age, both among men and women ($p < 0.0001$). There were a significant relationship of AO with following diseases ($p < 0.0001$ for all): arterial hypertension–64,4%, angina pectoris–15,18%, myocardial infarction–2,94%, stroke–2,97%, osteochondrosis–23,43%, pathology of the gastrointestinal tract–42,1%, ulcer of stomach and/or duodenal–13,63%, chronic bronchitis–18,54%, bronchial asthma–3,92%, rheumatoid arthritis–8,74%, cardiac rhythm disturbances–24,22%, kidney diseases–22,88%, thyroid diseases–15,91%, oncological diseases–4,22%, diabetes–7,43% (types 1 & 2). The number with AO were greater in poor/very poor families and in groups individuals with secondary special education and below ($p < 0.0001$ for all). Persons with AO were more likely to notice the influence of obesity, low physical activity, nutrition, stress on their health ($p < 0.0001$ for all). People without obesity smoked more often ($p < 0.0001$). We didn't find close relationship between obesity and alcohol consumption.

Tab.1. Prevalence of Abdominal obesity and BMI obesity in regions of Russian Federation by the data of epidemiological study ESSE-RF.

	Abdominal obesity, %	Obesity by BMI, %
Krasnoyarsk	56,07	32,98
Vladivostok	54,64	31,02
Volgograd	51,30	28,34
Vologda	46,31	28,21
Voronezh	67,00	44,49
Ivanovo	53,95	34,85
Kemerovo	63,66	35,62
Samara	43,03	22,56
St. Petersburg	57,95	27,34
Orenburg	52,54	30,59
Tomsk	58,94	31,13
Tyumen	50,21	40,65
the Republic of North Ossetia – Alania	56,90	38,78

Conclusions: Study results showed high prevalence of women abdominal obesity in all regions of RF. In most cases, their socioeconomic status was worse, they had comorbidities more often than people without of obesity. The prevalence of abdominal obesity was rather higher than obesity by BMI and people with abdominal obesity need more attention.

IMPACT OF OBESITY ON THE EFFECTIVENESS OF TREATMENT WITH A SINGLE-PILL COMBINATION OF PERINDOPRIL ARGININE/INDAPAMIDE. DATA ANALYSIS OF THE RUSSIAN PROGRAM, FORSAGE

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Objective: Efficacy of a single-pill combination of perindopril arginine/indapamide (Per/Ind) at full dose (10 mg/2.5 mg) in patients with arterial hypertension, depending on the initial body mass index (BMI).

Design and method: 1963 treated, uncontrolled hypertensive patients from the FORSAGE study (29 cities of the Russian Federation). These patients were divided into three groups according to their baseline BMI: 1) Normal BMI < 25 kg/m² (16.6% of patients), 2) Overweight with 25 < BMI < 30 kg/m² (48.7%) and 3) Obese with BMI > 30 kg/m² (34.7%); they were switched from a previously ineffective combined bi-therapy to Per/Ind single-pill combination at full dose (10 mg/2.5 mg). The use of beta-blockers in case of concomitant CAD was authorized. Patient evaluation was performed at 2 weeks, 1 month, and 3 months.

Results: Patients (mean age 59–60 y) were mainly women (64%). Most of them had a history of heart failure (73%) and 26% had angina pectoris. Patients who were overweight (59% women) or obese (72% women) presented with higher baseline values of total cholesterol and creatinine and had a decreased glomerular filtration rate, especially in the group with BMI > 30 kg/m². Left ventricular hypertrophy (85%), diabetes mellitus (22%), stress angina (31%), heart failure

(78%), history of strokes (8%), hypertensive crises (35%), and hospitalizations for hypertensive crises (18%) were more often detected in the group of obese patients. The highest values of blood pressure (BP) were observed in the group of obese patients. Changes in BP and rates of target BP achievement are presented in Table 1.

Patient groups	<25 kg/m ²	25-30 kg/m ²	P1	≥30 kg/m ²	P2	P3
SBP ± SD at baseline (mmHg)	168.1±0.5	169.8±0.3	0.0009	171.2±0.3	0.0009	0.0001
DBP ± SD at baseline (mmHg)	97.3±0.3	98.1±0.2	0.0226	98.8±0.2	0.0001	0.0164
SBP ± SD at 3 months (mmHg)	128.8±0.5	130.0±0.3	0.0233	131.8±0.3	0.0001	0.0001
DBP ± SD at 3 months (mmHg)	78.5±0.3	79.3±0.2	0.0237	80.1±0.2	0.0001	0.0041
SBP/DBP decrease in 3 months (mmHg)	39.3/18.8	39.8/18.8		39.4/18.7		
Rates of BP target achievement (<140/90 mmHg) after 3 months (%)	81.8±1.8	78.1±1.1	0.0839	70.9±1.3	0.0001	0.0001

Table 1: Blood pressure changes in patients treated with a single-pill combination of Per/Ind (10 mg/2.5 mg) by body mass index.

P1, significance of the difference of overweight vs. normal BMI group;

P2, significance of the difference of obese vs. normal BMI group;

P3, significance of the difference of obese vs. overweight group.

Data presented are mean ± SD

Conclusions: Switching from a previously ineffective anti-hypertensive therapy to a single-pill combination of perindopril arginine/indapamide at full doses significantly decreased BP and resulted in high rates of target BP achievement in all BMI groups, including in more than 70% of obese patients, usually the most difficult to control with more co-morbidities and risk factors.

POTENTIAL RELATION BETWEEN SERUM LIPOPOLYSACCHARIDE BINDING PROTEIN LEVELS AND NOCTURNAL BLOOD PRESSURE VARIABILITY IN MIDDLE AGED HYPERTENSIVE MALES

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Objective: Stability of the nocturnal arterial pressure is markedly affected by normal sleep with differential autonomic regulation during the different sleep stages. Nevertheless, the mechanism behind the association of sleep disruption and nocturnal blood pressure variability is still unknown in hypertensive population. Lipopolysaccharide binding protein (LBP) has been applied as a surrogate biomarker for gut-intestinal permeability in clinical, and may disrupt sleep architecture and balance of parasympathetic and sympathetic activity in human. We hypothesized swing of nocturnal arterial blood pressure might be followed by alteration of serum LBP levels.

Design and method: 39 primary hypertensive males were recruited with mean age 42.46 years, blood pressure 130.51/87.74mmHg and BMI 27.26 kg/m². All patients were confirmed to have no obstructive sleep apnea (defined by AHI < 10event/hour, average AHI 4.22events/h) via polysomnography. BPV was assessed by standard deviation (SD) and coefficient of variability (CV = SD/

mean × 100%) of BP measurements from 24-h ambulatory blood pressure monitoring. Subjects were divided into two groups via the median of LBP and stage 1 sleep (N1%). Sleep architecture was assessed by polysomnography. Serum LBP, Interleukin-1b (IL), IL-6, and Tumor necrosis factor-α (TNF-α) were measured by commercial laboratories using sandwich-type enzyme immunoassay kit.

Results: Hypertensive males with higher serum LBP showed significantly higher inflammatory status as assessed by IL-1b, and significantly prolonged sleep stage 1 than did those with lower LBP. Hypertensive males with higher circulating LBP levels showed significantly higher 24 h mean arterial pressure CV, and nocturnal SBPSD, DBPSD, mean arterial pressure SD, SBPCV, DBPCV and nocturnal mean arterial pressure CV, compared with those with lower circulating LBP levels. Subjects with prolonged N1% also showed similar results while compared to their counterparts. A significant correlation was observed between 1) serum LBP levels and nocturnal systolic and diastolic BPSD and nocturnal mean arterial pressure SD; 2) serum LBP levels and nocturnal systolic and diastolic BPCV and mean arterial pressure CV, and remained significant even after adjusting for age, AHI, BMI and mean BP.

Conclusions: increased serum LBP, prolonging N1%, might aggravate nocturnal BPV. Elevation in serum LBP might a potential predictor for nocturnal BPV in this middle-aged hypertensive males.

INCREASED EPICARDIAL ADIPOSE TISSUE AND ARTERIAL STIFFNESS, USING CARDIO-ANKLE VASCULAR INDEX IN SLEEP APNOEA

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Objective: OBJECTIVES: To clarify the relationships between severity of obstructive sleep apnea (OSA) and epicardial adipose tissue (EAT), in addition to discusses for arterial stiffness shown by cardio-ankle vascular index (CAVI).

Design and method: Consecutive 110 Japanese patients with obstructive sleep apnea who had CAVI test and computed tomography (CT) were included in this study. EAT, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were measured and assessed for severity of OSA.

Results: Neither the body mass index nor SAT showed any co-relation with severity of OSA. But there were significant positive co-relation between severity of OSA and VAT or EAT ($r = 0.17$ $p < 0.05$, $r = 0.18$ $p < 0.05$ respectively). In addition, severity of OSA and EAT were selected as contributing factor for CAVI.

Conclusions: These data suggested that OSA could be induced by visceral obesity. OSA could be invasive factor for arterial stiffness. EAT may have increased through visceral obesity, intermitted hypoxia and reoxygenation and increasing afterload such as arterial stiffness shown by CAVI. Suitable diet and sleep apnea treatment could be effective to reduce cardiac pericardial fat.

POSTER SESSION

POSTERS' SESSION PS09:

CEREBROVASCULAR DISEASE

COGNITIVE DYSFUNCTION IN UNTREATED MIDDLE-AGED PATIENTS WITH UNCOMPLICATED GRADE 1-2 ESSENTIAL ARTERIAL HYPERTENSION

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Objective: Hypertension is a risk factor for mild cognitive deterioration and vascular dementia. In recent years, neuropsychology has recognized the impact of vascular pathology on cognitive function, as well as the importance of early detection and prevention. The purpose of the present study was to identify the effect of vascular pathology—and more specifically, hypertension—on cognition in untreated middle-aged patients with uncomplicated grade 1–2 essential arterial hypertension compared to normotensive controls.

Design and method: 50 healthy volunteers (17 men, mean age 47.3 ± 5.5 years) and 103 hypertensive patients (46 men, mean age 51.2 ± 5.2 years) were recruited. All subjects underwent 24-hours blood pressure monitoring. Neuropsychological assessment included Montreal Cognitive Assessment (MoCA), Trail Making test (part A and part B), Stroop Color and Word Test, verbal fluency test, 10-item word list learning task.

Results: Hypertensive patients had lower mean MoCA score (28.4 ± 1.4 points vs 28.9 ± 1.3 points, $p = 0.02$), worse performance in TMT B (119.4 ± 42.5 vs 105.5 ± 31.4 ; $p = 0.03$) and higher TMT difference score (80.7 ± 42.5 vs 62.9 ± 27.9 ; $p = 0.002$), compared to controls. Significant correlations were found between mean nighttime pulse pressure and TMT B – TMT A score ($r = 0.261$; $p < 0.01$).

Conclusions: Untreated middle-aged patients with uncomplicated grade 1-2 essential arterial hypertension have worse task switching, compared to normotensive controls.

REDUCED WHITE MATTER INTEGRITY AND CEREBRAL PERFUSION AS POSSIBLE NEW EARLY MARKERS OF BRAIN DAMAGE IN PATIENTS WITH ESSENTIAL ARTERIAL HYPERTENSION

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Objective: New markers of brain damage (apart from white matter hyperintensities (WMH) must be found to optimize the patient management. Arterial spin labeling (ASL), a noninvasive perfusion sequence, allows to detect changes in cerebral blood flow (CBF) in the early stages of the disease. Diffusion tensor imaging (DTI) has been proposed as a marker of cerebral small vessel disease. The aim of this study was to examine whether the fractional anisotropy (FA) and CBF values changed in untreated middle-aged patients with uncomplicated grade 1-2 essential arterial hypertension compared to controls.

Design and method: 41 healthy volunteers (15 men, mean age 46.2 ± 4.6 years) and 41 untreated hypertensive patients (18 men, mean age 50.3 ± 6.7 years) were recruited. All subjects underwent brain MRI (MAGNETOM Skyra 3.0T, Siemens AG, Germany). Fazekas scale was used to quantify the amount of WMH. ASL CBF maps were used to calculate the perfusion defects. FA was used as a DTI index. Regions of interest included splenium and genu of corpus callosum, inferior frontal gyrus, centrum semiovale, lentiform nucleus, hippocampus, entorhinal cortex, parahippocampal white matter, superior and inferior longitudinal fasciculus, cingulate gyrus, thalamus, insula, corona radiata, optic radiation.

Results: WMH were found in 4 healthy controls (9.7%, Fazekas 1) and in 22 hypertensive patients (53.7%, Fazekas 1 in 20 patients (48.8%) and Fazekas 2 in 2 patients (4.9%), $p = 0.0005$). Hypertensive patients had lower CBF in the cortical plate of both frontal lobes of the brain (37.3 ± 6.7 vs 45.3 ± 3.5 ml/100 g/min;

38.02 ± 6.2 vs 45.8 ± 3.2 ml/100 g/min, $p < 0.0001$). Hypertensive patients with and without WMH had lower CBF compared to controls ($p < 0.0001$). Hypertensive patients had lower FA in splenium of corpus callosum ($p = 0.003$) and left inferior frontal gyrus ($p = 0.0003$). Hypertensive patients with WMH had lower FA in left inferior frontal gyrus ($p = 0.01$), genu of corpus callosum ($p = 0.04$), left lentiform nucleus ($p = 0.02$). Hypertensive patients without WMH had lower FA in left inferior frontal gyrus ($p = 0.001$) and splenium of corpus callosum ($p = 0.04$).

Conclusions: FA and CBF can be used as early markers of brain damage in patients with essential arterial hypertension.

STROKE RECURRENCE AND COMPLIANCE TO ANTIHYPERTENSIVE TREATMENT

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Objective: To evaluate whether hypertension awareness and compliance to antihypertensive treatment is associated with less recurrent stroke among stroke patients from an emergency hospital.

Design and method: 595 adult subjects (age range 28–104 years) admitted to the neurology department of an emergency hospital in 2016 with stroke were included. We tested whether hypertension and lack of hypertension awareness were associated with recurrence of stroke, and whether compliance to antihypertensive treatment was less frequent in recurrent stroke patients.

Results: Among those at first stroke (78.82%) 74.84% were hypertensives, with 93.44% awareness rate, but with 85.06% of cases compliant to treatment. Hypertension correlated with stroke recurrence ($\chi^2 = 4.002$, RR 1.510 CI95% 0.99–2.299, $p = 0.045$). Both compliance to antihypertensive treatment and hypertension awareness were more frequent among those with recurrent stroke (Mann Whitney $p = 0.001$, respectively, $p = 0.03$). On logistic regression, hypertension was the only predictor of recurrent stroke. For results see table.

Variables	P value	OR	95% CI	
Arterial hypertension	0.046	1.692	1.010	2.835
Diabetes mellitus	0.968	0.990	0.616	1.592
Dyslipidemia	0.528	0.793	0.387	1.628
Atrial fibrillation	0.878	0.967	0.629	1.487
Carotid plaque	0.798	1.057	0.690	1.621
Chronic kidney disease	0.578	0.890	0.591	1.340

Conclusions: Stroke, as the most frequent neurologic complication of hypertension, is often followed by recurrence. Our results underline that even awareness and compliance to antihypertensive treatment cannot fully protect from such major events, pointing at the high residual risk patients often carry despite adequate therapy. Often the first to occur in the cardiovascular continuum of disease, hypertension may manifest its effects years before other pathologies ensue, and this may explain its larger influence on cardiovascular events.

HYPERTENSION AND AGEING LEAD TO IMPAIRMENT OF MYOGENIC VASOMOTOR MECHANISM, HIPPOCAMPAL EXPRESSION OF GENES INVOLVED IN BETA-AMYLOID GENERATION AND COGNITIVE DYSFUNCTION

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Objective: Hypertension in the elderly can lead to dysfunctional autoregulation of cerebral blood flow (CBF), leading to increased risk of stroke and the development of Alzheimer's disease (AD), but the underlying mechanisms are still unknown. We hypothesized that hypertension and aging synergistically impair the myogenic constrictor response of cerebral arteries (CA), known to be involved in the autoregulation of CBF and as a consequence, an altered gene expression in the hippocampus will be observable.

Design and method: Hypertension was induced in young (3 mo) and aged (24 mo) C57BL/6 mice with chronic (4 wk) infusion of angiotensin II and changes in myogenic response of CA) and hippocampal mRNA expression of genes involved in amyloid precursor protein (APP)-dependent signaling, APP cleavage, A-beta processing and A-beta-degradation, synaptic function were assessed.

Results: In MCAs from young hypertensive mice, pressure-induced increases in SMC Ca-signal and myogenic tone were increased, both of which were inhibited by the cytochrome P-450 omega-hydroxylase inhibitor HET0016 and the transient receptor potential (TRP) channel blocker SKF96365. MCAs from aged hypertensive mice did not show adaptive increases in pressure-induced Ca-signal and myogenic tone and responses to HET0016 and SKF96365 were blunted. Aged hypertensive mice exhibited spatial memory impairments in the Y-maze and impaired performance in the novel object recognition assay. Hypertension in aging was associated with changes in hippocampal expression of APP-binding proteins, e.g., [Mint3/amyloid beta A4 precursor protein-binding family. A member 3 (APBA3), Fe65/amyloid beta A4 precursor protein-binding family B member 1 (APBB1)], amyloid beta (A4) precursor-like protein 1 (APLP1), muscarinic M1 receptor, and serum amyloid P component, all of which may have a role in the pathogenesis of late-onset AD.

Conclusions: Thus functional maladaptation of aged cerebral arteries to hypertension is due to the dysregulation of pressure-induced 20-HETE and TRP channel-mediated SMC calcium signaling, whereas the hippocampal gene expression signature observed in aged hypertensive mice provides important clues for future studies to elucidate the mechanisms by which hypertension may contribute to the pathogenesis of Alzheimer's disease.

BLOOD PRESSURE REDUCTION AND OUTCOME IN PATIENTS WITH HYPERTENSIVE CRISIS AND ACUTE ISCHEMIC STROKE

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Objective: Antihypertensive treatment and blood pressure (BP) reduction in the acute phase of stroke is controversial. The aim of the study was to analyze the BP dynamics and outcome in treated with antihypertensive medication patients with hypertensive crisis (HC) and acute ischemic stroke (IS)

Design and method: The study included 70 randomly selected in-hospital patients with acute ischemic stroke accompanied by HC at admission (systolic blood pressure /SBP/ > 180 mm Hg and /or diastolic blood pressure /DBP/ > 120 mm Hg). BP dynamics and its association with the clinical outcome was assessed.

Results: The mean baseline BP values of the studied patients were 205.5 ± 21.99 mmHg for SBP and 114.43 ± 13.59 mmHg for DBP. Almost all were treated with antihypertensive therapy and BP fell significantly in the next hours and days. The initial greater BP reduction in the first 12 hours was followed by more gradual fall. BP decreased with 1/4th at the 24th hour compared with the baseline. Patients with clinical improvement demonstrated lower levels of BP (significant at baseline, 12th hour, third day, and at discharge) and smoother BP decrease than those with worsening. Higher values of BP were observed in the persons with no improvement or deterioration than in those with improved status (significant for the SBP at the 24th hour, the 3rd and 4th day and at discharge and for the DBP at the 3rd, 4th day and at discharge). There were no statistically important differences in the outcome of patients with systolic and diastolic BP reduction at the 24th hour > 20% from the baseline and in those with no such reduction.

Conclusions: High BP might be associated with worse prognosis in the acute phase of stroke, although BP reduction with antihypertensive medication is debatable and usually not recommended, except for extremely elevated values. In this study patients with HC and acute ischemic stroke treated with antihypertensive drugs and lower values of BP showed better outcome than those with persistent high values. High BP in the acute phase of stroke should be reduced carefully.

WHICH COGNITIVE DOMAINS ARE AFFECTED IN HYPERTENSIVE PATIENTS? AN ANALYSIS ACCORDING TO AGE, SEX, DEPRESSION AND COMORBIDITIES

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Objective: We aimed in our study to investigate the prevalence of mild cognitive impairment and the affected domains in relationship with age, comorbidities and some cardiovascular risk factors among hypertensive patients.

Design and method: We enrolled 357 consecutive hypertensive patients (54.1% female, 45.9% male, mean age 67.86 ± 10.45 years). Montreal Cognitive Assessment (MoCA) and Mini Mental State Examination (MMSE) tests were used to evaluate cognitive status and the shortened 13 items form of Beck Depression Inventory (BDI-13) for detecting depression. MoCA's cognitive domains were studied, according to the presence or absence of comorbidities and risk factors such as diabetes, obesity, coronary heart disease, stroke, peripheral artery disease, atrial fibrillation, depression. Nonparametric Mann-Whitney U test was used for comparison of means. Statistical analysis was performed with the IBM SPSS v.20 program.

Results: We found MoCA < 26 in 70.6% (252 patients; mean score: 22.42 points, ± 4.72), MMSE < 24 in 19.6% (70 patients, mean score: 26.05 points, ± 3.24). Age negatively correlated with MoCA scores. The cognitive domains impaired by ageing were attention, visuospatial/executive, abstraction, delayed recall and language domains, while orientation and naming remained unaffected in most cases. Patients with former stroke (13.4%) had significantly lower scores in visuospatial/executive, attention, language and orientation domains, while those with atrial fibrillation (22.7%) in language and abstraction (p < 0.05). No significant difference was found in cognitive domains among patients affected or not by peripheral artery disease (11.2%), coronary heart disease (35.3%) and type 2 diabetes (38.7%). Depression was detected in 57.1% (mean BDI-13: 8.01, ± 6.04 points), depressive patients had lower performance compared to nondepressives, especially in visuospatial/executive, attention, language, abstraction and delayed recall domains. A gender related significant difference in the distribution of visuospatial/executive, naming and attention domains was present (p < 0.05), women had globally lower scores. Obese patients (47.89%) had significantly higher MOCA scores than non-obese patients, presenting better performance in visuospatial/executive and delayed recall domains.

Conclusions: Mild cognitive impairment is common among hypertensive patients. Aging and depression has negative impact on cognitive performances. Women may have greater risk for cognitive decline. Cardio- and cerebrovascular diseases may influence different domains of cognitive functions.

DIFFERENCES IN BIOMARKERS LEVELS AND BRACHIAL AND CENTRAL BLOOD PRESSURE DURING THE ACUTE PHASE OF STROKE BETWEEN LACUNAR AND OTHER ISCHEMIC STROKES SUBTYPES

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Objective: We aimed to evaluate the differences in biomarker levels and brachial and central blood pressure estimates during the acute and subacute phase of stroke, between lacunar infarcts and other ischemic stroke subtypes.

Design and method: Patients > 18 years old, with a first episode of ischemic stroke, admitted to our institution between July 2015 and July 2017 were consecutively included. Subjects with Rankin > 2 and patients with history of previous heart failure were excluded. Blood pressure (BP) was measured at admission and during the acute phase of stroke. Determination of proBNP, urinary albumin excretion (UAE) and an echocardiographic study were performed in all subjects. The aortic pulse wave velocity (aPWV) and 24 h brachial and central BP (24h-ABPM) were measured by means of Mobil-O-Graph device during the subacute phase of stroke.

Results: 71 subjects with a first episode of ischemic stroke were included, mean age: 64.7 ± 13.9 years, 62% men: 22 lacunar stroke (31%), and 49 cases (69%) with non lacunar ischemic stroke. The levels of proBNP were significantly lower in patients with lacunar stroke as compared as atherothrombotic and cardioembolic stroke (median: 36, 277 and 274 pg/mL, respectively; p = 0.009). After adjusting for age, patients with lacunar stroke had significantly higher levels of BP in the emergency department: systolic BP 173 ± 37 vs 153 ± 28 mm Hg respectively; p = 0.006, diastolic BP: 97 ± 21 vs 86 ± 16 mm Hg; p = 0.035, and during

the acute phase of stroke: systolic BP 142 ± 19 vs 128 ± 16 mm Hg; $p = 0.002$; diastolic BP: 79 ± 12 and 73 ± 12 mm Hg respectively; $p = 0.025$.

Regarding 24h-ABPM, patients with lacunar stroke showed higher values of daytime pulse pressure, daytime brachial systolic BP, daytime brachial diastolic BP and central BP estimates, after adjusting for age. No significant differences were observed in target organ damage between the different ischemic stroke subtypes.

Conclusions: Patients with a first episode of lacunar stroke had lower levels of proBNP and higher BP levels during acute and subacute phase of stroke, suggesting a closer relationship with hypertension.

EFFECT OF VERAPAMIL SUSTAINED RELEASE ON CEREBROVASCULAR REACTIVITY IN HYPERTENSIVE PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To investigate the effect of verapamil sustained release (SR) on cerebrovascular reactivity (CVR) in patients with hypertension (HT) and rheumatoid arthritis (RA).

Design and method: The study comprised 30 patients with HT of grade 1–2 and RA, aged 59.7 ± 9.1 years. All patients were treated with 120 mg or 240 mg verapamil SR for 24 weeks. Ambulatory 24-hour blood pressure (BP) monitoring and evaluation of CVR were performed twice: initially and at the end of the study. CVR was evaluated using transcranial Doppler ultrasound of the middle cerebral arteries (MCA) in the hyperoxia and hypercapnia tests. We measured MCA time average maximal blood flow velocity (TAMX), peak systolic velocity (Vps) at baseline, during 2 min inhalation of oxygen (O₂) and during 3 min recovery phase. The hypercapnia test was carried out according to the same protocol with inhalation of the 4% mixture of carbonic gas with air (CO₂). We used three parameters for CVR evaluation: index changes of flow velocity mean (IFVm), speed modification of velocity (SMFVm) and index of recovery for velocity (IR-Vmrec). $IFVm = (Vps2 - Vps0) / Vps0 \times 100\%$. $SMFVm = (Vps2 - Vps0) / 120$. $IR-Vmrec = Vps0 / Vps4$. Vps0 is starting parameter. Vps2 is the parameter during 2 minute of inhalation. 120 is time of inhalation in seconds. Vps4 is the parameter during 4 minutes of test. The differences in BP values and parameters for CVR evaluation were tested with Student's t-test for paired samples.

Results: Verapamil SR treatment reduced both systolic/diastolic office and 24-h BP by $14.1/8.2$ mmHg for office BP and $13.5/9.9$ mmHg for 24-h BP, all $P < 0.0000$. After Verapamil SR treatment, the parameters of MCA blood flow and CVR did not change either in the hyperoxia or in the hypercapnia tests compared with those before treatment.

Conclusions: Treatment with verapamil SR did not improve the parameters of CVR in hypertensive patients with RA.

PREDICTORS OF STROKE RECURRENCE IN HYPERTENSIVES IN AN EMERGENCY HOSPITAL

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Objective: To evaluate cardiovascular (CV) risk factors and therapeutic management as predictors of recurrent stroke among hypertensives from an emergency hospital.

Design and method: From 595 adult subjects (age range 28–104 years) admitted to the neurology department of an emergency hospital in 2016 with stroke, we selected hypertensives ($n = 456$). They were divided in two subgroups depending on history of previous stroke and propensity matched to control for age and sex. Logistic regression was used to evaluate CV risk factors and treatment strategy as predictors of recurrent stroke.

Results: The prevalence of hypertension among stroke patients was 76.63%. Propensity matching resulted in 208 hypertensives. CV risk factors and antihypertensive medication did not significantly differ among those with recurrent stroke versus first-time stroke event. In-hospital mortality was significantly higher in those with recurrent stroke ($\chi^2 = 4.837$, RR 1.150 CI95% 1.014–1.305, $p = 0.028$). For results see table.

Conclusions: When adjusting for age and sex CV risk factors and antihypertensive medication did not predict stroke recurrence in hypertensives, which may suggest either the lack of intensive risk control, or an important residual risk despite therapy in those who already suffered stroke. Recurrence of stroke is more likely to lead to higher in-hospital mortality.

Variables	P value	OR	95% CI	
Dyslipidemia	0.963	1.016	0.515	2.006
Diabetes mellitus	0.844	0.938	0.494	1.781
Atrial fibrillation	0.675	1.159	0.581	2.314
Carotid plaque	0.181	1.530	0.820	2.855
Chronic kidney disease	0.433	1.261	0.706	2.251
Spironolactone	0.100	0.251	0.048	1.303
Betablocker	0.360	1.345	0.713	2.538
Calcium channel blocker	0.899	1.056	0.455	2.452
Statin	0.290	0.619	0.254	1.504
Diuretic	0.986	1.006	0.527	1.920
ACEI/Sartan	0.156	0.610	0.308	1.208
Antiplatelet	0.552	1.278	0.569	2.870

THE ASSOCIATION BETWEEN CAROTID FLOW AND COGNITIVE FUNCTION IN THE COMMUNITY ELDERLY POPULATION

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Objective: Carotid hemodynamics, such as intima-media thickness and carotid flow velocity were associated with stroke events. However, the association between carotid hemodynamics and cognitive function remains not fully clear. We aimed to investigate the relationship between carotid flow velocity and cognitive function.

Design and method: A total of 744 elderly (more than 60 years) subjects completed the baseline and followed ultrasound examinations and those were evaluated cognitive function. Cognitive function was evaluated by MMSE and cognitive function impairment was defined by the MMSE less than 26. The peak-systolic velocity, end-diastolic velocity were measured in the common carotid arteries. Logistic regression was used to evaluate the association between carotid flow velocities, carotid diameters and cognitive function.

Results: A total of 744 elderly subjects completed all examinations during the followed period. The prevalence Cognitive function impairment (MMSE less than 26) was 13.3% ($n = 99$). The peak systolic velocity (PSV) and diastolic end velocity (EDV) were lower in those with cognitive function impairment (60.5 vs. 65.5 cm/sec, p -value < 0.001 for PSV and 19.7 vs. 22.1 cm/sec, p -value < 0.001 for EDV), and only peak-systolic velocity remains significant in the multivariable models. Moreover, those with lower carotid flow velocities (the lowest 10th of peak systolic velocity) had 9.69 fold risk (95% confidence intervals: 2.75–34.21) of cognitive function impairment, compared to those with the highest 10th of peak systolic velocity. The significant association remains in the multivariable model by adjusting for age, gender, education, brachial systolic BP, fasting glucose, and low density lipoprotein cholesterol.

Conclusions: Low carotid flow velocity, especially peak-systolic velocity was associated with cognitive function impairment. Lower carotid flow may involve the pathogen of cognitive function impairment in the general elderly population.

CEREBROVASCULAR RESERVE TEST IN HEALTHY VOLUNTEERS AND HYPERTENSIVE PATIENTS WITH DIFFERENT DURATION OF HYPERTENSION AND WITH APNOEA

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Objective: We compared different types of the cerebrovascular reserve (CVR) in healthy volunteers, patients with different duration of hypertension, and with sleep apnea.

Design and method: All participants of research have given the informed agreement. We used ultrasonography of transcranial Doppler's method in the middle cerebral arteries (MCA) from temporal window. We studied the changes of flow velocity mean (FVm) starting, during hyperoxia (inhalation 2 min 100% oxygen) and FmV in period of recovery (rec) (air-inhalation 3 min) in 228 patients (36–70Y) with hypertension and 44 healthy volunteers (HV) without stroke. Secondary hypertension were excluded by clinical and biochemical tests. At the time of vascular evaluation, none of the patients had a history or clinical evidence of diabetes, peripheral vascular disease, coagulopathy, or any disease predisposing them to vasculitis. HP were divided into 3 groups: hypertension duration (HD) < 5

years, HD > 5 years and apnea. We used Indexes of FVm; $IFVm = (Vm0 - Vm) / Vm0 \times 100$. Vm0, BP0 are starting parameters and Vm, BP are the parameters at period of inhalation.

Results: HV had the normal distribution of Index of FVm 95%CI [-23.1;-19.8]. The index of FVm differed significantly in HP compared to HV: -21.42 ± 1.27 and -11.32 ± 2.30 $p < 0.01$. Distribution of the index parameters showed the presence of three types of reactions arteries response to hyperoxic test: normal 95%CI [-27.1;-19.9], reduced 95%CI [-4.9;-16.6], and opposite reaction 95%CI [-2.3; 5.6] $c^2 =$ during hyperoxia. The frequency of occurrence of normal; reduced; opposite reactions were in the groups HD < 5Y 43.1; 55.2; 2.4% $c^2 = 17.53$, HD > 5Y 16.2; 64.1; 20.1% $c^2 = 72.3$, and sleep apnea 10.2; 23.4; 67.4 $c^2 = 6.44$ $p = 0.00$; $p = 0.00$; $p = 0.01$.

Conclusions: HP had different types of the CVR, it were normal, reduced, and opposite directions of the reactions during hyperoxia test. Patients had significantly less often normal reaction and significantly more often had opposite reaction, which had more than 5 years of hypertension, and with sleep apnea. The study needs further observations.

A FAST AND SIMPLE NEW QUESTIONNAIRE TO HIGHLIGHT THE COGNITIVE IMPAIRMENT IN HYPERTENSIVES: THE ASSOCIATION WITH ARTERIAL STIFFNESS

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Objective: The critical incidence of cognitive impairment in hypertensives leads into the need to adopt tools easy to use and able to precociously discern the neuropsychological deficit. Aim of the study was to verify, in relatively well-treated hypertensive patients, the discriminative ability of a brief questionnaire to discern the quality and the grade of a mild cognitive impairment and their association with the preclinical vascular damage.

Design and method: Following a pilot study performed in healthy and hypertensive subjects, an 18-item (NPI) questionnaire, with a good internal coherency ($\alpha:0.87$) and graded answers (never-very often: 1-4), exploring diverse neuropsychological abilities ascribable to different cerebral cortical areas, was administered to 375 grade1-2 hypertensives treated with ACEi or ARBs as monotherapy. In the patients, subdivided in tertiles, in order of the total score for cognitive impairment (CIStot), 196 with lower (LCIS), 120 with intermediate (ICIS) and 59 with higher (HCIS), but with similar education, metabolic assessment, history and hypertensive state (BPoff and ABPM), the preclinical vascular damage, structural as carotid intima-media thickness (IMT) and functional, as carotid-femoral pulse wave velocity (PWVcf), was determined.

Results: The analysis showed significant characteristics. ($m \pm s.d.$; * $p < .05$, ** $p < .01$, *** $p < .001$ vs LCIS; ° $p < .05$, °° $p < .01$, °°° $p < .001$ vs ICIS)

pts/v	AGE	SBP/DBPoff	SBP/DBPday	SBP/DBPnight	IMT(mm)	PWVcf(m/s)
LCIS	57±11	132±5/81±5	133±5/82±6	119±10/69±5	.89±0.2	8.8±2.9
ICIS	56±12	132±4/81±5	121±9/81±9	118±8/69±8	.91±0.2	10.1±1.4**
HCIS	57±12	133±5/80±4	123±11/78±9	108±12/64±8	.98±0.2	10.9±2.4***

pts/v	CIStot	NPI1	NPI3	NPI6	NPI7	NPI10
LCIS	20.9±2.4	1.2±0.6	1.6±0.8	1.3±0.6	1.2±0.5	1.1±0.5
ICIS	28.3±2.4***	1.4±0.6***	1.9±0.8***	1.5±0.6***	1.6±0.7***	1.5±0.7***
HCIS	39.9±4.4***°°°	2.0±1.1***°°°	2.3±0.9***°°°	1.9±0.8***°°°	1.9±0.9***°°°	1.8±1.1***°°°

In particular, psychophysical attitude (NPI1), brief-term memory (NPI3, NPI7) and problem solving (NPI6, NPI10) deficits are impaired in HCIS hypertensives. Pearson analysis pointed out the association between PWV and brief-term memory (.649***), and problem solving (.618**), attentive-cognitive functions under the control of frontal cortical areas.

Conclusions: The findings show that between relatively well-treated hypertensives, the mild impairment of attentive-executive capabilities are associate with the arterial stiffness, before the onset of a preclinical structural vascular damage, as IMT, and are detectable by a new rapid and easy-to-use screening tool.

GEOGRAPHIC VARIABILITY IN THE DECLINE OF THE INCIDENCE OF FATAL AND NON-FATAL STROKE

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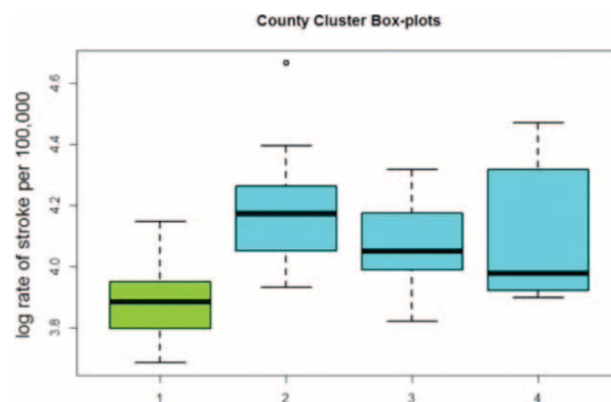
Objective: To examine whether the decline in incidence of fatal and non-fatal stroke is affected by characteristics of the population in different geographic areas.

Design and method: County specific data from the 21 counties in the state of New Jersey were obtained from the Robert Wood Johnson Foundation

County Health Rankings. The percentage of the population in each county with the following medical and socioeconomic risk factors was used in the analysis: persons under the age of 18, persons 65 years or older, female, smokers, physically inactive, obese, with diabetes, diabetic monitoring among diabetics, excessive drinking, college education, median household income, unemployed, uninsured, single parent household, areas with violent crime. The counties were lumped into 4 categories based on similarities of the above characteristics. The incidence in fatal and non-fatal stroke was compared among the 4 county clusters.

Results: Overall, the incidence of fatal and non-fatal stroke declined throughout the state. The incidence was significantly lower ($p < 0.05$) in cluster 1. There was no difference in the decline among the other 3 clusters (Figure). Compared to clusters 2, 3 and 4 in the aggregate, persons included in cluster 1 had higher household income, were more likely to have college education, and were less likely to be unemployed, to live in single parent households, to have diabetes, to be obese, to smoke, or to be physically inactive.

Conclusions: The incidence of fatal and non-fatal stroke was more pronounced among persons who had better risk factor profile and higher socioeconomic status. There were no significant effects of demographics (e.g. age, gender).



AN EXAGGERATED BLOOD PRESSURE RESPONSE TO EXERCISE IS COMMON IN THE SUBACUTE PHASE AFTER STROKE, BUT IS NOT AFFECTED BY RANDOMIZATION TO 12 WEEKS OF INTENSIVE AEROBIC EXERCISE

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Objective: The primary aim of this study was to explore peak systolic blood pressure levels attained during an ergometer exercise test in patients in the subacute phase after stroke. The secondary aim was to evaluate the impact of twelve weeks of twice-weekly intensive aerobic exercise on the systolic blood pressure response to exercise in these patients.

Design and method: We analyzed data from a clinical trial, in which 56 patients with a recent stroke were randomized to either participation in a twice-weekly intensive aerobic exercise program for twelve weeks (intervention group, $n = 29$), or to usual care (non-intervention group, $n = 27$). All patients performed a symptom-limited ergometer exercise test twice: prior to randomization (baseline, at a median of 22 days following the acute stroke) and after twelve weeks. Complete ergometer blood pressure data were obtained for 53 participants both at baseline and after twelve weeks

Results: At baseline 66 % of the patients exhibited an exaggerated exercise blood pressure response (peak systolic blood pressure greater than or equal to 210 mmHg in men or greater than or equal to 190 mmHg in women). An exaggerated blood pressure response occurred more frequently in patients with resting systolic blood pressure greater than or equal to 140 mmHg than in patients with resting systolic blood pressure lower than 140 mmHg (24/31 or 77.4 % vs. 11/22 or 50.0%, $P = 0.038$). At follow-up patients who had been randomized to the ex-

ercise program achieved higher peak work rate but peak systolic blood pressure remained unaltered.

Conclusions: We conclude that among patients with a recent stroke, it was common to have an exaggerated systolic blood pressure response during exercise. However, this response was not altered by participation in a 12-week program of aerobic exercise.

THE NEED OF BETTER ARTERIAL HYPERTENSION AND ATRIAL FIBRILLATION MANAGEMENT IN REDUCING STROKE INCIDENCE

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Objective: Strokes are among the most common causes of morbidity and mortality, and in individuals who suffered stroke, subsequent long-term neurological deficit in a larger or smaller range is also an important factor. Arterial hypertension and atrial fibrillation are the most common influencing factors of strokes. Numerous clinical and epidemiological studies have confirmed that elevated systemic blood pressure values are among the major risk factors for both ischemic and hemorrhagic stroke, and the effect of arterial hypertension is complex. Aim of the study was to point out the need to improve the early identification, elimination and treatment of risk factors for stroke, according to the valid recommendations of the European Society of Hypertension and European Society of Cardiology.

Design and method: Retrospectively, we analyzed a cohort of patients hospitalized for stroke during a three month period (July - September 2016) at the 1st Department of Neurology in Bratislava. The group consisted of 104 patients, from which ischemic stroke was diagnosed in 88 subjects (84.6 %) and hemorrhagic stroke in 16 subjects (15.4 %). The average age was 70.7 years. A history of previous stroke was in 18 (17.3 %) patients.

Results: Among the most important risk factors in addition to age, we found that arterial hypertension as the most common risk factor occurred in 96 subjects (92.3 %). Atrial fibrillation occurred in 34 patients (32.7 %), but only 14 patients (41.2 %) were treated with anticoagulant therapy before hospitalization. Hemorrhagic stroke during anticoagulant therapy was only in 1 patient, but ischemic stroke in 13 patients. In this group of patients with anticoagulant therapy who have evolved ischemic stroke in spite of this treatment, we found that in 7 patients (53.8 %) the treatment was underdosed and therefore ineffective.

Conclusions: Our results from real clinical practice points to the need to improve the effective management of arterial hypertension and atrial fibrillation, the most common influencing factors of stroke. It is necessary to improve the inadequate indication of anticoagulant treatment with consideration of the stroke risk calculation for atrial fibrillation (CHA2DS2-VASc Score) and bleeding risk calculator (HAS-BLED).

THE PREVALENCE OF MASKED HYPERTENSION AMONG OLDER PATIENTS WITH COGNITIVE COMPLAINTS

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Objective: Although the clinical relevance of masked hypertension ([MHT] defined as normal office BP, but elevated BP at home) is still debated, it has been associated with sustained hypertension and higher cardiovascular morbidity, both established risk factors for cognitive decline. Data about MHT in elderly with cognitive problems is scarce. Therefore, the aim of this study was to estimate the prevalence of MHT in older patients visiting a memory clinic and to examine the association between MHT and cognitive function.

Design and method: We studied 249 patients who attended our memory clinic. They were subjected to 7-day home BP measurements (Microlife WatchBP Home), twice in the morning and evening. Patients were included if they had at least 8 measurements left, after discarding measurements of day 1, and if office BP (single, supine) was available. The following definitions were applied: MHT (office BP < 140/90 mmHg; home BP > = 135/85 mmHg), normotension (office BP < 140/90 mmHg; home BP < 135/85 mmHg), hypertension (office BP > = 140/90 mmHg; home BP > = 135/85 mmHg), white-coat hypertension (office BP > = 140/90 mmHg; home BP < 135/85 mmHg). Characteristics of the group with MHT were compared to those with normotension. Statistical analyses were performed using independent samples t-test, Mann-Whitney U-test and chi-square test, using $P < 0.05$.

Results: From 202 patients (73.3 ± 9.3 years, 52% male) office and home BP was available. Office BP and home BP significantly differed (157/84 ± 23/10 mmHg and 139/79 ± 16/9 mmHg, respectively, $P < 0.0001$). The prevalence (with 95% CI) of MHT was 6.9% (3.4–10.4), corresponding to 14 patients. Normotension was observed in 12.4% (n = 25), hypertension in 55.0% (n = 111) and white-coat hypertension in 25.7% (n = 52). Characteristics of patients with MHT and normotension are shown in Table 1. We observed a trend ($P = 0.08$) for a lower cognitive score on the CAMCOG test battery in MHT compared to normotension.

Conclusions: Our findings show a lower prevalence of MHT compared to earlier studies performed in older people. Based on results from this relatively small group, patients with MHT may show decreased cognitive function compared to patients with normotension. However, further studies with larger numbers are needed to confirm this.

Table 1. Characteristics of patients with normotension and MHT

	Normotension (n=25)	MHT (n=14)	P-value
Age, mean (SD), yrs	70.0 (11.9)	75.6 (7.5)	0.12
Female, % (n)	48 (12)	36 (5)	0.46
BMI, mean (SD), kg/m ²	27 (5.5)	26 (3.9)	0.49
Use of antihypertensives, % (n)	36 (9)	86 (12)	0.01
History of CVD, % (n)	36 (9)	50 (7)	0.39
MMSE score, median (IQR)	26.0 (21.3–28.8)	24.5 (19.5–26.0)	0.27
CAMCOG score, median (IQR)	90.0 (71.5–94.8)	75.0 (68.0–81.0)	0.08
Office SBP, mean (SD), mmHg	126.5 (7.7)	125.7 (7.7)	0.77
Office DBP, mean (SD), mmHg	74.5 (7.5)	74.4 (7.7)	0.97
Home SBP, mean (SD), mmHg	118.0 (9.4)	144.5 (8.9)	na
Home DBP, mean (SD), mmHg	71.7 (6.0)	79.1 (8.0)	na
Diagnosis, % (n)			0.23
Dementia, all types	32 (8)	57 (8)	
Mild cognitive impairment	20 (5)	22 (3)	
Subjective memory complaints	36 (9)	7 (1)	
Other	12 (3)	14 (2)	

BP=blood pressure; MHT=masked hypertension; SD=standard deviation; BMI=body mass index; CVD, cardiovascular disease; MMSE=Mini-Mental State Examination; CAMCOG=Cambridge Cognitive Examination; SBP=systolic blood pressure; DBP=diastolic blood pressure. P-value derived from independent samples t-test for age, BMI and office blood pressure; from Mann-Whitney U test for MMSE and CAMCOG; and from chi-square test for sex, history of CVD and diagnosis.

HYPERTENSIVE STATUS AND CARDIOVASCULAR RISK FACTORS IN STROKE PATIENTS

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Objective: To evaluate cardiovascular (CV) risk factors in hypertensive versus normotensive stroke patients admitted to an emergency hospital.

Design and method: In 595 adult subjects (age range 28–104 years) admitted to the neurology department of an emergency hospital in 2016 with stroke, we evaluated prevalence of cardiovascular risk factors and differences in them between hypertensives versus normotensives.

Results: Hypertension was the most prevalent cardiovascular risk factor among stroke patients at 76.63% of cases. Diabetes mellitus was more frequently associated with hypertensive status, while carotid plaque was seen more in normotensives. Dyslipidemia, atrial fibrillation and chronic kidney disease were not significantly different among the subgroups. See table.

Variables	Hypertensives	Normotensives	P value
Dyslipidemia (10.1%)	46 (10.1%)	14 (10.1%)	p ns
Diabetes mellitus (23%)	114 (25%)	23 (16.5%)	p 0.038
Atrial fibrillation (34.1%)	161 (35.3%)	42 (30.2%)	p ns
Carotid plaque (35.5%)	152 (33.3%)	59 (42.4%)	p 0.049
Chronic kidney disease (39.7%)	179 (39.3%)	57 (41%)	p ns

Conclusions: Stroke patients have a very high cardiovascular burden, with hypertension, the first in the cardiovascular continuum, having probably accelerated effects on total risk by other factors, which here were insignificantly different between hypertensives and normotensives.

MORTALITY IN PATIENTS WITH STROKE AND BLOOD HYPERTENSION

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Objective: To carry out a retrospective descriptive study of hypertensive patients with cerebrovascular disease in a regional hospital.

Design and method: Transversal descriptive analysis of patients with arterial hypertension who suffered cerebrovascular disease admitted to our service from January to December 2015. A detailed study of all the risk factors suffered by patients was carried out. The population was divided into two groups according to the type of pathology, Ischemic vs Hemorrhagic and a descriptive study of the characteristics of each of the groups was carried out by means of their frequencies.

Results: There were a total of 106 patients, with an age of 71.08 ± 13.53 years, of which 52.8% were women. Of the total population, 83 patients (79%) comprised the group of ischemic stroke and 22 patients (21%) belonged to the group of hemorrhagic stroke. The mean stay of the patients was 9.99 ± 10.53 . Only 71.7% of patients had social security and 40.6% were Bere Ber race. Mortality was 16% (17 patients). 68.9% of the patients were HBP, 37.7% had DM and 22.6% DLP as outstanding comorbidities. Patients were divided between hypertensive and non-hypertensive patients, analyzing mortality in both groups without statistically significant differences being observed (17.80% vs 12.12%, $p < 0.333$). The patients were then divided between ischemic ICTUS and hemorrhagic stroke, analyzing the mortality dependent on hypertension in each of the groups. Within the ischemic ICTUS, no statistically significant differences were observed (12% vs 15.51%, $p < 0.482$). In the hemorrhagic ICTUS group, no statistically significant differences were found either (12.50% vs. 28.75%, $p < 0.380$).

Conclusions: In our study, we observed how patients with arterial hypertension who suffer a cerebrovascular accident have higher comorbidity and tend to have a more torpid clinical course with higher mortality. In all the series we observed a trend (more marked in the hemorrhagic stroke) to the mortality in patients with arterial hypertension without it becoming statistically significant, this is probably due to the small sample size, we are currently collecting data to see the results in a more truthful way

CLINICAL PROFILE OF HYPERTENSES IN EXTREME AGES OF LIFE

J. Osuna Sanchez, J. Ampuero Ampuero. *Hospital Comarcal de Melilla, Melilla, SPAIN*

Objective: To carry out a retrospective descriptive study of patients aged 90 years or older admitted to the Internal Medicine service with arterial hypertension.

Design and method: This is a cross-sectional descriptive analysis of patients older than 90 years admitted to internal medicine for any pathology from January to December 2016 with arterial hypertension. A detailed study was carried out of all the risk factors presented by the patients, the associated comorbidities, as well as personal history.

Results: There were a total of 109 admitted patients older than 90 years. Of which 67.9% were women. The mean age was 92.78 years (90–103). 18.3% of the patients were institutionalized, 57.8% were dependent for all the basic activities of daily life (ABVD) and 27.5% were partially dependent for all ABVD. 67.8% were ethnic Caucasians, 30.6% Berber and 1.6% were Jews.

With respect to personal background, 36.7% IRC; 40.4% ICC; 36.7% previous ischemic heart disease; 30.3% DM; 41.3% FA; 14.8% COPD; 30.3% dyslipidemia; 14.7% neoplasia (active or not); and an 18.3% history of stroke. As an important finding, 33.9% of patients presented cognitive impairment to some degree. 78.9% of the patients had presented at least one admission in the previous 12 months, and 27.9% 2 or more previous admissions. Up to 90.7% of patients had 2 or more pathologies at the time of admission. The mean hospital stay was 12.43 ± 9.52 days, 46.8% of the patients died.

Conclusions: As we advance in the findings in medicine, the patients in our services are older and have greater comorbidity. Within these comorbidities, arterial hypertension is one of the main ones.

POSTER SESSION

POSTERS' SESSION PS10:

ATHEROSCLEROSIS AND MOLECULAR FOUNDAMENTS

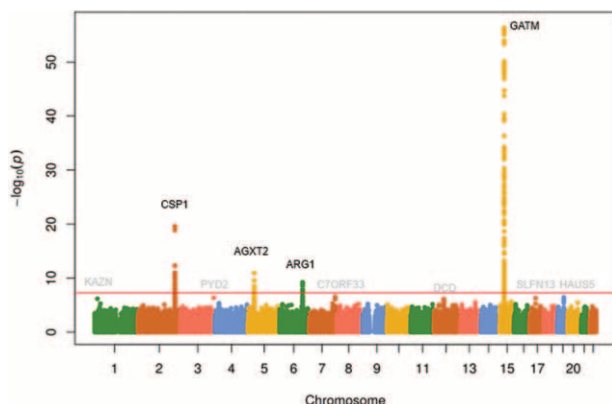
GENOME WIDE ASSOCIATION STUDY META-ANALYSIS OF HOMOARGININE USING THE HRC REFERENCE PANEL

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Objective: Data from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study and the 4D Study have shown that low homoarginine (HARG) is a significant risk factor for all-cause and cardiovascular mortality. In 2013, we performed a first genome wide association study (GWAS) meta-analysis on the genetic determinants of homoarginine concentration based on data from LURIC and the Young Finns study (YFS) and discovered three loci with genome-wide significance. In the meantime, new expanded and more accurate imputation reference panels have been released.

Therefore, our aim was to performed a meta-analysis of GWAS using the haplotype reference consortium (HRC) imputation reference panel to identify further genes which are involved in the regulation of HARG serum levels. Furthermore, we increased the sample size from ca. 5k to 6k.

Design and method: HARG was measured in serum stored at -80°C by a reversed phase high-performance liquid chromatography. Genotyping was done in LURIC and 4D by using the Affymetrix 6.0 array and a custom-built Illumina Human 670k BeadChip in YFS. Imputation to the HRC reference panel was performed using Minimac. SNPs were evaluated for association with HARG using linear regression analyses using the software PLINK2 with adjustment for age, sex and principle components. Meta-analysis was done using a fixed-effects, effective sample-weighted Z-score meta-analysis method, as implemented in the software METAL.



Results: In the meta-analysis, 391 SNPs were genome-wide significantly associated with HARG. These SNPs are located on chromosome 2 (CSP1), on chromosome 5 (AGXT2), on chromosome 6 (ARG1) and on chromosome 15 (GATM) (Fig. 1). This adds one significant locus to the previous meta-analysis. Another six loci showed suggestive association with P-values < 10E-6.

Gene set enrichment and tissue enrichment analyses using DEPICT did not results in any significant hits after FDR correction. Highest-ranking gene sets with p-values of 10E-4 were gene sets involved in dystonia, cellular hormone response, insulin resistance, carbohydrate and lipid metabolism. Highest-ranking tissues with nominally significant p-values were atrial appendage and heart atria.

Conclusions: In the meta-analysis four genomic loci reached genome-wide significance and a further six loci showed suggestive association.

SUBCLINICAL TARGET ORGAN DAMAGE IN HYPERTENSIVE SUBJECTS INCLUDED IN THE IBERICAN STUDY

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Objective: The general aim of IBERICAN study is to know the prevalence and incidence of cardiovascular risk factors and cardiovascular and renal disease in Spain. The aim of this abstract is to know the prevalence of subclinical target organ damage (TOD) in hypertensive patients respect non hypertensive patients in the population of the IBERICAN Study

Design and method: The IBERICAN Study is a longitudinal, observational, and multicentric study with subjects between 18 to 85 years of age, recruited in Primary Care (PC) and who will be follow up at least 5 years. The final sample size is estimated in 7,000 patients. We show the baseline characteristics of the patients in the first visit (n = 5,944). To define the TOD, we consider the ESH 2103 Guide criteria: pressure pulse in aged > = 60 mmHg, ankle/brachial index < 0.9, microalbuminuria: albumin/creatinine ratio (between 30 - 299 mg/g), glomerular filtration (CDK-EPI < 60 ml/min), left ventricular hypertrophy (electrocardiogram or ECHO).

Results: 2.873 hypertensive patients (prevalence: 48.3%), the mean age in the sample was 64.7 ± 12 years, 49.7% women, antiquity of hypertension 9.7 ± 6 years, BMI 31.1 ± 8.9 kg/m². Prevalence of TOD in hypertensive vs no hypertensive patients was 39.8% vs 13.3%, p < 0.001. With respect to the type of TOD: pressure pulse in aged > = 60 mmHg: 27.5% vs 7%, p < 0.001; ankle/brachial index < 0.9: 2.7% vs 1.3%, p = 0.196, NS; microalbuminuria: 11.7% vs 4.9%, p < 0.001; glomerular filtration (CDK-EPI < 60 ml/min): 13.5% vs 3.2%, p < 0.001; left ventricular hypertrophy: 6.9% vs 1.4%, p < 0.001.

Conclusions: Patients with hypertension in Primary Care have higher prevalence of subclinical target organ damage respect no hypertensive patients and for each of the types of the subclinical target organ damage according to the ESH 2103 Guide criteria. Is important the diagnosis of TOD, because they are high-risk cardiovascular patients.

IMPACT OF OBSTRUCTIVE SLEEP APNOEA AND TREATMENT RESPONSE ON IMMUNOSENESCENCE PARAMETERS IN HYPERTENSION

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Objective: Inflammation and immunosenescence (IS) have been considered to be associated with hypertension. (HTN) Obstructive sleep apnea (OSA) was also associated with chronic inflammation by repetitive oxidative stress. However, the relationship between immunosenescence parameters and treatment of HTN with or without OSA is unclear. We evaluate to demonstrate the association of chronic inflammation and IS parameters with OSA in hypertensive patients and the changes according to BP treatment.

Design and method: Multicenter longitudinal observational study from April 2013 to October 2015. A total of 131 Hypertensive patients (SBP > 140 mm Hg

or DBP > 90 mm Hg) were divided into OSA low risk and OSA high risk according to Berlin sleep apnea questionnaire. CD28 null and CD58 (+) fraction of CD8 T-cells were sampled at baseline in both groups. 87 patients among them were analyzed for baseline and 6 months follow-up immunosenescence parameters with treatment of HTN.

Results: Among 131 subjects, 88 patients (67.2%) were OSA high risk, and 43 patients (32.8%) were OSA low risk. CD28 null fraction of CD8 T cells in OSA high risk group was $35.1 \pm 18.3\%$ vs $43.9 \pm 19.9\%$ in low risk group with a p-value 0.014. CD58+ fraction of CD8 T-cells in OSA high risk group was $37.0 \pm 16.9\%$ vs $44.7 \pm 20.0\%$ in OSA low risk group with a p-value 0.023. HTN was controlled in 56 patients (64.4%). CD28nullCD8+ T cell was significantly decreased from $41.1 \pm 17.9\%$ to $37.5 \pm 18.8\%$ (p-value = 0.01) but CD57+CD8+ T cell was not correlated with HTN treatment. ($42.2 \pm 17.5\%$ vs $42.7 \pm 18.4\%$, p-value = 0.596). In multivariate analysis, only age was associated with change in CD28nullCD8+ T cell with greater reduction in CD28nullCD8+ T cell. (beta: 0.373, t = 2.412, p-value = 0.019).

Conclusions: CD28 null and CD58 (+) fraction of CD8 T-cell in hypertensive patients with OSA were paradoxically higher in patients without OSA. IS parameter, CD28nullCD8+ T cell was significantly decreased with HTN treatment, especially in younger patients.

LONG NON CODING RNAS IN PERIPHERAL BLOOD MONONUCLEAR CELLS IN HYPERTENSIVES WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION AND THEIR RELATION TO THEIR FUNCTIONAL CAPACITY

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Objective: Long non coding RNAs (lncRNAs) are emerging as important components of regulatory networks underlying cardiovascular development and pathophysiology. They exhibit distinctive roles in modulating tissue-specific epigenomic states that are critical for the transcriptional and epigenetic reprogramming that underpins heart failure (HF) pathogenesis. Our aim was to assess gene expression levels of the lncRNAs CARMEN and FENDRR in peripheral blood mononuclear cells (PBMCs) in hypertensive patients with heart failure with preserved ejection fraction (HFpEF) and to evaluate their association with their exercise capacity.

Design and method: Methods: We included 45 patients with essential hypertension and HFpEF (mean age 67 ± 8 years). Twenty one hypertensive patients without HFpEF (mean age 65 ± 12 years) were also included as controls. All patients underwent a cardiopulmonary exercise test (CPXT). PBMCs were isolated and lncRNAs' expression levels were determined by quantitative real-time reverse transcription polymerase chain reaction

Results: Results: Patients with HFpEF showed significantly higher CARMEN (27.93 ± 5.68 versus 11.6 ± 4.8 , p = 0.02) and FENDRR (45.72 ± 8.88 versus 16.01 ± 4.04 , p = 0.01) expression levels compared with the control group. For hypertensive patients with HFpEF, strong positive correlations were observed between CARMEN expression levels in PBMCs and peakVO2 and ($r = 0.46$, p = 0.001), VE/VO2 ($r = 0.45$, p = 0.002) as well as exercise duration ($r = 0.427$, p = 0.003). We also observed a weak but significant negative correlation between FENDRR expression levels in PBMCs and VE/VO2 ($r = -0.35$, p = 0.02).

Conclusions: Our data reveal that CARMEN and FENDRR expression levels in PBMCs of hypertensive patients with HFpEF may be related to their functional capacity. Further studies are needed to assess their role as therapeutic targets in those patients

NEGATIVE TREND IN ASSOCIATION OF UROMODULIN WITH BLOOD PRESSURE IN PREHYPERTENSIVES AND UNTREATED HYPERTENSIVES WITH NORMAL KIDNEY FUNCTION

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Objective: Uromodulin and minor G allele UMOD gene rs13333226 have been associated with blood pressure (BP), hypertension (HT) and better renal function. Our aim was to analyze the association of uromodulin and the frequency of G allele with BP and kidney function in untreated subjects with a normal glomerular filtration rate (GFR).

Design and method: From 894 participants of the ENAH follow up, a cohort group of 559 untreated subjects (men 55.8 %, cohort group mean age 38.6) with an eGFR > 60 ml/min/1.73m² (CKD Epi equation) were enrolled into the study. Subjects were divided in three subgroups: optimal BP (OBP; N = 107), prehypertension (PHT; N = 145) and HT (N = 307). UMOD genotyping rs12917707 polymorphism was performed by RT-PCR with the fluorescence-based TaqMan system, while urinary uromodulin levels were measured by Enzyme Linked Immunosorbent Assay (ELISA).

Results: We failed to find difference in uromodulin levels among BP categories. However, a negative association of uromodulin with systolic BP (NS) and diastolic BP ($r = 0.20$; p = 0.069) was observed in the entire group. No association between uromodulin and eGFR was noted. Uromodulin was found to be lower in women than men. The frequency of A and G alleles was 83.2% and 16.8%, respectively. No difference in the frequency of G allele was found among the BP categories. A trend of higher uromodulin was observed in homozygous for the G allele. No significant trend was observed between uromodulin and eGFR in the entire group.

Conclusions: There is trend of negative association of uromodulin with BP in middle-aged untreated subjects with normal kidney function. We did not find an association of uromodulin with eGFR. A trend of a higher uromodulin urine concentration was observed in subjects with the G allele of UMOD rs13333226.

IN VIVO FUNCTIONAL EVALUATION OF STIM1 AS A CANDIDATE GENE RESPONSIBLE FOR EXAGGERATED SYMPATHETIC RESPONSE TO STRESSES IN SHRSP: ESTABLISHMENT OF STIM1 KNOCK-IN SHRSP

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Objective: Increased activity of sympathetic nervous system is a possible mechanism related to development of severe hypertension in the stroke-prone spontaneously hypertensive rat (SHRSP). In the previous studies, we identified stromal interaction molecule 1 (Stim1) as a promising candidate gene responsible for the exaggerated sympathetic response to stresses in SHRSP. A nonsense mutation (p.Arg640X) was found in its coding sequence, resulting in expression of a truncated form of Stim1 and a decrease in store-operated calcium entry (SOCE) mediated by Orai1 or TRPC. In the present study, we generated Stim1 knock-in SHRSP (SHRSP-Stim1em1Kyo), in which the nonsense mutation was rescued by CRISPR/Cas9 system, to investigate whether Stim1 is a causative gene for hypertensive phenotype of SHRSP.

Design and method: SHRSP-Stim1em1Kyo was established by microinjection of gRNA, Cas9 mRNA and ssODN with target site sequence of rat Stim1 to embryos from SHRSP/Izm. SHRSP/Izm was used as control strain throughout the experiments. Cerebral astrocytes were cultured from newborn rats (1–3 days after birth) by a shaking method. The SOCE activity in the cultured astrocytes were evaluated by calcium imaging using Fluo-8 AM. Blood pressure (BP) was measured by tail-cuff method. Urine was corrected from a rat kept in a metabolic cage at room temperature/4°C for 6 h and urinary norepinephrine excretion (u-NE) was analyzed by HPLC in SRL (Tokyo, Japan). Changes in uNE with or without the cold stress was calculated as an indicator of sympathetic activity to the stress.

Results: Establishment of homozygous SHRSP-Stim1em1Kyo was confirmed by DNA sequencing and western blotting which showed expression of wild-type STIM1 protein in brainstem. The expression level in SHRSP-Stim1em1Kyo was significantly greater than that in SHRSP/Izm. Increased SOCE activity was found in astrocytes from SHRSP-Stim1em1Kyo compared with that from SHRSP/Izm. No significant differences were found in both SBP at 12, 16 and 20 weeks of age and changes in u-NE between the two strains.

Conclusions: Improvement of STIM1 function in SHRSP/Izm may not affect its sympathetic activity to the cold stress.

ASSOCIATION OF SERUM URIC ACID LEVELS WITH ARTERIAL STIFFNESS AND ENDOTHELIAL DYSFUNCTION IN A POPULATION OF NORMOTENSIVE TO EARLY-STAGE HYPERTENSIVE INDIVIDUALS

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Objective: Hyperuricemia appears to be associated with increased cardiovascular risk. Both accelerated vascular stiffness and endothelial injury caused by

increased oxidative stress have been postulated as contributing potential mechanisms. We investigated whether serum uric acid levels correlate with robust markers of arterial stiffness and endothelial dysfunction in a population of untreated individuals free from cardiovascular diseases, whose blood pressure ranged from normal to early-stage essential hypertension.

Design and method: Individuals free from cardiovascular comorbidities, who received no medication for any reason, were eligible to participate. Arterial stiffness was estimated by the carotid-femoral pulse wave velocity (PWV) measurement with applanation tonometry using the Sphygmocor device. Serum samples were drawn for the measurement of uric acid levels and other biochemical parameters. Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, was measured in serum samples using commercially available competitive enzyme-linked immunosorbent assay (ELISA) kit.

Results: A total of 241 individuals, 144 males and 97 females, with a mean age of 45.0 ± 11.2 years and mean systolic/diastolic blood pressure $138.8 \pm 18.4/88.7 \pm 12.0$ mmHg, participated in the study. Mean PWV was 7.9 ± 1.8 m/s, while serum uric acid and ADMA levels were 5.1 ± 1.4 mg/dl and 1.00 ± 0.39 mmol/l, respectively. Uric acid positively correlated with both PWV ($r = 0.152$, $p = 0.025$) and ADMA levels ($r = 0.141$, $p = 0.029$). After adjustment for other variables (age, gender, body mass index, HDL cholesterol, triglycerides, glomerular filtration rate) in the multivariate analysis for uric acid, an independent association between with ADMA levels was observed ($\beta = 0.200$, $p < 0.001$), whereas the association between uric acid and PWV was no longer significant.

Conclusions: In a population of untreated normotensive- to- early-stage hypertensive individuals, increased levels of uric acid are independently associated with endothelial dysfunction. On the other hand, the observed association between uric acid and arterial stiffness appears to be mediated by traditional cardiovascular risk factors. Uric acid might be implicated in the pathogenesis of cardiovascular diseases through endothelium-dependent mechanisms.

AN ANGIOTENSIN RECEPTOR BLOCKER, FIMASARTAN REDUCES VASCULAR SMOOTH MUSCLE CELL SENESENCE BY INHIBITING CYR61 AND ERK/P38MAPK/P53 SIGNALING PATHWAY

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Objective: Angiotensin II (Ang II) has been suggested to accelerate vascular senescence, however the molecular mechanism(s) remain unknown.

Design and method: We treated human coronary artery smooth muscle cells (hCSMCs) with Ang II and evaluated cellular senescence. We also evaluated the protecting role of Ang II type 1 receptor blocker (ARB), fimasartan.

Results: Senescence associated β -galactosidase (SA- β -Gal) positive cells significantly increased in Ang II-treated hCSMCs ($18.75 \pm 1.75\%$) compared with the control ($11.75 \pm 2.75\%$, $p < 0.05$). The effect of Ang II was significantly attenuated by pretreatment with fimasartan. Molecular markers related with cellular senescence, p53 and p16 expressions, were both significantly increased by Ang II (p53: 1.39 ± 0.10 , p16: 1.19 ± 0.06 fold vs control, both $p < 0.05$), which were completely suppressed by fimasartan (p53: 1.02 ± 0.07 , p16: 0.97 ± 0.07 fold vs control, both $p < 0.05$). Downstream molecules of Ang II type 1 receptor, cysteine-rich angiogenic protein 61 (CYR61) was rapidly and significantly induced by Ang II over 10 nM concentration (1.50 ± 0.17 fold vs control). In order to evaluate the effect of CYR61 on senescence, we transfected hCSMCs with adenoviral vectors expressing CYR61 (Ad-CYR61). Compared with a control, adenoviral vector expressing only green fluorescent protein (Ad-GFP) transfected hCSMCs, Ad-CYR61 transfected hCSMCs showed significantly increased SA- β -Gal positive cells ($33.0 \pm 3.1\%$ vs $9.5 \pm 1.3\%$, $p < 0.01$). Conversely, when we suppressed CYR61 expression by transfecting antisense CYR61 (Ad-AS-CYR61), Ang II-induced senescence was significantly decreased ($11.0 \pm 0.5\%$ vs $24.7 \pm 0.9\%$ in Ang II, $p < 0.01$). p53 expression by Ang II was significantly attenuated by Ad-AS-CYR61, whereas p16 expression was not regulated by CYR61 modulation. Lastly, we evaluated the signaling pathway above p53 and p16 by modulating ERK/p38 MAPK. Ang II significantly activated ERK1/2 and p38 MAPK, which was significantly blocked by fimasartan. ERK and p38 inhibition both regulated Ang II-induced CYR61 expression. However, p53 expression was only regulated by ERK1/2, whereas p16 expression was only attenuated by p38 MAPK.

Conclusions: In conclusion, Ang II induced vascular senescence by ERK/p38 MAPK – CYR61 pathway. And Ang II receptor blocker, fimasartan near completely protected Ang II induced vascular senescence.

CHANGES IN THE LEVEL OF LIPID AND INFLAMMATORY PARAMETERS AS PATHOGENETIC BASIS OF VASCULAR REMODELING IN PATIENTS WITH ARTERIAL HYPERTENSION AND METABOLIC DISORDERS

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Objective: To identify the relationship between inflammatory and lipid biochemical and structural parameters of vessel wall in patients with arterial hypertension (AH) and abdominal obesity (AO).

Design and method: 130 patients were included in the study and randomized into 2 groups. Group 1 included 77 subjects (mean age 47.39 ± 1.60 years) with AH degree I-III and AO. 53 subjects (mean age 47.29 ± 0.95 year) without metabolic disorders were involved in group 2 (control). The parameters of sphygmography and 24-hour blood pressure monitoring; biochemical parameters (total cholesterol, low-density lipoprotein cholesterol (LDL-cho), high-density lipoprotein cholesterol (HDL-cho), triglycerides (Tg), and inflammatory markers (homocysteine, hs-CRP, endothelin-1 and ceruloplasmin) were estimated.

Results: In group 1 there was revealed significant increase in sphygmography indices of arterial stiffness (pulse wave velocity (PWV) – normal value < 10 m/s and cardio-ankle vascular index (CAVI) – normal value = 9); as well as in mean 24-hour, mean daytime systolic BP (SBP) and in day time SBP variability. We detected significant increase in biochemical parameters (total cholesterol, LDL-cho, triglycerides level) and in inflammatory markers (homocysteine, hs-CRP, endothelin-1 and ceruloplasmin level), and decrease in HDL-cho compared to the patients of group 2.

In group 1 there were registered positive correlations between lipid and inflammatory markers with parameters of sphygmography and metabolic disorders (PWV, CAVI with LDL-cho, homocysteine, hs-CRP, endothelin-1, ceruloplasmin, body mass index and waist circumference).

In group 1 initially elevated levels of inflammation markers and lipid profile parameters revealed by Neural Networks method may predict a significant increase in the stiffness of vascular wall (predictive accuracy – 76.4%; sensitivity – 78.2%; specificity – 70.5%).

Conclusions: Changes in the level of atherogenic fractions of lipids and inflammation markers can be a pathogenetic link in the development and progression of the vascular wall stiffness, determining the development of cardiovascular complications.

THE RELATIONSHIP BETWEEN LEVELS OF ALDOSTERONE, ESTRADIOL AND SERUM MARKERS OF ENDOTHELIAL DYSFUNCTION IN HYPERTENSIVE WOMEN

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Objective: To study the relationship between plasma levels of aldosterone, estradiol and serum markers of endothelial dysfunction (ED) such as stable nitric oxide metabolites NO₂-+NO₃- (NOx), endothelin-1 (ET-1), homocysteine (HC), von Willebrand factor (vWF) in nondiabetic women with essential hypertension (EH).

Design and method: We examined 79 hypertensive, nondiabetic women (mean age 51.4 ± 6.5 y, mean EH duration 8.5 ± 7.6 y). 28% of the group were smokers, 54% were obese, 76% - with dyslipidemia. Regular menstrual function had 30% of the women, the rest of the group – postmenopausal (median duration of postmenopause was 5.7 ± 3.5 y). Circulating NOx levels were studied by spectrophotometry, ET-1, HC, vWF levels – by immunoenzyme assay, aldosterone and estrogen levels – by immunoenzyme assay. Statistical analysis was done using the Statistica 10.0 software.

Results: We compared the levels of ED markers in women with a normal (56%), and elevated levels of aldosterone (44%), as well as in women with a normal (62%) and low levels of estradiol (38%). Women with hyperaldosteronemia had higher concentration of NOx (45.3 ± 17.6 and 38.8 ± 16.5 mmol/l, respectively, $p < 0.05$), E-1 (1.4 ± 1.1 and 0.9 ± 0.8 fmol/l, respectively, $p < 0.05$) and vWF (1.6 ± 0.8 and 1.3 ± 0.9 mg/dl, respectively, $p < 0.05$). Aldosterone levels correlated with NOx ($r = 0.36$, $p < 0.05$), E-1 ($r = 0.3$, $p < 0.05$) and vWF ($r = 0.34$, $p < 0.05$) levels. Women with hypoestrogenemia had higher NOx (46.3 ± 16.9 and 37.5 ± 16.0 mmol/l, respectively, $p < 0.05$), E-1 (1.5 ± 1.1 and 0.8 ± 0.4 fmol/l, respectively, $p < 0.05$) and vWF (1.6 ± 0.9 and 1.2 ± 0.7 mg/dl, respectively, $p < 0.05$) levels as well. Estradiol levels correlated with NOx ($r = -0.6$, $p < 0.05$) and vWF ($r = -0.5$, $p < 0.05$) levels.

Conclusions: Our results suggest that women in perimenopausal period demonstrate hormonal disorders with elevation of aldosterone level and decline of estrogen levels.

gen level, which are related to the increase of a number of substances considered as the markers of endothelial dysfunction.

SUBSTANTIAL VARIABILITY ACROSS INDIVIDUALS IN THE VASCULAR RESPONSE AND NUTRIGENOMIC RESPONSE TO AN ACUTE INTAKE OF CURCUMIN: A RANDOMISED CONTROLLED TRIAL

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Objective: Curcumin exerts biological activities of interest in cardiovascular prevention. However, its vascular protective effect is still poorly investigated in humans. The present study aims to assess vascular effects of an acute intake of curcumin and its nutrigenomic impact in circulating immune cells.

Design and method: In a randomised, double-blind, crossover design, eighteen healthy smokers consumed a placebo or a 5-gram of curcumin. Before and two hours after the intake, vascular function measurements were performed by using flow-mediated dilation (FMD). In addition, endothelial function in the microcirculation and blood pressure were evaluated. Plasma curcumin concentrations and changes in gene expression in peripheral blood mononuclear cells (PBMC) were analysed.

Results: No significant effect of curcumin on FMD was observed when considering the entire study population ($p = 0.08$), mainly due to a high inter-individual variability. Interactions were found for gender and risk score, but not for plasma curcumin concentration, to explain this variability. A subgroup analysis according to the gender or the cardiovascular-risk score revealed a significant effect of curcumin on FMD in women ($\delta = 2.07 \pm 2.59\%$, $p < 0.001$) and in subjects presenting lower cardiovascular risk ($\delta = 1.45 \pm 0.97\%$; $p < 0.001$). Pulse pressure decreased significantly in men ($\delta = -5.06 \pm 7.21$ mmHg, $p = 0.009$) and in subjects presenting higher cardiovascular risk ($\delta = -4.81 \pm 4.54$ mmHg, $p = 0.04$). No change in gene expression was observed when data were analysed for all volunteers but changes in expression were observed when analyzed according to gender.

Conclusions: This clinical trial highlights that a substantial variability in efficacy of curcumin exists across individuals, with potential positive effects on endothelial function and pulse pressure.

THE EFFECT OF STATIN THERAPY ON MONOCYTE SUBPOPULATIONS IN PATIENTS WITH ARTERIAL HYPERTENSION AND OBESITY

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Objective: Association of arterial hypertension with obesity is an acknowledged risk factor of the development of coronary artery disease (CAD). Statins represent golden standard of management dyslipidemia in these patients. One of the mechanisms linking arterial hypertension, obesity and atherosclerosis is a low-grade inflammation. Recently it had been shown that minor subpopulations of monocytes with phenotype CD14loCD16+ and CD14+CD16+ are highly proatherogenic. The objective of the study was to evaluate influence of statins on composition of monocyte population in obese patients with arterial hypertension.

Design and method: A total number of 16 patients (7 men, 9 women; age 58.5 (54.8; 62.5) years; body mass index 30.9 (29.1; 32.8)) were recruited in the study. Among them 9 patients received statin therapy (atorvastatin in 7 patients (mean dose 18.6 mg); rosuvastatin in 2 patients (mean dose 10 mg)); 7 patients did not take statins. Lipid profile was determined by standard method, including measurement of total cholesterol, triglycerides, low density lipoproteins cholesterol (LDL-C) concentrations, and calculation of high density lipoproteins cholesterol (HDL-C) concentration and LDL/HDL ratio. Numbers of classical CD14hiCD16lo, non-classical CD14loCD16+ and intermediate CD14+CD16+ monocytes were determined by flow cytometry.

Results: Statin therapy allowed to obtain target values of LDL-C in the majority of patients in the study (2.9 (2.5; 3.4) mM vs. 3.6 (3.1; 4.3) mM in patients who did not take statins). Patients receiving statin therapy were characterized by lower numbers of CD14loCD16+ monocytes (5.4 (3.6; 8.1)% vs. 10.9 (8.5; 18.3)%; $p = 0.016$) and higher frequency of CD14hiCD16lo monocytes compared to patients without

statins in the course of medication (89.4 (82.9; 92.3)% vs. 79.3 (73.8; 84.4)%; $p = 0.023$). No differences were revealed in numbers of CD14+CD16+ monocytes. In total group of patients we revealed negative association between numbers of CD14loCD16+ monocytes and LDL-C concentrations in women, but not in men ($r = 0.857$; $p = 0.014$).

Conclusions: Statin therapy in patients with arterial hypertension and obesity is associated with low numbers of proatherogenic CD14loCD16+ monocytes and higher frequency of classical CD14hiCD16lo monocytes, which may be related to lipid-lowering effects of statins.

COMPARATIVE PROTEOMIC ANALYSIS IN MICRODISSECTED RENAL VESSELS OF HYPERTENSIVE AND NORMOTENSIVE RATS

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Objective: Systemic hypertension has a profound impact on the renal vascular physiology and functionality. Our goal was to identify the biological pathways and macromolecules of the renal arteriolar wall, which are involved with the development of hypertension.

Design and method: Tissue derived exclusively from renal vessels of 4 Spontaneously Hypertensive Rat (SHR) and 4 normotensive controls (Wistar Kyoto, WKY) at 20 weeks using Laser Capture Microdissection on 14 micrometer cryosections was used. High sensitivity proteomic analysis was performed in the microdissected homogenized material in order to detect early molecular alterations associated with hypertension of the renal vessels before the onset of vascular damage.

Results: Proteomic analysis revealed 688 proteins; 550 proteins were found in both groups, of which 58 proteins were differentially expressed (15 proteins were up-regulated and 43 proteins were down-regulated in SHR). 71 proteins were found exclusively in control WKY rats and 67 exclusively in SHR rats. Pathway enrichment analysis revealed 114 and 111 pathways in WKY and SHR, respectively and 106 common pathways in both groups. Many of the interesting differentially expressed proteins identified in our study are relevant to vascular tone regulation. Thus proteins involved with NO and vasodilation and affecting eNOS include Xaa-Pro aminopeptidase 1 (XPP1), N(G) N(G)-dimethylarginine dimethylaminohydrolase 1 (DDAH1), Dehydropteridine reductase (DHPR), whereas proteins involved with blood pressure regulation by the renin-angiotensin system include Glutamyl aminopeptidase/Aminopeptidase A (AMPE) and Aminopeptidase N (AMPN). Moreover, pathway enrichment analysis revealed that the eNOS activation pathway is dysregulated only in the hypertensive SHR animals.

Conclusions: Our study demonstrates that hypertension causes early proteomic changes in the renal vessels of SHR compared to WKY. These changes are relevant to vascular tone regulation and consequently may be involved in the development of vascular damage and hypertensive nephrosclerosis. Further studies are required to explore whether these pathways and molecules are involved with hypertensive nephrosclerosis and to identify components that could be considered new therapeutic targets

RELATIONSHIP BETWEEN LYMPHANGIOGENESIS, TISSUE MACROPHAGES EXPRESSION AND SUBCUTANEOUS SODIUM CONCENTRATION: EFFECTS OF HYPERSODIC AND HYPOSODIC DIET IN A NORMOTENSIVE RAT

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Objective: Salt retention is a condition associated with a mild inflammatory state. Recent researches pointed out the skin as central regulator of sodium balance besides the traditional "nephrocentric view". Hypertonic skin sodium storage is associated with osmotic and immunological dysregulation expressed by activation of tonicity-sensing pathways in macrophages, stimulation of lymphangiogenesis facilitating skin sodium clearance. The aim of this study is to evaluate in a model of normotensive rat the effect of two different dietary sodium regimens on the interstitial sodium levels, lymphangiogenesis and tissue macrophages expression.

Design and method: Two groups of normotensive rats (Wistar Kyoto) were fed for three weeks with two different dietary regimens, respectively, High Salt Diet (HSD, NaCl 8%) and Low Salt Diet (LSD, NaCl 0.08%). Interstitial subcutaneous sodium concentration was measured by microdialysis procedure. Tissue evaluation of Macrophage component, endothelial and lymphatic capillary density was

evaluated by Immunohistochemistry analysis. Macrophage was detected by anti CD-68 antibodies, vascular endothelial structures revealed by von Willebrand Factor antibodies and the lymphatic elements by Podoplanin (D2-40) antibodies.

Results: There was no significant difference between interstitial sodium concentration and sodium plasma levels (144mmol/L vs 146 mmol/L).

Histological differences were found in the two groups (HSD and LSD): measurements of lymphatic podoplanin (D2-40) component and endothelial structures were different (average of vessels number per mm2 (D2-40: HSD 3,90 vs LSD 2,08; von-Willebrand: HSD 6,04 vs LSD 4,62). Similarly, macrophage population average of number of cells per mm2 area was higher in HSD (CD 68+: 6,90) vs LSD (CD68+:5,65).

Conclusions: The effect of an high salt dietary intake bursts an inflammatory response supporting the idea that interstitial tonicity variations may be related to macrophage activation and, consequently, lympho-endothelial expression. HSD did not lead to any difference in interstitial sodium concentration assuming an adequate ability in drainage of skin sodium excess in a model of normotensive rat.

INCREASED HDL CHOLESTEROL LEVELS RELATE TO ENDOTHELIAL GLYCOCALYX INTEGRITY IN OLDER TREATED PATIENTS WITH ESSENTIAL HYPERTENSION

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Objective: Endothelial dysfunction indicates 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 (CVD). We aimed to investigate the role of increased HDL cholesterol levels (HDL-C), which usually are considered protective against cardiovascular disease, in endothelial glycocalyx integrity in older healthy hypertensive patients.

Design and method: One hundred-twenty (120) patients with arterial hypertension under treatment (mean age 66+9 years, females) and no history of previous cardiovascular disease were divided regarding HDL-C tertiles in two groups. In group HDLH, HDL-C was > 71 mg/dl (upper HDL-C tertile, n = 41, mean age 67+10 years, 6males). In group HDLL, HDL-C was < 71 mg/dl (two lower HDL-C tertiles, n = 79, mean age 66+9 years, 45 males). Increased perfusion boundary region (PBR) of the sublingual arterial microvessels (ranged from 5–9 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, central and brachial systolic and diastolic BP as well as PP, smoking habit, LDL-C levels and PWV. PBR 5–9 was significantly decreased in group HDLH (p = 0.04). In the whole population, HDL-C was inversely related with PBR 5–9 (r = -0.22, p = 0.01). In a multiple linear regression analysis model, using age, BMI, smoking habit, HDL-C, LDL-C and office SBP, as independent variables, we found that BMI (Beta = 0.25, p = 0.006) independently predicted PBR 5–9 in the whole population.

Conclusions: We found that endothelial function, represented by EG levels, seems to be protected even in older hypertensive patients with extremely increased HDL-C levels and no history of cardiovascular disease. The possible role of EG, as a novel cardiovascular risk index in essential hypertension, needs to be further evaluated.

CR6 INTERACTING FACTOR 1 DEFICIENCY PROMOTES ENDOTHELIAL INFLAMMATION BY SIRT1 DOWNREGULATION

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Objective: CR6 interacting factor 1 (CRIF1) deficiency impairs mitochondrial oxidative phosphorylation complexes, contributing to increased mitochondrial and cellular reactive oxygen species (ROS) production. CRIF1 downregulation has also been revealed to decrease sirtuin 1 (SIRT1) expression and impair vascular function. Inhibition of SIRT1 disturbs oxidative energy metabolism and stimulates nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)-induced inflammation.

Design and method: Therefore, we hypothesized that both CRIF1 deficiency-induced mitochondrial ROS production and SIRT1 reduction play stimulatory roles in vascular inflammation.

Results: Plasma levels and mRNA expression of proinflammatory cytokines (tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6) were markedly elevated in endothelium-specific CRIF1-knockout mice and CRIF1-silenced endothelial cells, respectively. Moreover, CRIF1 deficiency-induced vascular

adhesion molecule-1 (VCAM-1) expression was consistently attenuated by the antioxidant N-acetyl-cysteine and NF-κB inhibitor (BAY11). We next showed that siRNA-mediated CRIF1 downregulation markedly activated NF-κB. SIRT1 overexpression not only rescued CRIF1 deficiency-induced NF-κB activation but also decreased inflammatory cytokines (TNF-α, IL-1β, and IL-6) and VCAM-1 expression levels in endothelial cells.

Conclusions: These results strongly suggest that CRIF1 deficiency promotes endothelial cell inflammation by increasing VCAM-1 expression, elevating inflammatory cytokines levels, and activating the transcription factor NF-κB, all of which were inhibited by SIRT1 overexpression.

ATHEROSCLEROSIS PROGRESSION IN PATIENTS WITH BREAST CANCER IN THE SHORT-TERM PERIOD: THE EFFECT OF LIPOPROTEIN (A)

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Objective: The cardiovascular care of patients who have cancer, have received broad attention. Inflammatory status associated with malignancies and promoted atherosclerosis during cancer therapies have been established. Lipoprotein (a) [Lp(a)] is a proven risk factor for atherosclerosis (AS) progression. Lp(a) blood level is quite stable during proinflammatory conditions. We aimed to evaluate the association between Lp(a), IgM and IgG autoantibodies against apoB100-containing lipoproteins and its Cu2+ oxidized (ox) modifications with the progression of carotid AS in patients with breast cancer after 6 months of cancer therapy.

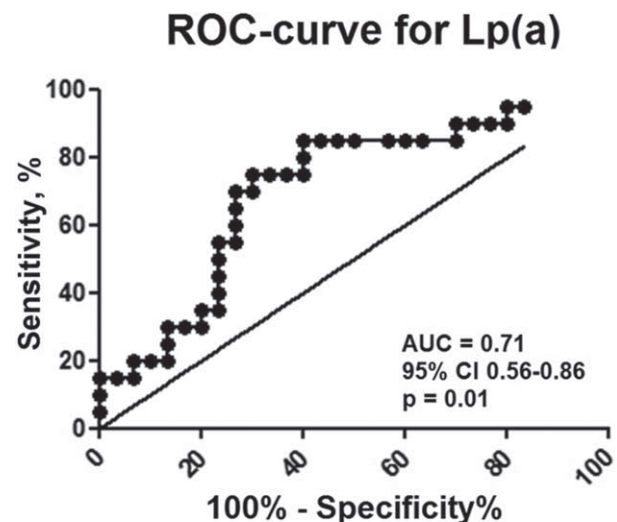


Figure 1. ROC-curve for Lp(a) plasma level.

Design and method: 50 women with newly diagnosed breast cancer (HER2-positive, stage II-III), mean age 50 (40;57) years were enrolled. Lipid profile, serum Lp(a), IgM and IgG autoantibodies against Lp(a) and low density lipoprotein (LDL) or oxLp(a) and oxLDL were assessed before the onset of neoadjuvant cancer therapy with trastuzumab, paclitaxel, doxorubicin, cyclophosphamide. Carotid intima-media thickness (CMT), the percentage of stenosis of the common carotid (CCA) and internal carotid (ICA) arteries was analyzed at baseline and after 6 months. New stenosis > 20% or increase of preexisting stenosis > 5% of carotid arteries was considered as AS progression. CMT increase was considered at > 0.1 mm.

Results: AS progression was revealed in 25 (50%) patients; CMT increase was observed in 20 (40%) patients. Patients with CMT increase had the higher values of Lp(a) concentrations at baseline (18.8 mg/dl (11.2;32.6) against 5.6 mg/dl (3.7;17.9), p = 0.01). Lp(a) plasma level above 11.5 mg/dl was a risk factor for CMT increase (OR 6.0 (1.7;21.2), p = 0.005; AUC 0.71 (95% CI 0.56–0.86, p = 0.01, figure 1). The conventional risk factors (age, BMI, arterial hypertension, smoking) as well as the plasma levels of total cholesterol, LDL, triglycerides, IgM and IgG autoantibodies against Lp(a), LDL or its oxidized modification did not possess the prognostic value for carotid AS progression in this 6-month study.

Conclusions: We speculate that Lp(a) level above 11.5 mg/dl in HER2+ breast cancer patients may indicate a predisposition to the progression of atherosclerosis in the short-term period of cancer treatment.

VASCULAR EFFECTS OF ANTI-CANCER CISPLATIN THERAPY

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Objective: Cisplatin-containing chemotherapy is an effective cure for the majority of men with testicular cancer. However, patients treated with cisplatin are at increased risk of cardiovascular events. It is not clear whether this reflects primarily early direct vascular toxicity, or a latent pro-atherogenic state. We hypothesised that cisplatin-containing chemotherapy induces acute endothelial injury and a prothrombotic state.

Design and method: We conducted a prospective study of patients with testicular cancer who attended the Beatson West of Scotland Cancer Centre. Patients were recruited into 3 groups according to management: (1) surveillance, (2) 1–2 cycles of adjuvant cisplatin-containing chemotherapy (3) 3–4 cycles of curative cisplatin-containing chemotherapy. Patients attended 6 visits over 9 months, each visit including an assessment of endothelial function by % flow-mediated dilatation (FMD) and collection of venous blood for analysis. Visit 1 was < 8 weeks following orchidectomy, visit 2 was < 24 hours after initial cisplatin cycle and subsequent visits were at 6 weeks, ³months, ⁶months and 9 months.

Results: 26 patients were recruited between January 2016 and August 2017. 9 patients were managed with surveillance, ⁷received 1–2 cycles of cisplatin and 10 received 3–4 cycles of cisplatin. In all patients receiving cisplatin, % FMD reduced from 15.0 ± 1.2 to 10.8 ± 0.7 within 24 hours ($p = 0.01$). On subsequent visits, % FMD was not significantly different from baseline. Serum cholesterol increased from 5.5 ± 0.2 to 7.2 ± 0.5 mmol/L at 6 weeks after receiving 3–4 cycles of cisplatin ($p = 0.01$). There was a trend to increasing serum triglycerides after cisplatin-containing chemotherapy.

Conclusions: Cisplatin-containing chemotherapy is associated with acute endothelial toxicity that recovers within 6 weeks, hypercholesterolaemia and a trend to hypertriglyceridaemia. Our observations may explain some of the early prothrombotic effects of cisplatin. These data should help define therapeutic strategies to prevent short- and long-term adverse vascular effects of cisplatin-containing chemotherapy.

GENE INTERACTIONS OF ALPHA-ADDUCIN AND LANOSTEROL SYNTHASE IMPACT RENAL IMPAIRMENT IN SALT SENSITIVE HYPERTENSION

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Objective: The genes involved in the development of renal damage and salt sensitive hypertension (SS) are unknown. Renal impairment is considered to be the major determinant of salt sensitive hypertension.

Design and method: We explored the roles of alpha-adducin (ADD1) and lanosterol synthase (LSS), genes coding for structural proteins of the cell membrane and Endogenous Ouabain (EO), respectively, on renal Na handling and their genetic interactions in a large cohort of naïve hypertensive patients (NHP) whose salt sensitive phenotype was characterized.

Acute saline load (NaCl 308 mEq/2 h e.v.) was performed in 774 NHP (age 44.95 ± 9.61 years), and functional and hormone renal parameters were tested.

Results: Under baseline conditions NHP carriers of the LSS AA genotype showed lower GFR ($n = 68$, 115.7 ± 4.6 ml/min) compared to LSS C carriers (124.6 ± 1.4 ml/min, $p = 0.066$). After an acute saline test, GFR increased in both groups, while the urinary volume and urinary creatinine were lower in LSS AA. Analysis of gene*gene interactions demonstrated that NHPs carrying both mutated GT ADD1 and homozygous for LSS C variants excreted the sodium load more rapidly than their ADD1*LSS mutated variants. On the other hand, an additive ($p = 0.003$) effect of ADD1 GT & LSS AA variants on the pressure-natriuresis relationship was observed, with a significant right shift along the x axis. Finally, circulating EO was modified according to the LSS variant: in SS LSS AA, EO rose significantly during the recovery while in SR LSS AA, EO was suppressed as were aldosterone and PRA.

Conclusions: The results demonstrate: 1. NHPs carrying the LSS AA genotype have reduced GFR under basal conditions; 2. Salt Sensitive LSS AA are EO non-modulators, since their circulating EO does not decline under circumstances

where the RAAS is suppressed; 3. The ADD1*LSS interaction identifies those NHPs with impaired renal Na handling.

ASSESSMENT OF THE CENTRAL HAEMODYNAMIC PARAMETERS DURING OESTROGEN-PROGESTERONE THERAPY IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Objective: It is known that women with polycystic ovarian syndrome (PCOS) or those during oestrogen-progesterone (OE-P) therapy can have impaired endothelial dysfunction. In two precedent studies we found a difference between augmentation index (AIx) observed and normal value, among patients with PCOS without OE-P therapy and those with OE-P therapy without PCOS: 6.3 and 7.3, respectively. This study was conducted to evaluate the response of the central haemodynamic parameters (CHP) in two groups of women with PCOS: during OE-P therapy and those without OE-P therapy.

Design and method: METHODS: In a retrospective cross-sectional study two groups of women with PCOS (58) were registered: 25 (average age 30) during OE-P therapy (average months of therapy 42) and 33 (average age 33, $p = 0.3$) without OE-P therapy and never treated. The CHP were assessed non-invasively by a SphygmoCor device (Atcor-Sydney, Australia), was made according to method's standard such as: Central Aortic Pressure (CAP), End-Systolic Pressure (ESP), Main Arterial Pressure (MAP), Pulse Pressure (PP), Augmentation Pressure (AP), and AIx. The AIx was evaluated in correlation to age in each patient. Body mass index in the groups with/without OE-P therapy was $27.3/31.4$ ($p = 0.06$). Tobacco consumption among women with/without OE-P was 44%/15%, respectively.

Results: Among women with OE-P therapy observed values of CAP, ESP, MAP, PP, AP were lowest than women without therapy. Systolic and diastolic pressure, and heart rate among women with OE-P therapy were lowest too. All the preceding values did not reach a statistically significant difference. Among women without OE-P therapy the highest values of CHP could be explained by the body weight highest. Interestingly, the difference measure between AIx observed and AIx normal value, according to age, between women with/without OE-P therapy ($8.5/6.6$) reached a statistically significant difference ($p = 0.05$). Women with PCOS during OE-P therapy presented AIx significantly highest than those without therapy, could be explained by the action of both factors on endothelium.

Conclusions: CONCLUSIONS: The OE-P therapy in women with PCOS increased the AIx, as a measure of peripheral vascular disease state, that could be an additional cause to develop hypertension in young women.

ASSOCIATION OF ENDOTHELIAL DYSFUNCTION IN MICROCIRCULATION USING LASER SPECKLE CONTRAST ANALYSIS WITH MARKERS OF ARTERIAL STIFFNESS

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Objective: Endothelial dysfunction has a key role in microcirculation promoting very early structural and vascular alterations that precede any clinically detectable vascular damage and contribute to the pathogenesis of hypertension. Small artery alterations though are interdependent with large artery lesions and interact in a vicious cycle that sustains and exaggerates vascular damage. It has been speculated that a common denominator in that cross-talk between micro- and macrocirculation is endothelial dysfunction. In this study we evaluated the association of endothelial dysfunction of skin microcirculation using Laser Speckle Contrast Analysis (LASCA) with central blood pressures (cBP) as recorded with the Mobil-O-Graph device, in treatment-naïve hypertensive patients.

Design and method: We studied a group of 31 untreated, hypertensive patients with new-onset essential hypertension, without cardiovascular comorbidities, mean age 50.3 ± 18.5 years. Central BPs were recorded in all subjects using the Mobil-O-Graph NG (IEM, Stolberg, Germany) device. In addition, microvascular blood flow of the skin forearm was evaluated using LASCA (PeriCam PSI NR System, Perimed Järfälla, Sweden). Results of microvascular flow are expressed as baseline Cutaneous Vascular Conductance (CVC), peak CVC and peak CVC minus baseline CVC. Pearson's and Spearman's correlations were used, based on the variable's normality of distribution.

Results: We observed a significant negative correlation between peak CVC and 24-hour cBP ($r = -564$ for central systolic BP [cSBP], $r = -458$ for central diastolic BP [cDBP]), day cSBP ($r = -560$), day cDBP ($r = -466$) and night cSBP ($r = -457$)

($p < 0.05$). In addition, peak CVC minus baseline CVC showed a significant negative correlation with all cBP parameters ($p < 0.05$). Baseline CVC showed a significant negative correlation with 24-h cSBP ($r = -482$) and day cSBP ($r = -488$) ($p < 0.05$).

Conclusions: A significant inverse relationship was revealed between most central BP parameters and markers of endothelial dysfunction of skin microcirculation in treatment-naïve patients with new onset essential hypertension. In this group of patients, the endothelial dysfunction of skin microcirculation may be already associated with a higher central hemodynamic load although the exact cause and effect relationship of this bidirectional communication between small and large arteries has not been fully elucidated yet.

THE SEVERITY OF INFLAMMATORY PROCESS AS A RISK FACTOR OF CARDIOVASCULAR COMORBIDITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: The aim of the study was to evaluate the association of the markers of inflammation and coexisting cardiovascular pathology in patients with rheumatoid arthritis

Design and method: 620 patients with RA (diagnosis according to ACR /EULAR) from the rheumatology in-patient clinic with the mean age of 43.4 ± 10 ; 95.4 % ACCP – positive patients, activity on DAS (Disease Activity Score) 28 II, III; 85.4 % female with the disease duration for about 3–15 years were enrolled in the trial. We assessed the level of IL-1 with the use of ELISA.

Results: The constructed model surfaces indicated the interdependence of IL-1, the activity of DAS 28 and the level of LDH in RA patients. The correlative and regressive analysis of the results showed the statistically significant correlation of TG, LDG, SBP and markers of inflammation IL-1, DAS 28: $p = 0.627$ ($p < 0.01$), $p = 0.527$ ($p < 0.01$), $p = 0.712$ ($p < 0.01$), $p = 0.776$ ($p < 0.01$), $p = 0.544$ ($p < 0.01$), $p < 0.514$ ($p < 0.01$) accordingly. The correlation coefficient between hs-CRP and the indicators of the lipid profile revealed similar interconnections.

Conclusions: According to the results of modeling, disease activity on DAS 28 and markers of inflammation (IL-1 and hs-CRP) as a markers of the severity of inflammatory process in RA patients are risk factors for developing atherosclerosis and AH. The analysis of inflammation indicators in RA patients allows to assess the risk of developing and progressing atherosclerosis and AH. The data enables to select the best possible personified therapy for such patients at the early stage of the disease.

POSTER SESSION

LATE-BREAKER POSTERS: SESSION 1

EYES ON HYPERTENSION: SEVERE MICROVASCULAR RETINAL DYSFUNCTION IN HYPERTENSIVE PATIENTS FAILING TO ACHIEVE BLOOD PRESSURE TREATMENT TARGETS

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Objective: Endothelial dysfunction is crucial in the development, progression, and prognosis of cardiovascular diseases. Small studies in restricted collectives have pointed toward altered retinal endothelial impairment in uncontrolled essential hypertension. There has been no dedicated study to hypertensive patients to this point in time. It was, thus, the aim of this study to evaluate retinal vessel endothelial function - an easily assessable vasculature - in patients with hypertension and evaluate it against structural and functional gold standards.

Rationale: To investigate micro- and macrovascular function in hypertensive patients who have not achieved blood pressure (BP) treatment goal.

Materials & Methods: 80 patients with ill-controlled hypertension (median age $69 \pm \text{IQR} = 15$ years, mean systolic BP $150.4 \pm \text{SD} = 11.4$ mmHg, diastolic BP 91.1 ± 9.4 mmHg) were prospectively recruited. 74 healthy individuals (HC) without any cardiovascular risk factors served as controls (age 56 ± 28 years, systolic BP $122.2 \pm \text{SD} = 9.9$ mmHg, diastolic BP 76.2 ± 7.1 mmHg). Microvascular retinal endothelial function was measured via dynamic retinal vessel analysis (DVA). This non-invasive technique measures mainly NO-dependent flicker light-induced dilatation of retinal arteries (FID). Other vascular outcome measures include retinal arteriovenous ratio (AVR), flow-mediated dilatation (FMD), and pulse-wave velocity (PWV), as well as analysis (PWA, Augmentation index, aortic blood pressure). To account for imbalanced possible confounders (age, sex, body mass index, LDL cholesterol, and fasting plasma glucose), an inverse probability weighted analysis (propensity score) was employed (R 3.4.3, package CBPS). Generalized linear models were used to test group differences in weighted models. Survey means and robust standard errors are reported for weighted analyses.

Results: Arterial retinal vascular function (FID) was significantly impaired in patients with ill controlled hypertension (HTN) compared to HC (mean FID $2.77 \pm 0.24\%$ vs. $3.86 \pm 0.24\%$, $p = 0.001$). Also, post-flicker constriction was found reduced in HTN ($2.77 \pm 0.24\%$ vs. $3.86 \pm 0.24\%$, $p = 0.046$). Static retinal vascular analysis revealed significantly ($p = 0.001$) lower AVR in HTN (0.818 ± 0.008 vs. 0.854 ± 0.007 , $p = 0.001$). PWV was significantly increased in HTN compared to HC (PWV 7.2 ± 0.2 ms⁻¹ vs. 8.7 ± 0.3 ms⁻¹, $p < 0.001$). Augmentation index at 75/min heart rate was 22.2% in HC versus 25.3 $\pm 1.5\%$ in HTN ($p = 0.045$). PWV correlated negatively with FIDart ($r = -0.24$, $p = 0.003$). FMD was reduced ($5.66 \pm 0.35\%$ vs. $6.23 \pm 0.42\%$) yet not significantly so ($p = 0.3$). Interestingly, FMD exhibited the often-reported negative correlation with vascular baseline diameter ($r = -0.45$, $p < 0.001$) but FID did not exhibit such a correlation ($r = -0.02$, $p = 0.84$). 61% of HTN (49/80 patients) received no drug therapy at examination, 3% received 3 or more antihypertensive drugs. Balance for potential confounders was achieved (maximum standardized mean difference 0.18 for LDL; sufficient overlap).

Discussion & conclusions: Our results demonstrate profound alterations in microvascular function of patients with hypertension. Whether these results have clinical or prognostic impact needs to be carefully evaluated in further clinical studies.

BLOOD PRESSURE CONTROL, TREATMENT AND THERAPEUTIC ADHERENCE IN HYPERTENSION, NON-VALVULAR ATRIAL FIBRILLATION AND ORAL ANTICOAGULANT TREATMENT TAO-PRES PROJECT

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Objective: To analyze the degree of blood pressure control in patients over 65 years, with hypertension (HT), non-valvular atrial fibrillation (NVAf) and oral anticoagulant therapy (OAC) in Primary Care (PC).

To analyze the clinical profile in this type of patients, coexistence with other cardiovascular risk factors (CVRf), differences by gender and age, as well as possible determinants of blood pressure control.

Design and method: Multicenter, descriptive, transversal, retrospective study. Tree urban and one rural PC centers collaborated in the project. All patients attended in any of the centers over 65 years, with diagnoses HT, NVAf and OAC were included. A systematic review of computerized medical history was made, taking anthropometric and analytical measurements, office blood pressure measurement, pharmacotherapy, risk scales and pharmacotherapeutic adherence.

Results: 1038 patients were included. Women 54.7%. The mean age was 81.4 years (SD 7.1), mean body mass index (BMI) 28.7 (SD 5.4), smoking 4.8%, enolism 5%, sedentary lifestyle 35.4%, cognitive impairment 12.3%. Coexistence with other CVRF: dyslipemia 53.7%, diabetes 30.2%. Target organ injury: Nephropathy 32.8%, left ventricular hypertrophy 20.1%, peripheral artery disease 8%. Cardiovascular events: stroke 19.8%, coronary heart disease 16.3%, heart failure 26.7%. Mean systolic blood pressure (SBP) 132.6 (SD 13.4), mean diastolic blood pressure (DBP) 74.4 (SD 9.2). Controlled blood pressure (BP) in 66.7% of patients according to global mean measurements, in 54.7% according to total registered measurements. Statistically significant differences: mean age of patients with controlled BP (82.1) vs uncontrolled BP (78.4) $p = 0.0001$; mean BMI of controlled patients (28.5) vs uncontrolled (29.4) $p = 0.04$; % diabetic patients controlled (74.5) vs uncontrolled (25.5) $p = 0.005$. The number of drugs was significantly higher in DM ($p = 0.005$), coronary heart disease ($p = 0.002$) and heart failure ($p = 0.001$). Most prescribed drugs were acenocumarol (65.7%) and beta blockers (43.5%). The overall pharmacotherapeutic adherence rate was significantly higher in women ($p = 0.003$) and nephropathy ($p = 0.001$).

Conclusions: The degree of blood pressure control was high respect to mean blood pressure measurements but suboptimal respect to total measurements. There is a high coexistence with other CVRF. Blood pressure control was better in older patients, lower BMI and DM.

SUBTYPES OF MASKED HYPERTENSION AND THEIR ASSOCIATIONS WITH TARGET ORGAN DAMAGE IN UNTREATED CHINESE PATIENTS

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Objective: Masked hypertension is office normotension in the presence of ambulatory hypertension, which can be subdivided into isolated daytime, isolated nighttime or day-night hypertension. However, no previous studies contrasted the subtypes of masked hypertension in their associations with target organ damage.

Design and method: Consecutive untreated patients referred for ambulatory blood pressure (BP) monitoring to our Hypertension Clinic were recruited. The cutoff values for daytime and nighttime hypertension were a BP of 135/85 mmHg and 120/70 mmHg, respectively. Measures of target organ damage, including left ventricular mass index (LVMI), carotid-femoral pulse wave velocity (cfPWV) and urinary albumin-to-creatinine ratio (ACR), were determined.

Results: The 1808 participants (mean age, 51 years; women, 52%) included 30.4% normotensive subjects, and 37.2% with masked hypertension, among whom 18% had isolated daytime hypertension, 12% isolated nighttime hypertension, and 70% day-night hypertension. After multivariate adjustment, patients with isolated daytime hypertension (7.9 vs 7.5 m/s, $P = 0.003$) had higher cfPWV than normotensive subjects. While patients with isolated nocturnal hypertension (0.79 vs 0.58 mg/mmol, $P = 0.002$) had higher urinary ACR than normotensive subjects. Patients with masked day-night hypertension had consistently higher cfPWV (7.8 vs 7.5 m/s, $P < 0.001$) and urinary ACR (0.74 vs 0.58 mg/mmol, $P < 0.001$) than normotensives. For LVMI, no difference ($P > 0.11$) between any subtypes of masked hypertension and normotension was observed.

Conclusions: Masked hypertension was prevalent in this untreated outpatient cohort. Masked daytime hypertension was associated with arterial stiffness while nighttime hypertension was associated with kidney damage and day-night hypertension with both target organ measures.

HOME BLOOD PRESSURE MONITORING AND E-HEALTH: INVESTIGATION BY FOCUS GROUPS OF PATIENTS' EXPERIENCE WITH THE HY-RESULT® SYSTEM

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Objective: Hy-Result is a web-based rule management software designed to help patients to comply with the home blood pressure measurement (HBPM) protocol and to self-interpret their results. The study Explore patients' experience using the Hy-Result® system.

Design and method: Three focus groups with 24 hypertensives patients, 5 general practitioners and 1 hypertension specialist were proposed to hypertensive patients who possess a blood pressure monitor at home and an internet access to use Hy-Result® for home blood pressure monitoring. A maximum variation sampling was performed and the analysis was thematic in a grounded theory approach. The researcher clustered patients' responses into sub-themes and themes which were compared to highlighted concepts and issues which had been checked by the hypertension expert

Results: 1) Functionality. Hy-Result® is easy to use for all patients. The main drawback is the need to transcribe blood pressure values in absence of automatic data transfer. 2) Medical content. Hy-Result® contains essential information on arterial hypertension and home blood pressure monitoring. According to user interpretation, Hy-Result® generated appropriate reactions: alert, reassurance, delay before going to doctor's office. For some patients information was obvious. 3) Feelings and expectations. Half of the patients trust Hy-Result®. They all agree that the application gives suggestions and not a diagnosis. Hy-Result® did not cause anxiety and the risk of exaggerated measurements have been discussed. 4) Physician-patient relationship. For patients, using Hy-Result® need to be a doctor's request. They are aware that Hy-Result® does not replace the judgement of the doctor. Physician-patient relationship did not change, doctor still have the main role in arterial hypertension management.

Conclusions: Hy-Result® is a validated, easy to use, e-health tool for hypertensive patients undergoing HBPM. It can be considered for hypertensive patients of all ages. Most of the patients welcomed it as a complementary tool to facilitate discussion with their physician. Some patients expressed their doubts about Hy-Result® considering that the system is only for people comfortable with technology. Patients are ready to use Hy-Result® on their doctors' requests. We still need to evaluate the opinion of medical professionals concerning the system.

NON DIPPING PATTERN OF SYSTOLIC BLOOD PRESSURE DIPPING, IN A PORTUGUESE HYPERTENSIVE POPULATION, IS HETEROGENOUS AND SHOULD BE REDEFINED

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Objective: Background In 2010 authors publish that non dipper pattern of systolic blood pressure was an heterogenous division, Bastos et al, 2010 Jul 1;12(7). We updated our population in terms of events and follow up and reanalysed.

Design and method: An hypertensive population n = 1200 (645 women), ageing 51 ± 12 years, BMI 27 ± 5 Kg/m², 53% under antihypertensive medication and without previous CV events were followed during 12.8 ± 5.1 years. There were 251 CV fatal/non-fatal events (147 strokes, 67 coronary, 37 others CV). Systolic blood pressure dipping (SBPD) can be analysed has a variable continuous or a has a dipping pattern (extreme dippers < 0.8 (ED) n = 76, normal dippers < 0.9 (D) n = 514, non-dippers > 0.9 < 1.0 (ND) n = 525 and reverse dippers > 1.0 (RD) n = 83).

Results: When we analysed ND pattern we found it heterogenous. ND was divided in ND1 (>0.9 < 0.95) n = 207 and ND2 (>0.95 < 1) n = 312. In a Kaplan Meier curve analysis free of CV events there were a worst survival for those ND1 compared to ND2 (log rank 5,6 p < 0.02) for Stroke (AVC) (log rank 5,3 p < 0.05). When SBPD were analysed including ND1 and ND2 in Kaplan Meier survival curves free of events RD > ND1 > ND2 > D > ED had worst CV events survival (log rank 26,9 p < 0.000), Stroke (log rank 18,7 p < 0.01), CV death (log rank 30,7 p < 0.000) global mortality (log rank 14,1 p < 0.01). ND1 has a similar behaviour has RD and ND2 has D.

In a multivariate Cox analysis, adjusted to age, gender, OBP, diabetes, BMI, CV therapy, SBPD including ND1 and ND2, was predictive of CV events (HR 0.87 (IC 0,77–0,99; p < 0,05) and CV death 0,65 (IC 0,43–0,98; p < 0,05).

Conclusions: In a Portuguese population, non dipping pattern is heterogenous and dividing it in ND1 and ND2 became more predictive of CV, Stroke, CV deaths and global deaths. Perhaps it's time to look for the non dipping pattern and re-define it in ND1 and ND2 for a more precise CV prognosis.

CLINICAL IMPACT OF A PHARMACEUTICAL PROFESSIONAL SERVICE INTERVENTION WITH OR WITHOUT A MULTI-COMPARTMENT MEDICATION IN NON-ADHERENT, UNCONTROLLED, CHRONIC HYPERTENSIVE, POLIMEDICATED PATIENTS IN SPANISH COMMUNITY PHARMACIES. SEFAC-SPD- VALOR STUDY

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Objective: Control of HBP in the spanish community is far from optimal (only about 50%), and has a negative impact on treatments efficacy and worsens clinical outcomes. Adherence to medication can substantially reduce this risk.

To determine the clinical impact of a pharmaceutical professional service intervention with or without a multi-compartment medication (MOD) in non-adherent uncontrolled chronic hypertensive polimedicated patients living at home and analyze the degree of adherence improvement and blood pressure control

Design and method: An epidemiological prospective multicenter trial to evaluate an intervention in community pharmacy on the managing of hypertension and adherence of treatment (Morinsky-Green Test), control group, pre and post measurements (1,3 and 6 months)

Results: Preliminary results in 75 and 51 valid patients at 3 and 6 months respectively, indicate that this service would help to increase adherence in non adherent patients (77% at 3 month and 76% at 6 month) with the use of MOD versus 30% at 3 month (p < 0,0001) and 30% at 6 month (p < 0,0017) in the control group. Blood pressure showed a reduction of 23,3 mmHg (p < 0,0001) for systolic blood pressure (SBP) and 7,75 mmHg (p < 0,0001) for diastolic blood pressure (DBP) in the MOD group; vs. 10,06 mmHg (p < 0,05) and 5,04 mmHg respectively in the control group. In addition, the number of antihypertensive drugs distributed to the patients diminished from 5,17 pills in the basal period to 1,86 pills (p < 0,0001) at 6 months in the MOD group and from 3,60 pills to 1,53 pills (p < 0,0019) in the control group. It's an ongoing trial, final results will be operational at the end of may 2018

Conclusions: The present study shows how a pharmaceutical professional service intervention thru a MOD as a tool versus a control group, increased in both arms significantly adherence in non-adherent HBP polimedicated patients, diminished HBP significantly and reduced de number of pills in a 6 months period of follow up. Differences were seen among arms due to the fact that pharmacist review the medication, evaluate interactions and maintain a continue follow up with patients in the MOD group

HYPERTENSION SELF-MANAGEMENT DIGITAL SYSTEM: IS DRUG SELF-REPORTING RELIABLE?

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Objective: e-health technology offers new possibilities for the self-management of home blood pressure measurements (HBPM). Hy-Result is a validated rule management system designed to help users to comply with the HBPM protocol and self-interpret their HBPM readings. The algorithm takes in account HBPM readings and patient characteristics and produces a PDF file with an automatized interpretation of the BP levels and educational information in plain language. When entering data (including risk factors and comorbidities), the patient can provide his current antihypertensive treatment in a non-mandatory free text field and send his report to the physician or nurse. We assessed the accuracy of the treatment self-reported by system users.

Design and method: Observational, cross-sectional, retrospective study. Included patients consulting in an ESH excellence centre who had used the web system and e-mailed their PDF report to the centre. We checked the accuracy of the self-reported treatment (number of drug classes, name, dosage, number of daily intakes) compared to the medical prescription recorded in the medical file.

Results: Ninety four patients (35% females, average age 53,3) e-mailed their PDF reports; 10 reports were excluded because treatment was not self-reported (4) or not recorded during the consultation (6). Full concordance on the 4 criteria was 73% for the remaining 84 patients (Table).

Errors were mostly related to dose and number of drug classes (omissions due to single-pill combinations).

Criteria of Anti-hypertensive Drugs reports (n=84)	Totally concordant (n; total %)	Minimal Error (n; relative %*)	Error (n; relative %*)	TOTAL errors (n; relative %*)
Name	84; 100%	0; 0%*	0; 0%*	0; 0%*
Dose	73; 87%	4; 13%*	7; 22%*	11; 34%*
Daily Intake	82; 98%	1; 0%*	1; 0%*	2; 6%*
Number of Substances	75; 89%	0; 0%*	9; 28%*	6; 19%*
TOTAL	61; 73 %	5; 6%	27; 32%	32; 100%

Minimal Error - typing, not doubtful; **Error** - omission, name or dose mistaken) . *relative % referring the total of errors (ex: minimal error in name/total errors)

Conclusions: When using Hy-Result, 90/94 (96%) of the patients self-reported their anti-hypertensive treatment in the electronic formulary. The number of drug classes, names, doses and daily intakes was perfectly concordant in 73 % of patients. Errors detected were related to number of drug classes and dose, mostly due to single-pill combinations. The majority of patients using the Hy-Result system e-mailed reliable information about their treatment. Patient empowerment for telemonitoring web based service is promising.

THE ASSOCIATIONS OF TARGET ORGAN DAMAGE WITH MORNING HYPERTENSION BY VARIOUS DEFINITIONS

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Objective: Morning Hypertension (MHT) can be defined based on ambulatory blood pressure (BP) monitoring (ABPM) or home BP monitoring (HBPM). In which definition MHT is more associated with cardiovascular outcome remains unknown.

Design and method: From 2010–2015, we consecutively recruited untreated outpatients from our Hypertension Clinic. MHT was an average BP of at least 135/85 mmHg in the morning defined either based on HBPM, or the diary (the first 2 h after awakening) or short-clock time interval (6–10 AM) on the day of ABPM, irrespective of the BP levels at other time windows. We assessed carotid-femoral pulse wave velocity (cfPWV) by SphygmoCor system, left ventricular mass index (LVMI) and carotid intima-media thickness (IMT) by ultrasonography, and urinary albumin/creatinine ratio (ACR) as measures of target organ damage.

Results: In the 1085 untreated patients (age 51.2 years), the prevalence of MHT were 63.7%, 65.1% and 48.7% based on the ABPM diary, short-clock time interval and HBPM, respectively. After adjustment for age, sex, and other cardiovascular risk factors, patients with MHT compared to normotensives had significantly ($P < 0.001$) increased cfPWV, urinary ACR and carotid IMT, irrespective of the definitions. In multivariate-adjusted continuous analyses, target organ measures were all positively associated with morning systolic BP recorded by ABPM and HBPM ($P < 0.002$), except for that of LVMI with home BP. After further including the systolic BP at other time windows in the models, morning systolic BP during 6–10 AM remained significantly associated with cfPWV ($\beta = 0.019$, $P < 0.001$), and home morning systolic BP was associated with cfPWV ($\beta = 0.024$, $P < 0.001$) and urinary ACR ($\beta = 0.012$, $P = 0.003$).

Conclusions: Irrespective of the definitions based on ABPM or HBPM, morning hypertension was associated with target organ measures.

HOME BP LEVELS AND ARTERIAL STIFFNESS IN PATIENTS WITH MILD TO MODERATE ARTERIAL HYPERTENSION

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Objective: Home BP monitoring (HBP) known to be a stronger predictor of cardiovascular morbidity and mortality than office BP measurements. The aim of this study was to find target HBP levels bases on subclinical TOD indicators.

Design and method: We studied the 39 patients (24 women, 15 men), with an average age of 52.0 ± 0.1 years. The average office systolic blood pressure (SBP) was 150.5 ± 3.1 mm Hg, diastolic blood pressure (DBP) was 94.2 ± 2.0 mm Hg, the mean heart rate (HR) was 67.1 ± 2.3 b. m. We measured pulse wave velocity (PWV, SphygmoCor), 24-h ambulatory BP (ABPM) and central BP (cSBP) (Mobilograph), cardio-ankle vascular index (CAVI, VaSera VS-1500). Patients were asked to self-measure blood pressure (HBP) three times at 1-min intervals every morning and evening for 7 days between 6 and 11 hours after taking the medications with a validated, automatic oscillometric device OMRON HEM-9210T. Participants received written instructions and individual guidance on how to measure BP correctly.

Results: So the average morning HSBP was 128.6 ± 2.3 mmHg, HDBP was 84.6 ± 1.7 mmHg, the HHR was 71.7 ± 2.3 b.m. The average evening HSBP was 130.0 ± 2.1 mm Hg and HDBP to 84.4 ± 1.7 mm Hg, heart rate 72.1 ± 2.1 mm

Hg. The 24-h SBP was 128.0 ± 2.1 mm Hg, 24-h DAT 81.9 ± 1.6 mm Hg, 24-h HR 72.3 ± 2.1 b.m., 24-h PBP 47.3 ± 2.2 mm Hg, 24-h cSBP 116.5 ± 4.8 mm Hg, 24-h Alx 75% $30.7 \pm 4.5\%$, 24-h PWV 8.0 ± 0.5 m/s. CAVI index was: R-CAVI 7.9 ± 0.3 , L-CAVI 8.0 ± 0.4 ; R-ABI 1.04 ± 0.3 , L-ABI 1.03 ± 0.3 . PWV by SphygmoCor was PWVe - 12.0 ± 2.3 m/s, PWVm - 8.6 ± 1.4 m/s, Alx75 - $24.1 \pm 5.4\%$, cSBP 110.6 ± 18.7 mm Hg.

Conclusions: We have found, that HBP target levels could be SBP < 130 DBP < 90 as those levels were not associated with arterial stiffening. We will include more subjects in order to confirm this results.

AVANAT'AGE STUDY: EVALUATION OF VASCULAR AGE IN HYPERTENSIVE PATIENTS IN MOROCCO

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Objective: High blood pressure is one of the most important risk factors for cardiovascular morbidity and mortality. The study aims to evaluate the evolution of vascular age in hypertensive patients under treatment with a fixed combination of perindopril and amlodipine in Morocco

Design and method: Non-interventional study on an open cohort carried out in general practice in Morocco, under conditions of usual management of hypertension over a period of 3 months.

Results: 400 patients were recruited, of whom 62.5% were women. Their mean age was 62.2 years, their average blood pressure (BP) was 173.2 ± 17.7 mmHg/ 92 ± 10.8 mmHg. At baseline, 64% were treated with the lowest dosage (5/5) of the fixed combination as compared to 58% at 3 months. The mean vascular age was 69.7 ± 12.3 years at inclusion.

After a 3-month treatment with the fixed combination at any of its four dosages (5/5, 5/10, 10/5, or 10/10 mg) a mean decrease in vascular age of 8.3 years ($p < 0.0001$) was achieved. This decrease was observed with an average of 11.3 ± 5.8 in BP grade 3 vs. 7.2 ± 3.6 in BP Grade 2 patients and 3.7 ± 1.9 at grade 1. A mean reduction of BP of $35/13$ mm Hg compared to baseline was observed ($p < 0.0001$). The normalization rate at 3 months was 49.7% considering 140/90 mmHg as target BP. The fixed combination was well tolerated with an adverse event rate of 1.5% ($p < 0.0001$).

Conclusions: This study demonstrates the efficacy and tolerability of the fixed combination of perindopril and amlodipine in reducing vascular age (associated with a BP reduction and control) in hypertensive patients under usual clinical practice conditions in Morocco.

RENAL DENERVATION ON BLOOD PRESSURE VARIABILITY AND BLOOD PRESSURE LEVELS: TWO YEARS OUTCOMES

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Objective: Therapy-resistant hypertension (RHTN) is associated with major adverse cardiovascular events. Increased sympathetic drive is considered to be one of mechanisms of resistance to antihypertensive treatment and associated with high blood pressure level. Sympathetic hyperactivity is also linked to increased blood pressure variability (BPV) resulting in worse prognosis. Renal denervation (RDN) reduces sympathetic activity and BP in some patients with RHTN, however data on the impact of the procedure on BPV are lacking.

Aim of the present study was to assess effect of RDN on blood pressure levels and BPV during 2-years follow-up.

Design and method: The study enrolled 22 consecutive patients (mean age 56 ± 10.2 years, ⁹males) with confirmed true RHTN (mean of 4.2 ± 1.4 antihypertensive drugs intake) who underwent bilateral RDN procedure (Symplicity RDN System, Medtronic, USA). BP and BPV (by means of average real variability) were assessed by ABPM (BPLab, Petr Telegin, Russia) at baseline, 12-month and 24 month after procedure.

Results: In overall population there was a decrease of both office and 24-hour SBP at 12 months after RDN (-26 ± 20.2 mmHg; -17.4 ± 10.8 mmHg; respectively, $p < 0.05$ for all), however further reduction at 24-month follow-up was only for "office" SBP (-22.8 ± 23 mmHg; $p < 0.02$ and -22.6 ± 17.6 mmHg; $p = 0.3$ respectively). 24-hour BPV decreased from 18.8 ± 4.4 mmHg to 17 ± 4.2 mmHg (-2.6 ± 3.7 mmHg, $p < 0.0001$) after 12 months and continued to decline to 15.36 ± 2.9 mmHg (-3.3 ± 2.5 mmHg, $p < 0.001$) two years after procedure. In 15 patients RDN provided decrease of BP level > 20 mm Hg, in 7 patients resulted in 10 mm Hg decrease. Both groups had a significant reduction of BPV in 24-month (-5.0 and -1.3 mmHg respectively; $p < 0.001$). There was a positive correlation between change of SBP, 24-h SBP and 24-h BPV at 24-month visit compared to baseline ($r = 0.654$ for office SBP/BPV; $p = 0.02$ and $r = 0.628$ for 24-h SBP/BPV; $p = 0.02$).

Conclusions: RDN resulted in significant reduction of 24-BPV in patients with both marked and moderate decrease of blood pressure level indicating additional positive impact on adverse prognostic features of hypertension.

APPLICATION OF A CENTRAL ILIAC ARTERIOVENOUS COUPLER DEVICE IN SEVERE TREATMENT-RESISTANT ARTERIAL HYPERTENSION: A FOUR-YEAR FOLLOW-UP

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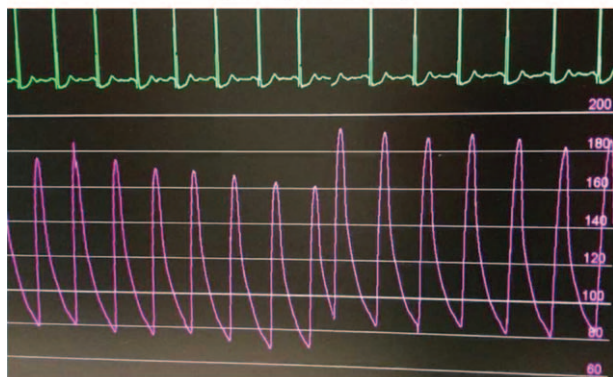
Objective: The application of a central iliac arteriovenous coupler device leads to a reduction of blood pressure (BP) due to a decrease in total vascular resistance and improvement of arterial compliance in patients with resistant hypertension. However, long-term efficacy and safety need to be further explored. We report on the first case of 4-year follow-up in a patient treated by coupler implantation, who underwent repeated right heart catheterization.

Hemodynamic changes measured by right heart catheterization during follow-up

Date of right heart catheterization	RAP [mmHg] (s/d/m)	PAP [mmHg] (s/d/m)	CI (Fick) [l/min/m ²]	PVR [dyn x sec /cm ⁵]	CABP [mmHg] (s/d/m)
Baseline examination, 16/Dec/2013	11/10/7	36/13/21	2.6	160	214/105/141
0.5-year follow-up, 23/Jun/2014	13/9/7	39/13/23	3.0	129	214/92/133
3.5-year follow-up, 13/Jul/2017	14/13/12	56/20/35	4.1	114	165/70/105

RAP – right atrial pressure, PAP – pulmonary artery pressure, CI – cardiac index, PVR – pulmonary vascular resistance, CABP – central aortic blood pressure, s – systolic, d – diastolic, m – mean.

Immediate increase/decrease of blood pressure after closure/opening of the anastomosis (approximately 30 mmHg each way)



Design and method: A patient with treatment-resistant hypertension was admitted to hospital in 2013. Despite treatment with 6 anti-hypertensive drugs, his BP was poorly controlled. 24-hour ambulatory blood pressure monitoring (ABPM) revealed a mean BP of 153/93mmHg. Previously, he had undergone renal denervation, which did not lead to a significant BP decrease. Therefore, an arteriovenous coupler device was implanted in our catheterization laboratory, causing a periinterventional BP decrease from 198/90 to 163/69mmHg. The patient was discharged with a BP of 122/71mmHg. After 3 months, there was a sustained BP decrease (-14/9mmHg), whereas later, it was fluctuant (office BP: 147–173/85–95mmHg, ABPM: 153-166/81–94mmHg) probably due to medication non-adherence (3/6 drugs), confirmed by a urinary toxicological screening test. One year later, the patient was hospitalized with iliac venous stenosis, which was treated by venoplasty and stenting. After 3.5 years, our patient complained about progressive dyspnea and weight gain. Follow-up right heart catheterization showed an increase in pulmonary artery-, right atrial- and wedge-pressure as well as cardiac index and a decrease in pulmonary vascular resistance. Central aortic pressure had also decreased from 214/105 (baseline) to 165/70mmHg, indicating device effectiveness. An invasive closure maneuver led to an immediate BP increase (+30mmHg) and a similar decrease after re-opening of the anastomosis, verifying

its functionality. To unload the right ventricle, an intensive diuretic therapy was introduced, leading to clinical improvement.

Results: This is the first case of 4-year follow-up in a patient with treatment-resistant hypertension who underwent coupler implantation, leading to a significant BP decrease. We proved a proper long-term function of the device and demonstrated changes in hemodynamic parameters related to volume congestion, which were resolved by an intensified diuretic therapy.

ANALYSIS OF 24 HOURS BLOOD PRESSURE PATTERN IN NONHYPERTENSIVE CHRONIC HEART FAILURE PATIENTS

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Objective: Ambulatory blood pressure monitoring (ABPM) permits the evaluation of 24 hours blood pressure pattern. It is well defined the prognosis value of the abnormalities in the circadian variation in hypertensive patients. In the pathophysiology of heart failure, neurohumoral mechanism plays an important role. Nevertheless, the circadian variation in nonhypertensive heart failure patients has not been well evaluated.

Design and method: We studied 80 patients with a clinical diagnosis of nonhypertensive CHF. They were followed-up by the Heart Failure Unit. We performed a 24-h ambulatory blood pressure monitoring as well as an echocardiogram and analytical test.

Results: A total of 80 patients. Mean age: 62,7 ± 12. Males: 72,5%. Mean BMI: 29,6 ± 5 Kg/m². Mean time of follow-up of CHF: 69 ± 66 months. Associated risk factors: dyslipidemia 25% Diabetes 20% obesity 45% active smoking 30%, ex-smoking 27,5%.

Therapeutic regimen applied: RAS blockers 85%; betablockers 92,5%; loop diuretic 75%; spironolactone 35%; statins 55%; antiplatelet/anticoagulant drugs 75%, nitrates 20%, digoxin 30%

The 24 h ABPM measurements are in table 1.

The majority of CHF patients (77,5%) have an abnormal pattern of ABPM, as it is shown on table 2.

Table 1.

Mean ABPM (mmHg)	24 hours	Daytime	Nighttime
Systolic BP	107,7 ± 13,8	109,6 ± 14,2	104,5 ± 14,5
Diastolic BP	64,4 ± 7,8	66,4 ± 8,8	60,4 ± 7,6

Table 2.

Patterns of ABPM	Global
Dipper n(%)	18 (22,5)
Non-dipper n(%)	46 (57,5)
Riser n(%)	16 (20)
Extreme dipper n(%)	0 (0)

Conclusions: Nonhypertensive heart failure patients had, in majority, an abnormal circadian rhythm of blood pressure. It is well known the prognosis values of this alterations. This highlights the high cardiovascular risk and the neurohumoral alterations of this patients with chronic heart failure, whether they are hypertensive or not.

IS THERE A RELATIONSHIP BETWEEN VITAMIN D3 AND HYPERTENSION AND THE NUMBER OF ANTIHYPERTENSIVE DRUGS USED?

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Objective: In our study we wanted to search is there a relationship between vitamin D3 and hypertension and the number of antihypertensive drugs used.

Design and method: In our study we wanted to search is there a relationship between vitamin D3 and hypertension and the number of antihypertensive drugs used. A total of 2279 patients were enrolled in the study. 71.8 % of the patients were female and 28.2 % were male. 839 (36.8%) of patients were not using blood pressure medication. 292 of (12.8 %) of patients were using 1 antihypertensive drug, 643 of (28.2 %) of patients were using 2, 408 of (17.9 %) of patients were using 3, 77 of (3.4 %) of patients were using 4, and 20 of patients (0.9%) were using 5 antihypertensive drugs. The age of patients was in the range of 30–90. The ages of women ranged from 30 to 89 and the ages of males ranged from 38 to 90 years. Vitamin D3 levels of patients were in the range of 4.52–40.5 ng/mL. Vitamin D3 levels of patients were between 4.52–36.5 ng/mL in non-hypertensive patients and 5.63–40.5ng/mL in patients with hypertension.

Results: There was no significant relationship between vitamin D3 level and blood pressure presence ($p=0.083$). Also there was no significant relationship between vitamin D3 level and the number of antihypertensive drugs used ($p=0.349$).

Conclusions: Further work in this subject is necessary.

RELATION BETWEEN PULSE WAVE AND HEART FAILURE IN HYPERTENSIVE PATIENTS

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Objective: The increased central aortic stiffness has been identified as an independent risk factor for heart failure and end-organ damage. Carotid-femoral pulse wave velocity (PWV) measures the stiffness over large part of the aorta, and objective of this study is evaluate the relation between carotid-femoral pulse wave and cardiac parameters.

Design and method: We compared three groups of hypertensive patients with the same age and sex: SD - with systolic dysfunction, DD - with diastolic dysfunction and NLV - with normal LV function. All participants underwent a comprehensive echocardiographic study including carotid artery sonography, and assessments of arterial stiffness and wave reflections. Patients with uncontrolled hypertension, uncontrolled diabetes mellitus, recent myocardial infarction (within 3 months), atrial fibrillation, valvular heart disease, recent stroke (within 3 months) or established peripheral artery disease were excluded. The model was ANOVA oneway and regression analysis.

Results: There are no differences in sex, office and ambulatory Diastolic Blood Pressure (DBP). The office and ambulatory systolic blood pressure (SBP), aortic systolic (ASBP) and diastolic blood pressure (ADBP) are different among the three groups (SD SBP 118.2 ± 18.6 ; DD SBP 136.1 ± 21.3 ; NLV SBP 128.7 ± 18.3 , $p < 0.01$), (SD ASBP 108.8 ± 17.6 ; DD ASBP 124.1 ± 20.4 ; NLV ASBP 116.8 ± 16.2 , $p < 0.01$), (SD ADBP 65.4 ± 9.5 ; DD ADBP 80.1 ± 11.1 ; NLV ADBP 73.1 ± 11.7 , $p < 0.01$). The carotid-femoral pulse wave velocity were different (SD PWV 12.7 ± 4.3 ; DD PWV 13.6 ± 4.1 ; NLV PWV 11.6 ± 3.3 , $p < 0.01$) and central augmentation index (SD CAI 23.2 ± 14.1 ; DD CAI 26.2 ± 13.5 ; NLV CAI 21.3 ± 13.3 , $p < 0.01$). We found a relation between PWV and left ventricular mass index, and between CAI and relation A/E waves and E/E'.

Conclusions: The present study expanded the usefulness of carotid-femoral pulse wave velocity and central augmentation index as a risk factor for cardiovascular disease in patients with advance disease. We found that these parameters can be used to establish a relation to cardiac function in patients with hypertensive disease and could be used to predict the vascular lesions that these patients might have.

AMBULATORY BLOOD PRESSURE MONITORING AFTER ONE CARDIOVASCULAR EVENT IN PREDICTION OF A SECOND CARDIOVASCULAR EVENT

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Objective: In patients with previous cardiovascular (CV) event it is not clear whether Ambulatory Blood Pressure Monitoring 24 H (ABPM) has prognostic value for recurrence. The objective was to compare ABPM values after a first CV event between patients with (2EV) and without (1EV) a second CV event and to evaluate if ABPM has a role in secondary prediction.

Design and method: We studied 187 hypertensive patients with ABPM after a first CV event. ABPM data in 2EV vs 1EV were compared.

Results: Of the 187 patients (74.3 % male) ageing 66.6 ± 10.7 years, followed for 2.3 ± 1.9 years, 158 were 1EV and 29 were 2EV. In the 2EV, mean age was 67.2 ± 9.5 and 72.4% were male. Comparison of the ABPM parameters between the 2EV vs 1EV showed: 24H systolic blood pressure (SBP) (134 ± 15 vs 125 ± 13 mmHg, $p=0.002$), day SBP (138 ± 15 vs 129 ± 13 mmHg, $p=0.002$), night SBP (128 ± 18 vs 118 ± 16 mmHg, $p=0.003$), 24H pulse pressure (PP) (62 ± 13 vs 55 ± 13 mmHg, $p=0.004$), day PP (63 ± 13 vs 55 ± 14 mmHg, $p=0.005$) and night PP (62 ± 14 vs 53 ± 14 mmHg, $p=0.003$).

The Cox model, adjusted for gender and age, showed correlation with recurrent events for: 24H SBP (HR = 1.032, 95CI 1.005–1.060, $p=0.021$), day SBP (HR = 1.026, 95CI 1.001–1.052, $p=0.043$), night SBP (HR = 1.031, 95CI 1.007–1.055, $p=0.011$) and 24H PP (HR = 1.046, 95CI 1.013–1.081, $p=0.007$).

In the survival analysis, the 24H SBP ROC curve showed an AUC of 0.627 ($p=0.003$). The value of 124 mmHg was the best cutoff of SBP (sensitivity 82.7, specificity 51.2) for prediction of secondary CV events. The survival Kaplan Meyer curve showed a worse prognosis for the 2EV with 24H SBP > 124 mmHg (log rank 6.032, $p=0.014$) (not observed in the 135 mmHg 24H SBP Kaplan Meyer, $p=0.224$).

Conclusions: In patients with previous cardiovascular events, higher values of 24H, daytime and night-time SBP are more predictive of cardiovascular events. In our 2EV population, a 24H SBP higher than 124 mmHg is more predictive of secondary events.

INTER-ARM DIFFERENCES IN BLOOD PRESSURE AND MORTALITY: INDIVIDUAL PATIENT DATA META-ANALYSIS AND DEVELOPMENT OF A PROGNOSTIC ALGORITHM (INTERPRESS-IPD COLLABORATION)

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Objective: Study-level meta-analyses have associated inter-arm differences (IAD) in systolic blood pressure (SBP) with increased mortality. However key areas of investigation remain, such as determining the additional contribution of IAD to prognostic risk estimation for cardiovascular and all-cause mortality, and determining the minimum value for IAD that defines elevated risk. We are conducting an individual participant data (IPD) meta-analysis to address these questions.

Design and method: Systematic review and IPD meta-analysis; we identified prospective studies that measured SBP in both arms during recruitment, and invited contribution of eligible datasets to the Collaboration. Study datasets were cleaned and combined into a single dataset for analyses. A non-random sample of four datasets were reserved for model validation; remaining data were analysed in fixed effect 1-stage meta-analyses with multivariable time-to-event regression modelling. Analyses of IAD dichotomised using cut-offs by 1mmHg increments from 0 to 20 mmHg, adjusted for age, gender and baseline SBP, were compared to identify a lower limit of IAD associated with increased all-cause mortality using random effects 2-stage models.

Scientific Data

Searches to January 2017 yielded 4448 unique citations, 152 full texts were screened, 60 potentially relevant datasets were identified and their authors contacted. Data from 24 studies (57,434 eligible individual adult patients) were received.

Results: In complete case analysis of 35,900 records (the derivation cohort), absolute systolic IAD was associated with increased all-cause mortality: fully adjusted hazard ratio (HR) 1.01, 95% confidence interval (95%CI) 1.00 to 1.02 per mmHg of IAD. Other significant model variables were age, gender, baseline SBP, current smoking, total cholesterol, ethnicity, and diagnoses of hypertension or diabetes. Incremental analyses of 50,661 records showed increasing HRs associated with rising IAD cut-offs, and suggested that an IAD of 7 mmHg or more is associated with increased risk of all-cause mortality.

Conclusions: This IPD meta-analysis confirms the role of systolic IAD as an independent risk marker for all-cause mortality, with a threshold of 7 mmHg as a lower limit for increased mortality risk. We continue to model cardiovascular outcomes and will present full results to the meeting.

URINE ALBUMIN-TO-CREATININE RATIO IS ASSOCIATED WITH ASYMPTOMATIC INTRACRANIAL ATHEROSCLEROTIC STENOSIS IN HYPERTENSIVE PATIENTS

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Objective: Intracranial atherosclerotic stenosis (ICAS) contributes to nearly 50% of stroke in China, especially in patients with hypertension. Urine albumin-to-creatinine ratio (ACR) has been related to stroke and other atherosclerotic cardiovascular diseases. However, there is limited information about the effect of ACR on early impairment of cerebral vessels. Hereby we assessed the association between ICAS and ACR in a stroke-free hypertensive population.

Design and method: Computed tomography angiography was performed to detect atherosclerotic stenosis of intracranial arteries in 889 hypertension patients. A random spot urine was sampled to evaluate ACR. Logistic regression was carried out to analyze the association of ACR with the presence, extent and lesion number of ICAS. Risk factors which we previously identified were also added in the adjustment to determine whether the association of elevated ACR with ICAS was independent.

Results:

	ICAS	No ICAS	P
N (%)	194 (21.8)	515 (58.2)	
Age (years)	46.1 (8.1) (4.8-51.0)	44.0 (8.4) (3.7-48.3)	<0.001
Male (%)	189 (97.4)	231 (44.9)	<0.001
BMI (kg/m ²)	23.1 (3.2) (2.4-33.4)	24.0 (3.2) (2.7-27.7)	0.009
SBP (mmHg)	138.1 (23.3) (108.3-168.3)	134.3 (22.1) (111.7-156.9)	<0.001
DBP (mmHg)	72.1 (14.4) (58.0-86.2)	71.1 (12.1) (57.9-84.3)	0.586
Asymptomatic (%)	107 (54.6)	473 (91.5)	0.006
Strokeless (%)	91 (47.7)	194 (37.9)	0.027
Diabetes (%)	101 (52.0)	101 (19.3)	<0.001
LDL (mmol/L)	3.0 (2.3) (1.5-4.5)	2.9 (2.0) (1.3-4.6)	0.875
HDL (mmol/L)	1.1 (0.4) (0.3-1.5)	1.2 (0.4) (0.3-1.6)	<0.001
Uric acid (mmol/L)	371 (75.7)	371 (71.7)	0.189
ACR (mg/g)	31.4 (17.6) (8.1-58.1)	23.1 (13.1) (4.7-47.7)	0.007
ACR >30mg/g (%)	179 (92.0)	228 (44.3)	0.001
aOR (95%CI) for ACR >30mg/g	82.1 (37.0-186.3)	94.8 (38.2-240.4)	<0.001
aOR (95%CI) for ACR >30mg/g	112.0 (46.0-273.0)	112.0 (46.0-273.0)	0.001

ICAS: Intracranial atherosclerotic stenosis; BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; ACR: urine albumin-to-creatinine ratio.

	N (%)	OR (95%CI)	P
ACR (mg/g) >30	179 (23.8)		
ICAS Absent	124 (6.5)	1.00	
ICAS present	179 (20.0)	1.65 (1.21-2.27)	0.002
ICAS severity		1.57 (1.16-2.12)	0.004
1-100%	119 (13.4)	1.36 (1.03-1.79)	
31-100%	39 (4.4)	42 (4.7)	
ICAS lesion		1.58 (1.16-2.15)	0.003
1-2	140 (15.8)	1.55 (1.17-2.05)	
3+	18 (2.0)	23 (2.6)	

Discontinued by logistic and/or proportional odds comparison logistic regression. Adjusted for age, sex, BMI, SBP, DBP, LDL, HDL, uric acid, smoking history, aOR and intracranial stenosis.

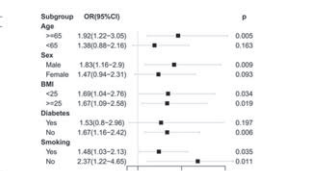


Figure 1. Sensitivity analysis on the association of ACR and ICAS by age, sex, BMI, diabetes and smoking history. Patients were stratified by age, sex, BMI, diabetes and smoking history and adjusted for age, sex, BMI, diabetes and smoking history. Adjusted for age, sex, BMI, SBP, DBP, LDL, HDL, uric acid, smoking history, aOR and intracranial stenosis were reported.

Variable	OR	95%CI	P
Age	1.11	0.96-1.29	0.156
Sex	0.97	0.82-1.15	0.211
BMI	1.10	1.01-1.19	0.006
Diabetes	1.00	1-1	0.924
Smoking	1.58	1.1-2.17	0.012
SBP	1.13	0.98-1.3	0.100
DBP	1.01	1-1.02	0.014
LDL	1.01	1.00-1.01	0.014

Discontinued by logistic and/or proportional odds comparison logistic regression. Adjusted for age, sex, BMI, SBP, DBP, LDL, HDL, uric acid, smoking history, aOR and intracranial stenosis.

There were 336 patients (37.8%) with ICAS. Elevated ACR (≥ 30 mg/g) was associated with ICAS after adjustment of confounding factors (OR = 1.65, 95% CI: 1.21–2.27). This association remained significant in patients who were male, ≥ 65 years and without diabetes. Patients with elevated ACR were more prone to develop moderate to severe stenosis (OR = 1.57, 95%CI: 1.16–2.12) and more lesions (OR = 1.58, 95%CI: 1.16–2.15). The association of elevated ACR with ICAS was independent of previously discovered risk factors.

Conclusions: Our findings suggested that ACR was associated with asymptomatic ICAS in an aged stroke-free hypertensive population. ACR may serve as a convenient and independent early marker of ICAS in clinical practice.

DIFFERENCES IN LABORATORY FINDINGS OF HYPERTENSIVE PATIENTS DEPENDING ON RISK FACTORS, SETTLEMENT AND AGE

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Objective: Hypertension is a chronic disease with growing incidence. Monitoring of laboratory parameters is important in global cardiovascular risk assessment of hypertensive patients and prevention of complications. Evaluation and comparison of laboratory results and risks in patients included in distinct age groups and those from urban and rural settlements.

Design and method: The study was conducted on 127 hypertensive patients during the first three months of 2017 at an urban outpatient unit specialized on cardiovascular diseases. Serum samples of patients were processed with Konelab20XTi analyzer using photometric method. Glycemia and lipid profile, kidney and liver function were determined. Urine tests were performed using the HandUReader equipment. Statistical processing of data was made using the GraphPad InStat program. Threshold of significance was set at $p < 0.05$.

Results: Mean age of the patients was 63 years, 56.7% were male subjects. Significant difference ($p = 0.0475$) occurred between serum HDL-cholesterol concentration of rural (average 75.6 mg/dl \pm 12.5 SD) and urban patients (average 49.1 mg/dl \pm 13.0 SD). Significantly higher serum urea levels were found in the rural subgroup (mean: 44.3 mg/dl \pm 13.0 SD) compared to those from urban settlements (mean: 36.4 mg/dl \pm 15.0 SD). Pathological urine compounds were found in 43.3% of rural patients and in 29.9% of urban subjects. Significant difference could be observed between the comorbidities present in these subgroups:

diabetes was twice as frequent in the rural subgroup compared to urban subjects, prevalence of dyslipidemia was three times higher in the urban group compared to rural patients. Significant difference could be observed between creatinine-based glomerular filtration rate (average 57.7 mL/min) of elderly subjects (>70 years) compared to higher values of younger patients, especially those under 60 years of age. No significant difference could be noticed between glycemia, serum uric acid, triglyceride, total cholesterol concentration and transaminase activity of different subgroups based on age or settlement.

Conclusions: We can conclude that rural patients present higher protective HDL-cholesterol level compared to urban subjects and lower prevalence of dyslipidemia, probably related to their different diet, this might also be the background of their higher serum urea concentration.

AVANT'AGE STUDY: EVALUATION OF CARDIOVASCULAR RISK IN PATIENTS TREATED WITH A FIXED COMBINATION OF PERINDOPRIL AND AMLODIPINE IN MOROCCO

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Objective: the measure of vascular age, according to the SCORE algorithm, is used to estimate the cardiovascular mortality risk. The proposed study outlined the benefits of a fixed combination of perindopril and amlodipine on the reduction of cardiovascular mortality risk.

Design and method: Non-interventional study on an open cohort carried-out in general practice in Morocco, under conditions of the usual management of hypertension, over a period of 3 months, using the SCORE algorithm.

Results: The cardiovascular risk was calculated for a total of 378 patients. Their mean age was 62.1 years, their average blood pressure (BP) was 173.2 \pm 17.9 mm Hg/92.3 \pm 10.7 mmHg. The mean vascular age was 69.7 \pm 12.4 years at baseline. After 3-months treatment with the fixed combination, at any of its four dosages (5/5, 5/10, 10/5, or 10/10 mg), the predicted 5-year risk of cardiovascular mortality was significantly lower as shown in Figure 1. Only 1.9% of patients were at very high risk after 3 months, against 12% at inclusion ($p < 0.0001$), this evolution was mirrored by a decrease of 35 \pm 16.9 mmHg of systolic BP and 13 \pm 12.0 mmHg ($p < 0.0001$) of diastolic BP. The fixed combination was well tolerated with an adverse event rate of 1.5% ($p < 0.0001$).

Conclusions: The AVANT'AGE study showed that the fixed combination of perindopril and amlodipine allow a significant reduction of the risk of cardiovascular mortality at 5 years by reducing and controlling BP of hypertensive patients under usual clinical practice conditions in Morocco.

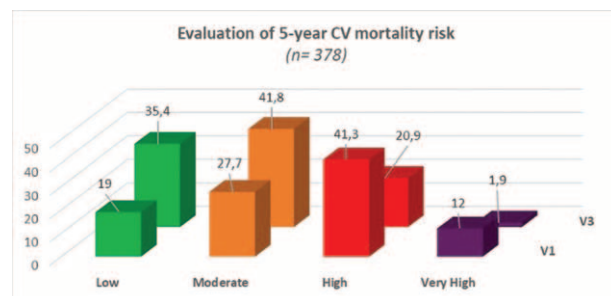


Figure 1: Evaluation of the 5-year cardiovascular mortality risk between V1 and V3

CLINICAL AND BIOCHEMICAL CORRELATIONS OF HYPERURICEMIA IN ESSENTIAL HYPERTENSION.

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Objective: Arterial hypertension and metabolic syndrome are clinical conditions leading to cardiovascular complications secondary to atherosclerosis. Hyperuricemia as a one of components of metabolic syndrome might directly damage arterial wall and cause atherosclerosis. Matrix metalloproteinases are involved in many processes associated in arterial wall damage and formation of atherosclerotic plaque. Their role in vascular pathology connected with hyperuricemia is unknown. Aim of the study was to identify clinical and biochemical differences between patients with mild primary arterial hypertension with and without hyperuricemia with a particular evaluation of the wide spectrum matrix metalloproteinases serum activity.

Design and method: Among patients with essential arterial hypertension (AH) stage 1 or 2 never treated by antihypertensive, hypolipemic or hypouricemic therapy we distinguished two groups. Asymptomatic hyperuricemia was defined as a serum uric acid over 356 μmol/l in females and over 416 μmol/l in males. The study participants were divided into two groups. Group 1 (G1) involves patients with asymptomatic hyperuricemia and AH, group 2 (G2) consisted of patients with normal uric acid and AH. We obtained in both groups anthropometric and clinical data including office and 24-hour ABPM. Several measures of subclinical organ damage were also obtained. In all the patients we assessed basic laboratory parameters and matrix metalloproteinases activity (MMP1, MMP2, MMP3, MMP9, TIMP1).

Results: Hypertensive, hyperuricemia patients in G1-group have: higher diastolic and systolic nighttime blood pressure (SBP: 119 mmHg vs. 113 mmHg, $p = 0.037$; DBP: 72 mmHg vs. 67 mmHg, $p = 0.043$), BMI (29.75 kg/m² vs. 26.70 kg/m², $p = 0.002$), higher waist circumference (97 cm vs. 87 cm, $p = 0.003$) and higher triglycerides (1.56 mmol/l vs. 1.20 mmol/l, $p = 0.032$), metalloproteinases 3 activity (MMP3) (19.41 ng/ml vs. 14.29 ng/ml, $p = 0.01$) than patients without hyperuricemia in G2-group. Among analyzed subclinical organ damage parameters was observed negative correlation between decrease eGFR below 90 ml/min/1.73 m² and uric acid concentration ($R = -0.37$, $p < 0.05$). Considering analyzed MMPs activity only MMP3 activity was higher in G1 than G2. Serum uric acid concentration in univariate linear regression remained in significant association with MMP3 activity ($R^2 = 0.09$, $B = 0.3$, $p = 0.002$). This relationship was still significant after adjustment to age sex and BMI.

Conclusions: Patient with essential arterial hypertension and hyperuricemia are characterized by higher prevalence of other metabolic syndrome components as a visceral obesity and hypertriglyceridemia. Uric acid concentration is associated with MMP3 activity, which is metalloproteinase initiating the cascade of other metalloproteinases responsible for degradation of structural vascular wall fibrous proteins.

ADVANTAGE OF MOCA AS COGNITIVE ASSESSMENT OVER PEBL IN HYPERTENSIVE PATIENTS WITH MILD COGNITIVE IMPAIRMENT

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Objective: Correlations between blood pressure (BP), pulse wave velocity (PWV) and the Montreal Cognitive Assessment test (MOCA) with Berg's Card Sorting Test (BCST) from battery of Psychology Experiment Building Language in hypertensive patients with mild cognitive impairment (MCI). The usefulness of MOCA and BCST in assessing the cognitive disorders.

Design and method: 32 patients with hypertension and MCI qualified by MOCA. The global cognitive assessment based on the neuropsychological tests: MOCA and BCST (computerized version of the Wisconsin Card Sorting Test). In BCST the percentage of correct (CA) and incorrect answers (IA), perseverative answers (PA), perseverative (PE) and non-perseverative errors (NPE) were assessed. The score MCI in MOCA test is ≤ 26 . The ambulatory blood pressure monitoring and PWV were performed. The Pearson test was used to analyze the correlation, the t-student test to the statistical analysis.

Results: The mean systolic BP was 126.75 ± 12.83 mmHg and the mean diastolic BP 76.94 ± 7.94 mmHg. The mean PWV was 11.83 ± 1.73 m/s and MOCA was 24.06 ± 9.98 points. The mean value of CA was $75.49 \pm 8.69\%$, IA $24.5 \pm 8.7\%$, PA $38.42 \pm 7.46\%$, PE $17.1 \pm 7.1\%$ and NPE $7.42 \pm 2.7\%$. PWV correlated with score of MOCA ($r = -0.743$, $p < 0.05$) and has positive correlation with BP. MOCA has significant correlation with SBP ($r = -0.4867$) and DBP ($r = -0.4913$). We showed: negative correlation MOCA with percentage of CA; positive with IA, PA, PE and NPE. BP has negative correlation with CA; positive with IA, PA, PE and NPE. PWV has negative correlation with IA, PA and PE; positive with CA and NPE.

Conclusions: Lower pressure values are associated with more correct answers of BCST. The higher PWV indicates higher BP and lower MOCA result. Surprising correlations with BCST: the higher PWV is associated with the more correct answers, while the lower is with larger percentage of incorrect answers; the higher MOCA result, more errors and less correct answers. Arterial stiffness contributes to MCI in hypertensive patients, so more research are needed to decide if computerized form of cards sorting test is useful to recognize the executive function disorders. The study indicates that MOCA is better in the assessment of cognitive function.

ARTERIAL STIFFNESS AS A PROGNOSTIC FACTOR FOR HYPERTENSIVE ENCEPHALOPATHY

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Objective: Although hypertension (HT) is a well-established risk factor for stroke, it is also known about hypertensive encephalopathy (HE) when neurologic sequelae of chronic HT appear as multifocal/diffuse MRI findings and can be asymptomatic. The aim of this study was to assess vascular markers as prognostic factors for HE.

Design and method: We evaluated 127 (75 male) patients aged 63 (57;68) with HT. Neurological exam included assessment of motor functions, coordination, cognitive functions etc. The brain MRI images of these patients were reviewed. Arterial stiffness indices (pulse wave velocity, PWV; augmentation index, AIx; arterial stiffness index, ASI) were obtained using oscillometry-based method during 24-h ABPM (Vasotens technology).

Results: Baseline characteristics of patients are shown in table 1.

Table 1
Baseline characteristics of patients

History of hypertension, years, n (SD)	11 (8)
Grade I of HT, n (%)	26 (21)
Grade II of HT, n (%)	69 (54)
Grade III of HT, n (%)	32 (25)
Non-disabling subcortical minor stroke in the past, n (%)	44 (35)
Diabetes mellitus, n (%)	26 (21)
Left ventricular hypertrophy, n (%)	115 (90)
Hemodynamically significant brachiocephalic arterial stenoses, n (%)	19 (15)
HE, n (%)	30 (24)

Stepwise discriminant analysis defined a model of the 6 signs that determine HE (Wilks' Lambda: 0.34199 approx. $F(12,82) = 4.8516$ $p < 0.0001$) including 24-h PWV > 8.2 m/s; ASI > 171 ; minor stroke in the past; history of hypertension > 15 years; 24-h mean BP > 104 mmHg; 24-h pulse pressure > 55 mmHg. There were statistically significant correlations between vascular markers (PWV, ASI, AIx) and the severity of MRI structural changes in brain (number of foci, severity of leukoariosis, enlargement of subarachnoid and of perivascular spaces, ventricular enlargement).

Conclusions: Along with previous stroke, duration of HT history, mean and pulse BP, such vascular markers as arterial stiffness indices have an independent association with HE.

INCIDENCE AND PREDICTORS OF NEW ONSET TYPE 2 DIABETES AMONG HYPERTENSIVE-OBESE PATIENTS

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Objective: Objectives: Calculate the incidence rate and predictors of progression to new onset Type 2 diabetes mellitus (T2DM) in hypertensive patients. Methods: An analytical retrospective cohort study was conducted in 9 primary care centers located at urban area of Qatif. It included 438 high risk patients with essential hypertension, 234 (53.4%) obese and 204 (46.6%) non-obese, who had normal fasting blood glucose and hemoglobin A1c or at prediabetes stage at baseline. Participants were followed for a mean duration of 38.3 months (1399.3 person-years). T2DM was diagnosed based on the American Diabetes Association criteria. Incidence rates for T2DM was calculated and its predictors were estimated using the Cox proportional hazards model.

Design and method: The incidence rate for new onset T2DM among all, obese and non-obese patients with essential hypertension were 82.9 (95% confidence interval (CI): 68.8–99.1), 100.7 (95% CI: 79.5–125.9), and 63.8 (95% CI: 46.7–85.1) per 1,000 person-years respectively. Yearly incidence of T2DM was the highest in the first and second years of follow up. It was 10.3% and 11.4% among obese, respectively, while it was 7.3% and 9.5% among non-obese, respectively. After two years of follow up, yearly incidence continued rising among obese patients, only. Predictors of new onset T2DM were female gender, family history of diabetes, dyslipidemia, fasting blood glucose and body mass index.

Conclusion: In hypertensive patients, new-onset T2DM was highest in the first two years of follow up, particularly among obese patients. Targeting modifiable risk factors is mandatory to decrease the chance of onset.

FERNANDEZ' STROKE: HYPERTENSION AND HYPOTENSION AND CARDIOVASCULAR RESOLUTIONS

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Objective: Practitioners/Researchers presently do not know that the knowledge of the coverage determinations of High Blood Pressure Oxygen Stroke(s)/Hemorrhage or

of Low Blood Pressure Oxygen Stroke(s)/Syncope (BP < 70/40) including their ICD Codes, are missing from their Diagnosis and Treatment of Syncope (BP > 200/110? or BP < 70/40). The following organizations must Correct the ICD's, and the Manuals or Guidelines involved in the Diagnosis and Treatment of Syncope in order to reduce the Systemic Number of Cryptogenic Strokes, Number of Syncope, Mortality and Morbidity Rates, and Medical Costs:

- HHS (MAC), 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients with Syncope
- VA/DoD (Champions) Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting
- European Society of Cardiology (ESC) (Chairperson), Guidelines for the Diagnosis and Management of Syncope (Version 2009)
- WHO (Unknown), International Classification of Diseases (ICD) (For the Practitioner to Diagnose and Treat Syncope (BP < 70/40) and get paid).

Design and method: This original contribution of all new, currently-updated, evidenced-based epidemiology is presently available in the clinical setting with knowledge of Syncope/Stroke/Transient Loss of Consciousness in the Fernandez' Stroke report. SCIENTIFIC DATA

A prolonged (6) year Blood Pressure Monitored Fernandez' Madam X Syncope Clinical Study was conducted in contrast to the conventional strategy-based-on-laboratory testing and resulted in:

- A Class of Recommendation (COR) of I (beneficial, useful, effective),
- A level of evidence of A (by its observation in any clinical setting).

Results: This Stroke report has translated this knowledge into actionable-recommendations of what to do when a person faints, provides new strategies, describes an effective mechanism-specific treatment, conclusively identifies the specific risks to the patient, guides the therapy, and reduces Syncope/Stroke/Transient Loss of Consciousness recurrences.

Conclusions: All the Practitioner has to do is monitor the patient's Blood Pressure and follow the treatment procedures. This will mitigate the Syncope symptoms but will not cure any other underlying diseases; And when the Issuers for the ICD's, Manuals and Guidelines make their corrections the Syncope systemic number of falls, strokes, mortality, morbidity, and medical costs will decrease.

NON-SURGICAL PERIODONTAL TREATMENT IMPROVES CARDIOVASCULAR ADAPTATION TO ORTHOSTATIC CHALLENGE IN THE SHORT-TERM

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Objective: Periodontal health status influences systemic health, and periodontal treatment (PT) has been shown to improve systemic inflammation and endothelial dysfunction. The latter has been associated with orthostatic intolerance. We hypothesized that single-stage scaling (SSS) and full mouth disinfection (FMD) may affect cardiovascular (CV) response to orthostatic challenge in otherwise healthy subjects who needed non-surgical PT (NSPT).

Design and method: 20 age-sex-BMI-matched patients (10 M;10F) aged 42.3 ± 13.9 years who needed NSPT underwent SSS (n.12) or FMD (2 sessions 48 h apart; n.8) based on disease severity. Systolic and diastolic BP (SBP, DBP; mmHg) and heart rate (HR; bpm) were measured with a validated automatic device (Omron M6 Comfort It) in clino- (3x) and orthostatism (within 1¢ after standing) before and after each treatment and 7 days after completion of treatment. Within- and between-group analyses were performed. Data were expressed as mean \pm SD. Significance level was set at $p < 0.05$.

Results: Overall, baseline CV parameters were as follows: SBP 120.2 ± 13.9 mmHg, DBP 74.6 ± 11.6 mmHg, HR 70.1 ± 11.6 bpm in clinostatism; SBP 126.8 ± 14.5 mmHg, DBP 82.2 ± 7.8 mmHg, HR 77.7 ± 12.3 bpm in orthostatism. No statistical difference was observed between treatment groups. Soon after each treatment session (acute effect), a non-significant increase in BP and a reduction in HR were observed in the population overall compared to baseline (clinostatism: SBP $+1.18$ mmHg, $p = 0.52$; DBP $+2.05$ mmHg, $p = 0.18$; HR -4.93 bpm, $p = 0.0001$; orthostatism: SBP $+3.25$ mmHg, $p = 0.26$; DBP $+3.1$ mmHg, $p = 0.11$; HR -2.15 bpm, $p = 0.07$). Seven days after treatment (final effect), a significant (except for oDBP) decrease in the CV parameters compared to the basal condition was observed in the population overall in both conditions (clinostatism: SBP -5.48 mmHg, $p = 0.03$; DBP -4.27 mmHg, $p = 0.01$; HR -48 bpm, $p = 0.002$; orthostatism: SBP -6.22 mmHg, $p = 0.01$; DBP -1.05 mmHg, $p = 0.59$; HR -4.33 bpm, $p = 0.03$). No statistical difference was observed in the acute or late effects on CV parameters between treatments.

Conclusions: NSPT determined a significant delayed reduction in BP and HR that persisted after orthostatic challenge, irrespective of treatment. These results are in line with previous findings on endothelial-mediated effects of NSPT. Longer follow-up is needed in order to verify any longer persistence of these effects and their potential impact on CV health.

ORAL PRESENTATIONS IN POSTER AREA

COMPLICATIONS AND COMORBIDITIES

NIGHT-TIME HEART RATE NON DIPPING: CLINICAL AND PROGNOSTIC SIGNIFICANCE IN THE GENERAL POPULATION

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Objective: Studies addressing the association between a reduced drop of heart rate (HR) at night with subclinical organ damage and cardiovascular events in the general population are scanty. We evaluated this issue in subjects enrolled in the Pressioni Monitorate E Loro Associazioni (PAMELA) study.

Design and method: At entry 2,021 subjects underwent diagnostic tests including laboratory investigations, 24-h ambulatory blood pressure (BP) monitoring and echocardiography. Participants were followed from the initial medical visit for a time interval of 148 ± 27 months. To explore the association of circadian HR rhythm and outcomes participants were classified in the primary analysis according to quartiles of nocturnal HR decrease. In secondary analyses the population was also classified according non-dipping nocturnal HR (defined as a drop in average HR at night lower than 10% compared to day-time values) and next in four categories: (1) BP/HR dipper, 2) BP/HR non dipper, 3) HR dipper/BP non dipper, 4) HR non dipper/BP dipper).

Results: A flattened circadian HR rhythm (i.e. lowest quartile of night-time HR dip) was independently associated to left atrial (LA) enlargement, but not to left ventricular hypertrophy; moreover, it was predictive of fatal and non-fatal cardiovascular events, independently of several confounders (hazard ratio 1.8, CI: 1.13–2.86, $p < 0.01$ vs highest quartile).

Conclusions: A blunted dipping of nocturnal HR is associated to preclinical cardiac damage in terms of LA enlargement and is predictive cardiovascular morbidity and mortality in the general population.

EFFECTS OF BACKGROUND STATIN THERAPY ON LOCAL RIGIDITY PARAMETERS IN PATIENTS WITH STEMI

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Objective: to analyze the carotid artery stiffness parameters in patients with STEMI.

Design and method: 85 patients were included in the study: 75 men and 10 women. The main group received atorvastatin 80 mg/day, the comparison group received atorvastatin 20 mg/day. The first group included 46 patients (41 men and 5 women), the average age was 51.2 ± 9.5 years. The second group consisted of 39 patients (36 men and 3 women), aged 52.7 ± 8.2 years. The groups were matched by age, sex, height, BMI, office BP.

The structural and functional arterial properties were evaluated using common carotid arteries (CCA) ultrasound by MyLab90 scanner (Esaote, Italy). The measurements were carried out using the technology of radiofrequency (RF) analysis which includes two programs: RF-QIMT and RF-QAS. The following parameters of local carotid stiffness were studied on 7–9th day and 24 weeks later: QIMT - intima-media thickness (um), stiffness indices α and β , CC-coefficient of transverse compliance (mm²/kPa), Aix augmentation index (%), local pulse wave velocity (PWV) (m/s), using a high-frequency probe (13–14 MHz).

Results: In the first group initial IMT value was 756.6 ± 134.2 um, after 6 months of therapy a decrease to 670.9 ± 128.9 um was found, which corresponds to regression by 11% ($p < 0.05$). The coefficient of transverse compliance - CC increased by 11% ($p < 0.05$): from 0.85 (0.63, 1.12) to 0.94 (0.79, 1, 13) mm²/kPa. There was a decrease in PWV measured locally in the carotid arteries at 6% ($p < 0.05$): from 7.2 (6.3, 8.7) to 6.8 (5.8, 7.2) m/s, $p < 0.05$. The stiffness index β

in the same group significantly decreased from 9.3 (7.5, 12.5) to 8.1 (6.0, 10.4) by 13%, respectively ($p < 0.05$).

These parameters have not changed after 6 months of therapy in the 2nd group. The Aix has significantly increased in both treatment groups: in the 1st group - from 1.2 (0; 4) to 4.2 (2.5, 8.5)%, $p < 0.05$; in the 2nd - from 1.06 (-0.14, 2.6) to 4.9 (2.3, 6.3)%, $p < 0.05$.

Conclusions: high-dose atorvastatin therapy has a significant positive effect on stiffness parameters of carotid arteries and IMT in STEMI patients according to radiofrequency analysis of the ultrasound signal.

EFFECTS OF BARIATRIC SURGERY ON ENDOTHELIAL FUNCTION IN EXTREMELY OBESE PATIENTS

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Objective: Endothelial function assessed through flow-mediated dilation (FMD) declines in obese patients and is connected with higher level of cardiovascular events. The aim of the study was to assess the changes in endothelial function after bariatric surgery in extreme obese patients.

Design and method: We included patients with severe obesity who met the eligibility criteria and underwent bariatric surgery (Sleeve Gastrectomy and Roux-en-Y Gastric Bypass). Anthropometric variables, laboratory investigations, intima media thickness (IMT) of carotid artery M-mode studies (GE Vivid 3 Ultrasound), flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD) were assessed before, 10 days and 6 months after the intervention. Statistical analysis was performed using general linear models and Spearman correlation.

Results: Data from 96 patients (mean age 43.45 ± 11.5 years, 42.7% men) were analysed. BMI decreased from 47.09 ± 6.24 kg/m² to 35.7 ± 5.4 kg/m² after 6 months (no significant change occurred after 10 days). Significant increase of mean FMD was observed after half a year (7.53 ± 5.48 vs 11.09 ± 7.65 %, $p < 0.05$) with no significant change in 10 day time. NMD (14.7 ± 10.3 vs 14.7 ± 7.5 vs 15.7 ± 13.07 %) and IMT (0.59 ± 0.12 vs 0.59 ± 0.12 vs 0.58 ± 0.12 mm) did not differ in follow up. There were no correlations between FMD nor NMD and BMI, weight and levels of hsCRP, glucose, HbA1C, insulin, leptin, adiponectin.

Conclusions: Improvement of endothelial function after bariatric surgery is an additional factor reducing cardiovascular risk among extremely obese subjects.

DETECTION OF ATRIAL FIBRILLATION DURING ROUTINE 24-HOUR AMBULATORY BLOOD PRESSURE MONITORING IN THE ELDERLY: COMPARISON WITH 24-HOUR ELECTROCARDIOGRAPHY

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Objective: To assess the diagnostic accuracy of a novel oscillometric 24-hour ambulatory blood pressure (ABP) monitor (Microlife WatchBP O3 Afib) with implemented algorithm for automated atrial fibrillation (AF) detection during each ABP measurement in elderly hypertensives.

Design and method: Elderly subjects (age > 64 years, or 50–64 years, untreated or treated for hypertension, with stroke history or suspected arrhythmias) were subjected to simultaneous 24-hour ABP monitoring and 24-hour electrocardiography (ECG).

Results: One hundred subjects (mean age 70.6 ± 8.2 [SD] years, men 53%, hypertensives 85%, 17 with permanent AF, 4 paroxysmal AF, 79 non-AF) were analyzed. Among a total of 6,410 valid ABP readings, 1,091 (17%) were taken in ECG AF rhythm. In reading-to-reading ABP analysis, the sensitivity, specificity and accuracy of the ABP monitor in detecting AF was 93%, 87% and 88% respectively. In non-AF subjects, 12.8% of the 24-hour ABP readings indicated false positive AF, of whom 27% were taken during supraventricular premature beats. There was a strong association between the proportion of false positive AF readings and that of supraventricular premature beats ($r = 0.67$, $p < 0.001$). In paroxysmal AF and non-AF subjects, the receiver operating characteristics curve (area under the curve 0.83, $p < 0.01$) showed that positive AF readings at 15% during

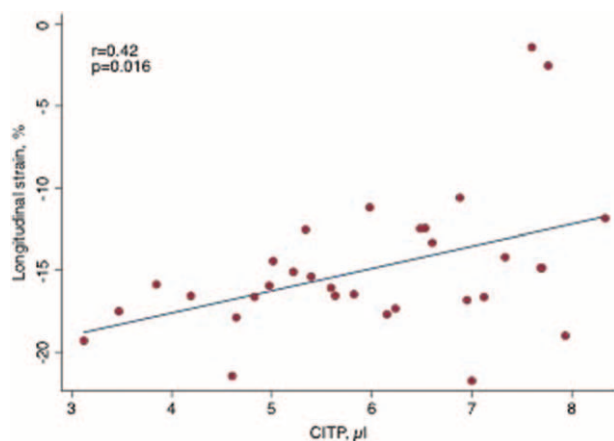
24-hour ABP. monitoring had 90% sensitivity and 77% specificity for detecting AF. (episode of any duration in 24-hour ECG).

Conclusions: A novel 24-hour ABP monitor with AF detecting algorithm has high sensitivity and moderate specificity for AF screening during routine ABP monitoring in elderly hypertensives. AF detected in 15% or more of the 24-hour ABP readings in elderly hypertensives should mandate 24-hour ECG monitoring for suspected AF.

CARDIAC MAGNETIC RESONANCE-DERIVED STRAIN ANALYSIS AND MOLECULAR BIOMARKERS OF FIBROSIS IN HYPERTENSIVE HEART DISEASE

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Objective: Preclinical cardiac dysfunction can be assessed using cardiac magnetic resonance (CMR) imaging-derived strain analysis. Molecular biomarkers of fibrosis have shown association with clinical outcomes, preclinical target organ damage and histologically proven myocardial fibrosis. The aim was to investigate the relationship of CMR-assessed strain with circulating biomarkers of fibrosis in hypertensives with left ventricular hypertrophy (LVH).



Design and method: CMR and assessment of biomarkers of fibrosis were performed in CVD-free hypertensives with positive ECG-derived criteria for LVH. Longitudinal, circumferential and radial strain were assessed using CMR-feature tracking. The concentrations of molecular biomarkers of collagen synthesis (PICP, PIIINP) and collagen degradation (C1TP, MMP-1) were measured using commercial kits. Pearson's correlation and multiple linear regression analysis controlling for gender, age, height, weight, heart rate and 24-h systolic BP were performed in order to assess the relationship between available variables.

Results: 36 hypertensives (83% males, mean age 50.6 ± 4.3) underwent CMR imaging, and strain analysis was performed in 33 participants. Correlation models

showed a significant relationship of longitudinal strain with C1TP; In fully adjusted regression models, longitudinal strain was associated with C1TP ($\beta = 0.46$, $p = 0.025$, $R^2 = 0.25$) (figure 1), and circumferential strain was inversely associated with MMP-1 ($\beta = -0.38$, $p = 0.047$, $R^2 = 0.32$). PICP and PIIINP were not independently associated with strain parameters.

Conclusions: Myocardial strain was associated with molecular biomarkers of collagen degradation: A decrease in longitudinal or circumferential strain (i.e., "less negative" values) was related to higher levels of C1TP and lower levels of MMP-1, respectively.

20-YEAR TRENDS OF CHARACTERISTICS AND OUTCOMES OF STROKE PATIENTS WITH ATRIAL FIBRILLATION

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Objective: The accurate knowledge of secular trends in prevalence, characteristics and outcomes of patients with ischemic stroke (IS) and atrial fibrillation (AF) allows better projections into the future. We aimed to report the overall, age- and sex-specific secular trends of characteristics and outcomes of patients with acute IS and AF between 1993 and 2012 in the Athens Stroke Registry.

Design and method: We used Joinpoint regression analysis to calculate the average annual percent changes and 95% confidence intervals.

Results: Among 3314 stroke patients, 1044 (31.5%) had AF. Between 1993–2012, there was an average annual reduction of 0.8% (95%CI:-1.5%;0.0%) in the proportion of AF-patients among all AIS patients, whereas the proportion of newly-diagnosed AF-patients among all AF-patients increased annually by an average of 7.1% (95%CI:5.4%;8.9%). Among all AF-patients, there was an average annual reduction of 2.9% (95%CI:-2.7%;-3.2%) in the proportion of previously-known AF-patients, followed by an annual average reduction of 2.4% (95%CI:-1.2%;-3.6%) in the proportion of previously-known AF-patients not receiving any antithrombotic treatment at admission. During that period, there was an increase in the average annual proportion of previously-known AF-patients treated with anticoagulants (6.4%, 95%CI:1.2;11.9%) and aspirin (2.3%, 95%CI: -0.4;5.0%) at admission; an average annual increase in the proportion of AF-patients who were prescribed anticoagulant was apparent both for patients with mRS < 4 (3.5%) and mRS:4–5 (7.2%), while the proportion of AF-patients who were prescribed aspirin or no antithrombotic at discharge was annually reduced (5.8% for mRS < 4; 1.6% for mRS:4–5 and 7.1% for mRS < 4; 5.3% for mRS:4–5 respectively). Stroke recurrences were annually reduced by an average of 5.8% (95%CI:-8.6;-3.0%), along with cardiovascular events (6.5%, 95%CI:-8.3;-4.7%) and deaths (7.9%, 95%CI:-9.2;-6.5%).

Conclusions: Between 1993 and 2012, the proportion of AF-patients on proper antithrombotic treatment and the rate of newly-diagnosed AF increased significantly. Rates of stroke recurrence, cardiovascular events and mortality reduced significantly.

ORAL PRESENTATIONS IN POSTER AREA

DIAGNOSIS AND TREATMENT

ANTI-INFLAMMATORY FACTOR DEL-1 PROTECTS FROM ANGIOTENSIN II-DEPENDENT VASCULAR REMODELING AND HYPERTENSION

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Objective: Hypertension is the leading cause of mortality worldwide. Critical contributor to pathophysiology of hypertension is vascular remodeling, which is mediated by angiotensin II (ANGII) driven T-cell inflammation and production of interleukin 17 (IL-17). Thus, anti-inflammatory approaches have been proposed as a potential therapeutic strategy.

We tested the role of an endogenous anti-inflammatory factor, developmental endothelial locus-1 (Del-1), in prevention of ANGII-induced vascular remodeling and hypertension.

Design and method: Mice overexpressing endothelial Del-1 (Del1 Tg) and WT mice which were repetitively injected with soluble Del-1 (50 mg/per injection) were used. Hypertension and vascular remodeling were induced with ANGII infusion using osmotic minipumps (Alzet[®]) for 4-weeks. Systolic blood pressure (SBP) was measured via tail-cuff method. Aortic remodeling was assessed by quantification of adventitial fibrosis, elastin and medial thickness. Aortic inflammatory cells were quantified with flow cytometry, whereas endothelial dysfunction was assessed using Mulvany myography.

Results: After 4-weeks of ANGII infusion, Del-1 Tg mice had lower ($P < 0.01$) SBP compared to WT littermates. Del-1 Tg mice had less ($P < 0.01$) aortic medial thickness, less adventitial collagen ($P < 0.01$) and more elastin ($P < 0.01$) area compared to WT mice. MMP2 activity was significantly ($P < 0.01$) less in Del-1 Tg mice than in WT. Endothelium-dependent relaxation of aorta was stronger ($P < 0.01$) in Del-1 Tg mice than in WT. Del-1 Tg mice had less ($P < 0.05$) CD45+ leukocytes, TCR β + T-cells, as well as CD4+ T-helper and CD8+ T-cytotoxic cells in aorta compared to WT mice. TCR β +IL-17+ double positive T-cell count was also less ($P < 0.05$) in Del-1 Tg than in WT mice. Injections of soluble Del-1 in WT completely protected from ANGII-induced development of hypertension and aortic remodeling. Del-1 injected mice had lower ($P < 0.05$) SBP compared to vehicle treated mice. Del-1 injections resulted in less aortic medial thickness ($P < 0.05$) and adventitial collagen area ($P < 0.05$), as well as lower MMP2 ($P < 0.05$) activity. Endothelium-dependent relaxation was stronger ($P < 0.01$) in Del-1 injected mice.

Conclusions: Our findings demonstrate that Del-1 protects from ANGII-dependent development of hypertension and vascular remodeling via limitation of inflammation and maintaining of endothelial function. Its proof of efficacy via exogenous injections presents Del-1 as a potential therapeutic agent.

HIGH SODIUM CONCENTRATION MODULATES DENDRITIC CELLS IMMUNE FUNCTIONS

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Objective: Excessive Na⁺ intake is associated with the development of hypertension and increases skin sodium concentration [Na⁺] (up to 200 mM). The transfer of dendritic cells (DCs) from hypertensive to normotensive leads to the development of hypertension in animals. DCs modulate both the innate and adaptive immune response. However, the effect of high [Na⁺] on DCs remains unclear in humans.

Design and method: DCs derived from human blood monocytes, differentiated for 6 days in RPMI 10% fetal calf serum (FCS) supplemented with GM-CSF (66 ng/ml) and IL4 (25 ng/ml) then stimulated during 48 h with LPS (2.5 or 50 ng/ml) at different [Na⁺] (140 vs 200 mM). We studied DCs morphological changes by confocal microscopy, analyzed cell viability, expression of CD25, CD83, CD86 and CD80 costimulatory markers, FITC-DEXTRAN endocytosis, reactive oxygen species (ROS) production and CCR7 chemokine receptor expression by flow cytometry. We studied DCs CCL19-driven chemotaxis using transwell migration assay with 8 mm pore size. We measured secreted cytokines (IL-12p70, IL-6, IL-23, IL-10, TGF- β) using ELISA. We also looked for MAP Kinase activity and SGK1 expression by western blot.

Results: At high [Na⁺] of 200 mM as compared to normal [Na⁺] 140 mM, we found that DCs viability was maintained (over $84.5 \pm 5\%$). DCs morphology changed towards a more elongated aspect. CD25, CD83 CD80 and CD86 expression significantly decreased ($-67.7 \pm 32.3\%$, $-60.4 \pm 14.5\%$, $-25 \pm 20.8\%$, $-13.6 \pm 10.3\%$, respectively, $p < 0.0001$). There were also less ROS production (-36.1 ± 12.3 , $P < 0.005$) and a persistence of endocytosis capacity ($+108.3 \pm 44.6\%$, $P < 0.005$). CCR7 expression ($-59.3 \pm 15.3\%$, $P < 0.0001$) and CCL19-driven chemotaxis ($-49.7 \pm 25.6\%$, $P < 0.0005$) index significantly decreased. Cytokines measurement showed a reduced secretion of IL-12p70, IL-6 and IL-23 ($-78.5 \pm 9\%$, $-66.6 \pm 9.2\%$, $-90.4 \pm 7.12\%$, respectively, $p < 0.0001$) and an increase of IL-10 and TGF- β ($+111 \pm 51\%$, $+191.1 \pm 110.4$, respectively, $P < 0.005$). At high [Na⁺] reduced phosphorylation of p38 ($-43.13 \pm 25\%$, $P < 0.03$) leads to a higher ERK $\frac{1}{2}$ protein phosphorylation ($+30.572 \pm 11.6\%$, $P < 0.0078$) and greater expression of SGK1 protein ($+35.078 \pm 11.5\%$, $P < 0.015$).

Conclusions: High [Na⁺] concentration downregulates pro-inflammatory human DCs immune response to LPS and inhibits their migration towards lymph nodes, through MAP Kinase signaling pathway and SGK1-related mechanisms. However, the implication of these changes in the development of hypertension remains unknown.

CLASSIFICATION OF NOCTURNAL BLOOD PRESSURE PROFILE USING FUZZY SYSTEMS

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Objective: Implement a fuzzy inference system for a nocturnal profile classification model, for knowing the nocturnal blood pressure behavior of the patients and with this gain knowledge of the current health condition of such patients, in order to prevent a cardiovascular event.

Design and method: A fuzzy system for the classification of nocturnal blood pressure is implemented, and this because the original tests that were performed with a traditional system of rules did not produced the desired results. The fuzzy system was empirically designed based on a medical article of nocturnal hypertension, in which the author defines that in order to obtain the profile of nocturnal blood pressure, the information of the ABPM obtained in the day and night should be separated. From which the quotient to obtain the night profile of patients is calculated, and from this the range of each membership function is obtained, which are those that provide us each level of classification. The fuzzy system has two inputs which are the quotient of the systolic pressure and the quotient of the diastolic pressure and as output the night profile of the patient.

Results: Tests were performed with a group of 200 patients, comparing the results of the traditional system rules with the fuzzy system, and having better results with the second, because the traditional system rules requires precise information. Tests are carried out with different architectures in which different types of membership functions were used, such as: trapezoidal and Gaussian, having better results with the fuzzy system with trapezoidal membership functions. A random sample of 30 patients was collected obtaining 90% of correct classification with the fuzzy system in comparison with the traditional system rule, which correctly classified 53.3% of the patients, with a standard deviation of 3.86. The table shows the comparison of the different experiments, being those marked with bold those that classified correctly.

Conclusions: Fuzzy logic allows us to handle inaccurate information, which helps us obtain good results, which can be noted in the reported experiments, where this type of classification is more efficient than the traditional system rules.

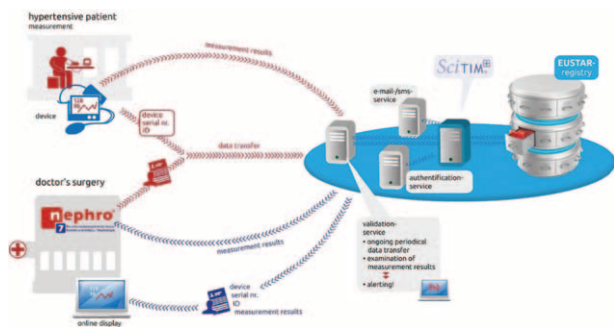
Systolic	Diastolic	Average	Real	Fuzzy System	Traditional system Rules
0.81	0.73	0.77	Extreme Dipper	Dipper	-
0.94	0.93	0.935	Non Dipper	Non Dipper	No Dipper
0.91	0.8	0.855	Dipper	Dipper	-
0.92	0.88	0.9	Non Dipper	Non Dipper	-
0.89	0.78	0.835	Dipper	Dipper	-
0.95	0.89	0.92	Non Dipper	Non Dipper	-
0.94	0.91	0.925	Non Dipper	Non Dipper	No Dipper
0.91	0.8	0.855	Dipper	Dipper	-
0.93	0.85	0.89	Dipper	Dipper	-
0.88	0.81	0.84	Dipper	Dipper	Dipper
0.95	0.91	0.93	Non Dipper	Non Dipper	No Dipper
0.77	0.79	0.78	Extreme Dipper	Extreme Dipper	Dipper extremo
1.00	0.89	0.94	Non Dipper	Non Dipper	-
0.88	0.83	0.85	Dipper	Dipper	Dipper
0.96	0.89	0.92	Non Dipper	Non Dipper	-
0.94	0.87	0.91	Non Dipper	Dipper	-
0.99	0.91	0.95	Non Dipper	Non Dipper	No Dipper
0.88	0.74	0.81	Dipper	Dipper	-
1.07	1.11	1.09	Reverse	Reverse Dipper	Dipper reverso
0.95	0.93	0.94	Non Dipper	Non Dipper	No Dipper
0.91	0.83	0.87	Dipper	Dipper	-
1.10	1.12	1.11	Reverse	Reverse Dipper	Dipper reverso
0.80	0.72	0.76	Extreme Dipper	Extreme Dipper	Dipper extremo
0.89	0.88	0.89	Dipper	Dipper	Dipper
0.82	0.80	0.81	Dipper	Dipper	Dipper
0.84	0.80	0.82	Dipper	Dipper	Dipper
0.92	0.89	0.91	Non Dipper	Non Dipper	-
0.88	0.86	0.87	Dipper	Dipper	Dipper
0.85	0.80	0.83	Dipper	Dipper	-
0.93	0.88	0.90	Non Dipper	Dipper	-

EUSTAR: EUROPEAN SOCIETY OF HYPERTENSION TELEMEDICINE IN ARTERIAL HYPERTENSION REGISTER 2018: DESIGN AND RATIONALE

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Objective: Failing to reach blood pressure (BP) goals is a major problem in treatment of hypertension, causing a high socioeconomic burden, sequel morbidities and strongly increased mortality. Recent studies demonstrated that interventional decentralized telemonitoring (idTM®) can strongly improve BP management in hypertension including high risk patients. In the EDiMed-Project (efficiency analysis of services in telemedicine) - supported by German Ministry for education and research - the cost-benefit ratio was analyzed and a positive socioeconomic impact was found.

Design and method: This project aims at establishing a telemonitoring system that allows to extend this service to all European Excellence centers for hypertension treatment and ultimately to all physicians treating hypertensive patients in Europe. For this effort, the unique software SciTIM® providing highest standard of data security was developed for the register to allow: Making idTM® available to physicians and patients across Europe Establishing telemedical standards for selected hypertensive indications Establishing a system for collections of high quality epidemiologic data from daily medical practice Establishing a digital interface for direct interaction between specialists and general practitioners



Results: Register nucleus started with 6 ESH-centers in 2018. The corresponding SciTIM software have been tested since May 2017 at the Nephrological Center Göttingen GbR. After completion of the test phase the EUSTAR register will be

extended to other centers. To integrate data directly from the data management systems the project will generate interfaces to the most commonly used medical data management systems. In addition, system will provide a user interface to physicians, enabling to monitor their patient's telemonitoring progress at first time directly in their electronic health records and specific rules to pro-actively alert staff members via daily reports.

Conclusions: The EUSTAR consortium will establish a register based on needs of medical specialists under the aegis of the ESH. A database will be created that allows safe and standardized exchange of data. The System will include interfaces for data collection from medical measurement devices and be open for all possible providers and also for other data than the first two parameters blood pressure and body weight.

RELATIONSHIP BETWEEN UNATTENDED AND ATTENDED BP VALUES AND PRECLINICAL ORGAN DAMAGE

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Objective: It has been suggested that measurement of “unattended” or “automated oscillatory (AOBP)” blood pressure values may provide advantages over conventional BP measurement; some hypertension guidelines now suggest this approach as the preferred one for measuring office BP. Data on the relationship between AOBP and cardiovascular events are much less solid as compared to those obtained with the standard BP measurement; on the other hand, some study suggested that AOBP might be more strictly correlated with hypertensive target organ damage than “attended” BP.

The aim of our study was to evaluate the relationship between “attended” or “unattended” BP values and target organ damage in 261 subjects attending the outpatient clinic of an ESH Excellence Centre.

Design and method: BP values were measured by the physician with an automated oscillometric device (Omron HEM 9000Ai, mean of 3 measurements), after 5 minutes of rest; thereafter, the patient was left alone and unattended BP was measured automatically after 5 minutes (3 measurements at 1 minute interval).

Results: Patient's mean age was 61 ± 16 yrs, mean BMI 26.1 ± 4.2 , 60% were female, 88 % had a previous diagnosis of hypertension (64% treated). Systolic unattended BP was lower as compared to attended SBP (130.1 ± 15.7 vs 138.6 ± 17.2 mmHg). Left ventricular mass index (LVMI) was similarly correlated with unattended and attended SBP ($r = 0.132$ and $r = 0.133$, $p < 0.05$, respectively). LVMI was similarly correlated with unattended and attended pulse pressure (PP) ($r = 0.277$ and $r = 0.299$, $p < 0.05$, respectively). Carotid IMT was significantly and similarly correlated with both attended and unattended BP values (CBMax-IMT: $r = 0.172$ and $r = 0.153$ for attended and unattended SBP, $p < 0.05$ and $r = 0.459$ and $r = 0.436$ for attended and unattended PP, $p < 0.001$). The differences between correlations were not statistically significant.

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

AN HIGHER WHITE-COAT EFFECT IN THE FIRST HOURS OF AMBULATORY BLOOD PRESSURE MONITORING IS ASSOCIATED WITH MORE BLOOD PRESSURE PEAKS DURING THE WHOLE DIURNAL PERIOD

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Objective: White-coat effect (WCE) is a common finding also in ambulatory blood pressure monitoring (ABPM) and like in office blood pressure (BP) measurement can determine an over-diagnosis of arterial hypertension. In our previous work we found that WCE magnitude (WCEm) is correlated with an higher BP variability during the entire 24-hours ABPM period but the effective BP load remain to be established.

Design and method: We analysed 421 ABPMs (M/F 146/275) characterized by the first systolic BP value at least 10 mmHg higher than mean diurnal systolic BP (mDSBP). WCEm was evaluated as the mean value of the first two hours of recording, both for systolic and diastolic BP (sysWCEm and diaWCEm, respectively). The diurnal BP load was estimated with BP peaks, i.e. the number of systolic and diastolic BP values respectively 10 and 5 mmHg higher than mDSBP and mean diurnal diastolic BP (mDDBP). We evaluated the correlations between

WCEm, BP peaks and drug classes (angiotensin-converting enzyme/angiotensin receptor blockers, beta-blockers, calcium channel blockers, thiazide diuretics, alpha-blockers, central alpha-agonists and anti-aldosterone) with a multivariate regression analysis with a p-value < 0.01 considered as statistically significant.

Results: Mean age was 65 ± 1 years (M/F $66 \pm 1/64 \pm 1$ years, n.s.) and overall mDSBP and mDDBP were 137 ± 1 and 79 ± 0.5 mmHg, whereas sysWCEm and diaWCEm were respectively 150 ± 1 and 86 ± 1 mmHg, without gender differences. Systolic and diastolic peaks were respectively 12.5 ± 0.1 and 13.5 ± 0.1 ; only the first was directly correlated with age ($r = 0.21$;

$p < 0.01$) whereas neither of the two was correlated with drug therapy. Both systolic and diastolic peaks were significantly correlated with sysWCEm (respectively $r = 0.17$ and $r = 0.19$; $p < 0.01$) but not with diaWCEm; they were also correlated with mDSBP and mDDBP (respectively $r = 0.35$ and $r = 0.31$; $p < 0.01$).

Conclusions: In patients with an higher sysWCEm, systolic and diastolic BP peaks are increased confirming an influence of WCE on the entire diurnal period of ABPM, suggesting that in patients with WCE the alarm reaction persists well beyond the two initial hours of recording alarm.

ORAL PRESENTATIONS IN POSTER AREA

EPIDEMIOLOGY AND MANAGEMENT

CLINICAL SIGNIFICANCE OF ELEVATED ANKLE-BRACHIAL INDEX DIFFERS DEPENDING ON THE AMOUNT OF APPENDICULAR MUSCLE MASS: THE J-SHIP AND THE NAGAHAMA STUDY

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Objective: Low ankle-brachial index (ABI) is associated with cardiovascular risk factors. In contrast, the clinical implication of high ABI is less understood, though several cross-sectional studies reported that high ABI was associated with cardiovascular risk factors. From our preceding study, we suspected that body composition may be a determinant for high ABI, and consequently modulate the clinical significance of high ABI.

Design and method: Datasets of two studies employing independent cohorts, the anti-aging study cohort (n = 1,765, 65 ± 9 years) and Nagahama study (n = 8,039, 58 ± 13 years), were analyzed in this study, in which appendicular muscle mass was measured by computed tomography and bioelectrical impedance analysis, respectively. Brachial and ankle blood pressure were measured using a cuff-oscillometric method.

Results: In the anti-aging study cohort, there was a significant correlation between the thigh muscle cross-sectional area (CSA) and ABI (r = 0.310, p < 0.001). The association of thigh muscle area (b = 0.387, p < 0.001), but not fat area, was independent of body mass index (p = 0.662) and other possible covariates, including systolic brachial blood pressure (p = 0.054), carotid hypertrophy (p = 0.559), and arterial stiffness (b = 0.102, p = 0.001). Although there was a significant sex-differences in the thigh muscle area, muscle CSA was identified as an independent determinant for ABI (b = 0.286, p < 0.001, VIF = 4.87) even in a sex (women: b = -0.087, p = 0.055, VIF = 4.19) included regression model. This positive association was replicated in the Nagahama cohort. When the subjects were subdivided by 75 percentiles of ABI and appendicular muscle mass, multinomial logistic regression analysis identified insulin resistance as an independent determinant for elevated ABI with normal muscle mass (coefficient = 0.134, p = 0.010), whereas insulin resistance was inversely associated with elevated ABI in cases with high muscle mass (coefficient = -0.268, p = 0.001).

Conclusions: Appendicular muscle mass was a strong determinant for ABI. The clinical background, particularly insulin resistance, of individuals with elevated ABI might differ based on the amount of muscle mass.

CAUTIOUS PATIENTS, CAREFUL PHARMACISTS. DO YOU HAVE TO TAKE YOUR NEW ANTI-HYPERTENSIVE MEDICATION TO EXPERIENCE THEIR SIDE EFFECTS?

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Objective: The burden of hypertension in primary care is high and alternative models of care, such as pharmacist management, have shown promise. However, data describing outcomes from routine consultations between pharmacists and hypertensive patients are lacking.

The aim of this study was to identify factors associated with referral of patients from pharmacies to general practice (GP), within the first two weeks of starting a new anti-hypertensive medication.

Design and method: Multivariate logistic regression conducted on data from community pharmacies in all regions of England.

Data were obtained from the 'New Medicines Service' conducted by community pharmacists between 2011 and 2012. Analyses were conducted on 131,419 patients. Fifteen predictors were included in the model, grouped into 3 categories: patient reported factors, demographic factors and medication related factors.

A subsequent content analysis of 1,200 pharmacist clinical consultation notes were also conducted to detect any variation in pharmacist care delivery and to better understand the reasons for referral.

Results: Mean patient age was 65 (±13 years) and 85% of patients were of white ethnicity. A total of 5,895 (4%) patients were referred by a pharmacist to a GP within the first two weeks of starting a new anti-hypertensive medication. Patients reporting side effects (adjusted OR 11.6 [95% CI 10.8–12.4]) were most likely to be referred. Prescriptions for alpha-blockers were associated with referral (adjusted OR 1.28 [95% CI 1.12–1.47]) while patients receiving angiotensin-II receptor blockers were less likely to be referred (adjusted OR 0.89 [95% CI 0.80–0.99]). The content analysis highlighted that providing the necessary assistance, reassurance and follow-up were features seen among consultations resulting in pharmacist management without the need for referral to general practice. However, variation in patient management was observed, highlighting the need to improve the advice given to patients who report medication concerns during early pharmacotherapy.

Conclusions: Most patients were followed up by pharmacists without the need for referral. Patient reported side effects, medication related concerns and medication class prescribed influenced referral. These data are reassuring that additional pharmacist involvement does not increase medical workload appreciably and support further development of pharmacist-led hypertension interventions.

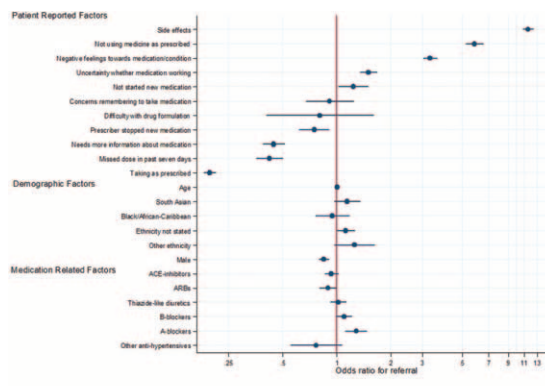
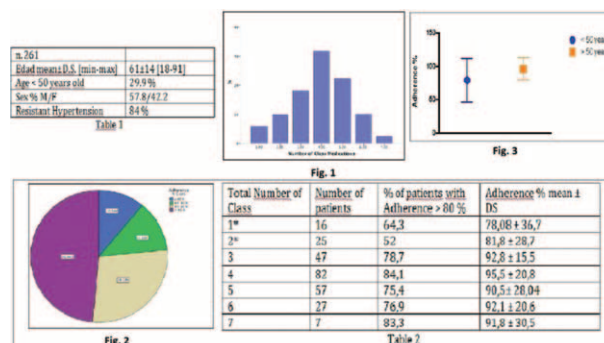


Figure 1 - Coefficient plot showing adjusted odds ratios of included predictors

DETECTION OF NON-ADHERENCE TO ANTI-HYPERTENSIVE TREATMENT THROUGH THE USE OF THE ELECTRONIC PRESCRIPTION SYSTEM IN PATIENTS REFERRED TO A TERTIARY HYPERTENSION CLINIC

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Objective: To know and evaluate the level of adherence to antihypertensive treatment through the information provided by the electronic prescription computerized system.



Design and method: A retrospective, cross-sectional study was conducted in the tertiary hypertension clinic of the Bellvitge's Hospital. Patients visited from June 2015 to July 2017 and with resistant hypertension diagnosis and/or aged less than 50 years were included. The data analyzed from the electronic prescription included: class of drug, prescribed dose and number of boxes collected in pharmacy each month. Adherence to the medication was evaluated during a 24-month long follow-up using the formulas: Number of theoretical boxes = (starting treatment date – final date of follow-up) × (daily intake unit)/(number of tablets of each box). Adherence (%) = number of boxes actually dispensed/number of theoretical boxes × 100. The data analysis was performed using the SPSS package, a level of significance $P < 0.05$ was set in all cases.

Results: We included 261 patients according to criteria. The average age was 61 ± 14.2 years, being 29.9% under 50 years. 84% of patients had resistance hypertension. (Table 1). Figure 1 shows the distribution by amount of drug classes. We detected an adherence to medication of less than 80% in 23.4% patients, between 80–95% in 28.1% and >95% in 48.4% (Fig 2).

Patients treated with < 2 classes of drugs had lower adherence (cut-off > 80%) compared to those taking > 3 classes (58.1% vs. 79.8% $p < 0.001$).

Also, we observed an inverse correlation between age and adherence ($r = 0.25$ $p < 0.0001$). Patients under 50 years had lower (average) adherence to those over ($79.1 \pm 32.2\%$ vs $96.2 \pm 17.3\%$ $p < 0.0001$). (Fig. 3)

Conclusions: The low adherence rates detected with electronic prescription computerized system were similar to values published in previous studies based on more complex methods (use of questionnaires, urinary metabolites, electronic boxes). Despite its intrinsic limitations, our method allowed to detect an high percentage of non-adherence.

In our cohort, younger patients and those who take fewer drugs presented the lowest levels of adherence.

DISCREPANCIES IN CARDIOVASCULAR RISK STRATIFICATION IN HYPERTENSIVE PATIENTS – RESULTS FROM THE SWISS HYPERTENSION COHORT STUDY (HcCH)

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Objective: The Swiss Hypertension Cohort Study (HcCH) is a prospective observational study initiated by the Institute of Primary Care at the University of Basel to investigate current hypertension management in Switzerland. The objective of this sub-analysis of HcCH was to compare risk stratification according to two established cardiovascular (CV) risk assessment models in Swiss hypertensive patients.

Design and method: 1004 patients aged 18 years or older and diagnosed with/treated for arterial hypertension were enrolled by 91 general practitioners from 12 cantons in Switzerland between 2005 and 2013. Blood pressure, medical history, comorbidities, laboratory results, lifestyle measures, medication, and clinical events were recorded at baseline and during annual follow-up visits. CV risk was graded into low, moderate, high, and very high risk using the 2013 European Society of Hypertension (ESH) risk chart for 10 year CV mortality and morbidity risk and the SCORE chart for 10 year CV mortality risk according to the 2016 European Society of Cardiology prevention guidelines. Patients with diabetes mellitus, reported CV diseases and/or missing data required for CV risk stratification were excluded from the analysis. Furthermore, patients with missing data that are necessary for risk stratification were also excluded. Interrater agreement between CV risk models was determined using Cohen's kappa.

Results: Baseline parameters of 367 patients were included into this sub-analysis of HcCH. Distribution of CV risk categories according to ESH and SCORE risk charts is given in Table 1. There was a poor agreement (Cohen's $\kappa = 0.117$, $p < 0.01$) between the SCORE and ESH risk stratification models.

Table 1:

Risk model	SCORE					Total
	CV risk	low	moderate	high	very high	
ESH	low	7	51	2	0	60
	moderate	8	73	8	0	89
	high	13	120	57	5	195
	very high	0	19	4	0	23
Total		28	263	71	5	367

Conclusions: Important discrepancies were found between the results of CV risk stratification according to ESH and SCORE models. The SCORE risk model classified about half of the study Population into a lower risk category compared to the ESH risk model, with the majority of misclassified patients being female. The results of this analysis indicate that the application of the SCORE CV risk stratification model alone may lead to significant underestimation of CV risk leading to inadequate therapeutic management and worsening of prognosis in, particularly high or very high risk, hypertensive patients.

MARKERS OF ARTERIAL STIFFNESS AND SUBCLINICAL VASCULAR DAMAGES IN OBESE CHILDREN

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Objective: We aimed at investigating the influence of weight excess and traditional cardiovascular risk factors on vascular structure and function in a sample of obese children.

Design and method: Overweight or obese children (BMI > 90th percentile for sex and age) included in this observational study underwent office and ambulatory BP measurements (ABPM) and the assessment of carotid intima-media thickness (cIMT), endothelial function by the Flow Mediated Dilation (FMD) technique, carotid distensibility (cDC) by ultrasounds and stiffness index (SI) by digital photoplethysmography.

Results: Sixty-six obese and 4 overweight children were enrolled (age 11.5 ± 2.4 years; female n: 30). Carotid IMT directly correlated with 24h- and nighttime SBP; cDC showed inverse correlations with BMI and waist circumference and 24h-BP. Unexpectedly, SI resulted inversely related with several indexes of weight excess. Most of these correlations remained significant after adjustment for age, sex, BMI and BP. In a replication set of 40 obese children SI, but not Pulse Wave Velocity (PWV), was still inversely associated with BMI.

Conclusions: These data suggest that arterial structure and elasticity are negatively affected by weight excess and BP levels, even in childhood. Surprisingly, SI might not be a reliable marker of vascular stiffness in obese children, because this measure is probably confounded by other factors including vasodilation.

ORAL PRESENTATIONS IN POSTER AREA

MECHANISMS OF HYPERTENSION

SUBCLINICAL RENAL DAMAGE IS ASSOCIATED WITH A REDUCED CHOROIDAL THICKNESS IN PATIENTS WITH PRIMARY HYPERTENSION

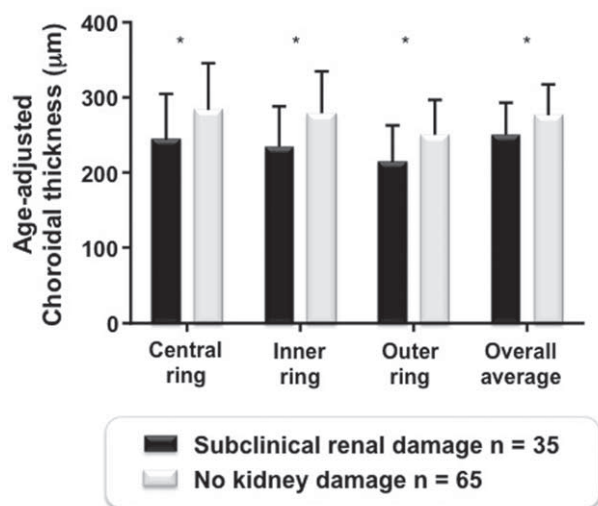
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Objective: The retina is considered the easiest accessible window to study the state of the systemic microcirculation, even if the choroid is the most important vascular layer of the eye. Our understanding of the choroid has been greatly increased in last years since the introduction of advanced techniques of optical coherence tomography (OCT). Our study was aimed to assess choroidal thickness by using Swept-Source OCT (SS-OCT) in essential hypertensive patients (EHs) with and without subclinical renal damage (SRD).

Design and method: We enrolled 100 EHs of which 65 without kidney damage and 35 with SRD. In all the participants SS-OCT and a routine biochemical work-up were performed. Glomerular filtration rate (GFR) was estimated by the CKD-EPI equation (eGFR). SRD was defined, by the presence of microalbuminuria or eGFR between 30 and 60 mL/min/1.73 m². OCT measurements were performed according to the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol, that divides the macula into 9 subfields. The circular grid consists of 3 concentric rings. The inner and outer rings are further divided into quadrants: temporal, nasal, superior, and inferior.

Furthermore, we calculated the average of the individuals values of the four quadrants separately for the inner and the outer ring. The average of all the 9 regions of the ETDRS grid (including the inner, the outer and the central rings) was also calculated.

Results: EHs with SRD showed thinner choroidal thicknesses than those without kidney damage (all $p < 0.05$), even after adjustment for age (figure). Overall choroidal thickness correlated significantly and directly with eGFR ($r = 0.36$) and negatively with urinary albumin excretion ($r = -0.39$). The association of choroidal thickness with SRD was confirmed in multiple logistic regression analyses once the effect of age, anti-hypertensive therapy and triglycerides was accounted for. The odds ratio of having SRD associated with a standard deviation increase of overall choroidal thickness was 0.43 (0.24–0.75, 95% confidence interval; $p = 0.007$).



Values are given as means + SD

* 0.05 < p < 0.01

Conclusions: Our study confirms the close relationships between changes in ocular microcirculation and renal dysfunction.

TRANSGLUTAMINASE-2 CONTRIBUTES TO REACTIVE OXYGEN SPECIES PRODUCTION IN MICE INFUSED WITH ANGIOTENSIN-II

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Objective: Transglutaminase type II (TG2) is a pleiotropic enzyme that exhibits various activities and it is involved in diverse biological functions, including cell signaling, cytoskeleton rearrangements, displaying enzymatic activities. We previously demonstrated that TG2 may contribute to angiotensin II-induced reduction of NO bioavailability as well as to the impaired vascular functional and structural alterations induced by angiotensin II. Here we hypothesized that TG2 may contribute to increased production of reactive oxygen species (ROS) in the vasculature of angiotensin-II-treated mice.

Design and method: TG2-knockout mice (TG2-K/O, 8 weeks old, n = 6) and age-matched wild type (WT) control mice were treated or not with angiotensin-II (400ng/kg/min) for 14 days. TG2 activity in aorta was measured by ELISA. ROS production in aorta was evaluated by dihydroethidium staining. The expression of angiotensin type I receptor (AT1R), TG2, NOX-1, and ERp72 (the positive modulator of NOX-1) was evaluated in aorta by immunoblotting, coimmunoprecipitation analysis was also performed.

Results: As expected, TG2-K/O lacked TG2 expression and activity. Angiotensin-II significantly increased (2-fold) TG2 expression and activity only in WT. AT1R expression in aorta was not influenced by Angiotensin II treatment in both WT and TG2-K/O mice. ROS production was similar in WT and TG2-K/O and increased only in angiotensin-II-treated WT (+9%, $p < 0.01$). NOX-1 and ERp72 expression was similar in WT and TG2-K/O. Angiotensin-II significantly increased NOX-1 (+23%, $p < 0.01$) and ERp72 (+29%, $p < 0.01$) only in WT. Only in aorta from WT and not from TG2-K/O, TG2 was successfully immunoprecipitated by AT1 and ERp72, indicating that TG2 is able to interact with both proteins, and suggesting that it may be involved in angiotensin II-induced NOX modulation and ROS production.

Conclusions: Angiotensin-II increased ROS production and NOX-1 expression and activation only in presence of TG2 in WT. TG2 interacts with both AT1R and ERp72. Thus, TG2 may contribute to NOX-induced ROS production in mice treated with angiotensin-II.

RETINAL ARTERIOLAR MICRO-CONSTRICTIONS EVALUATED WITH ADAPTIVE OPTICS: A NOVEL MARKER IN HYPERTENSION

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Objective: Retinal arteriolar remodeling is an early marker of subclinical target organ damage in arterial hypertension. Through adaptive optics which is totally noninvasive and highly accurate, it is possible to measure changes in arteriolar diameter within 1 mm accuracy. The aim of this study was to evaluate a new marker describing internal diameter variability of the supero-temporal arteriole in hypertensive patients before and after blood pressure control.

Design and method: Adaptive Optics RTX1[®] Camera (ImagineEye, Orsay, France) was used to capture three consecutive images along the supero-temporal arteriole. Wall Thickness (WT) and internal diameter (ID) were measured to calculate Wall-to-Lumen Ratio (WLR) and Wall Cross-Sectional Area (WCSA). A coefficient of variation (CV) for ID was calculated for each group by the following formula: (standard deviation ID/mean ID)*100 over three consecutive measurements. Subjects with a CV ID > 75% were classified as irregular. Uncontrolled hypertensive subjects in the irregular group were given an antihypertensive pharmacological treatment and were reevaluated 1 month after.

Results: 44 patients were analyzed (mean age 47.7 ± 11). Median CV ID in the irregular group was 11% [IQR 9.0–15.0] as compared to 2.0% (regular group) [IQR 1.0–4.0], $p < 0.001$. Patients in the arteriolar irregular group had an increase in home blood pressure (148.3/96.3 vs 130.7/ 82.6 mmHg, $p < 0.01$). They had

significantly decreased ID (82.24 ± 13.5 vs 89.9 ± 14.8 , $p = 0.01$) and increased WLR (0.311 ± 0.07 vs 0.262 ± 0.04 , $p = 0.025$) whereas no differences were observed in WT and WCSA.

At one-month follow-up, along with a significant blood pressure reduction, which was associated with arteriolar enlargement and WLR reduction, a decrease in median ID CV was observed ($11\%[\text{IQR } 9.0\text{--}15.0]$ to $4.2\%[\text{IQR } 1.8\text{--}6.05]$, $p = 0.014$).

	Regular (n=31)	Irregular (n=13)	P
CV ID	2.0 (1.0-4.0)	11 (9.0-15.0)	<0.001
Wall - μm	28.8 \pm 16.4	24.7 \pm 3.7	0.591
Lumen Diameter - μm	89.9 \pm 14.8	82.24 \pm 13.5	0.01
Wall-to-Lumen Ratio	0.262 \pm 0.04	0.311 \pm 0.07	0.025
Wall Cross Sectional Area - μm^2	3268 \pm 1614	3707 \pm 896	0.772

Table 1. Study population retinal remodeling indexes according to regularity.

	Baseline (n=13)	1 month follow-up (n=13)	P
Home SBP - mmHg	148.3 \pm 22.8	136.9 \pm 15.8	0.05
Home DBP - mmHg	96.3 (88.4-104.9)	92.1 (86.7-96.9)	0.01
Wall - μm	24.7 \pm 3.7	24.8 \pm 3.2	0.591
Lumen Diameter - μm	82.24 \pm 13.5	86.24 \pm 11.7	0.01
Wall-to-Lumen Ratio	0.311 \pm 0.07	0.303 \pm 0.05	0.025
Wall Cross Sectional Area - μm^2	3707 \pm 896	3746 \pm 828	0.772
CV ID	11 (9.0-15.0)	4.2 (1.8-6.05)	0.014

Table 2. Retinal remodeling indexes modifications after therapeutic intervention in the irregular group.

Conclusions: Arteriolar micro-constrictions are observed in a subset of hypertensive patients with the use of adaptive optics camera. A decrease in blood pressure is accompanied with their disappearance. Beyond classical retinal microvascular remodeling indexes, Adaptive Optics may allow the definition of novel markers of microvascular remodeling that are associated with hypertension.

FIMASARTAN REDUCES ANGIOTENSIN II-INDUCED CELLULAR SENESENCE IN HUMAN CORONARY ARTERY SMOOTH MUSCLE CELLS BY INHIBITING CYR61 AND ERK/P38MAPK/P53 SIGNALING PATHWAY

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Objective: Angiotensin II (Ang II) has been linked to vascular senescence; however, the molecular mechanism(s) by which this occurs remain unknown. We hypothesized that Ang II induced vascular smooth muscle cell (SMC) senescence by regulating the expression of cysteine-rich angiogenic protein 61 (CYR61). Also, we evaluated the role of Ang II type 1 receptor blocker (ARB), fimasartan in vascular senescence.

Design and method: We treated human coronary artery smooth muscle cells (hCSMCs) with Ang II and measured senescent cells by senescence associated β -galactosidase (SA- β -Gal). To evaluate the effect of CYR61 on calcification, VSMCs were transfected with adenoviral vectors expressing CYR61 (Ad-CYR61) at 100 multiplicities of infection (mois). As a control, an adenoviral vector expressing only green fluorescent protein (Ad-GFP) was used.

Results: SA- β -Gal (+) cells were increased in Ang II group ($18.75 \pm 1.75\%$) compared with the control ($11.7 \pm 2.75\%$), which was significantly attenuated by fimasartan administration ($6.5 \pm 1.0\%$). Molecular markers related with cellular senescence, p53 and p16 expressions, were both significantly increased by angiotensin II (p53: 1.39 ± 0.10 , p16: 1.19 ± 0.06 fold vs control, both $p < 0.05$), which were completely suppressed by fimasartan (p53: 1.02 ± 0.07 , p16: 0.97 ± 0.07 fold vs control, both $p = 0.002$). In addition, it was confirmed that CYR61 was induced by AngII. As CYR61 was independently increased, the number of SA- β -Gal positive cells was increased ($33.0 \pm 3.1\%$ vs $9.5 \pm 1.3\%$ in control), and as CYR61 was inhibited, the number was decreased ($11.0 \pm 0.5\%$ vs $24.7 \pm 0.9\%$ in AngII). Also, Fimasartan inhibited the activation of ERK and p38 MAPK by Angiotensin II. As ERK was inhibited, CYR61 and p53 decreased, And as p38 MAPK was inhibited, CYR61, p53 and p16 decreased.

Conclusions: In conclusion, fimasartan provides anti-senescence effect by suppressing CYR61 and ERK/p38 MAPK/p53 signaling pathway in hCSMCs. In addition, this anti-senescence effect will be a basis for identification of pleiotropic effect by ARBs.

CARDIORESPIRATORY EFFECTS OF HIGH TEMPERATURE ELECTRONIC CIGARETTES VAPING

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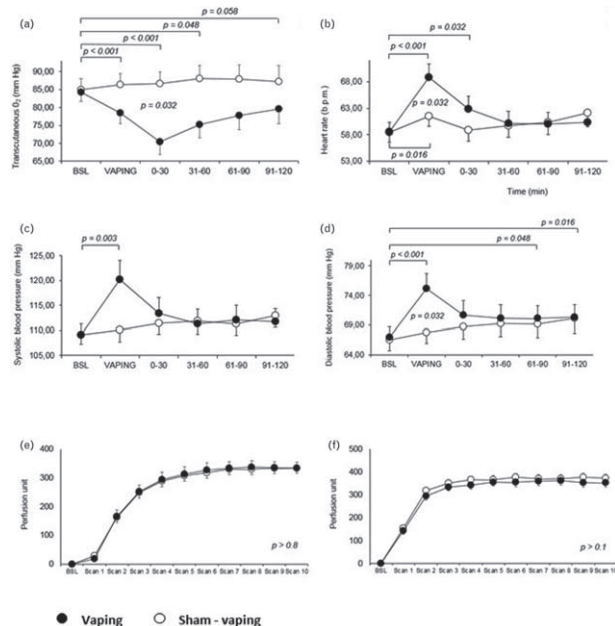
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Objective: The new generation of electronic cigarettes (e-cigarettes) deliver high energy to heat the carriers allowing vaporization process, mainly composed of propylene glycol (PG) and glycerol (GLY). At high temperature, PG and GLY undergo combustion instead of vaporization, and produce volatile carbonyls, which are strong cardiovascular toxicants.

The primary study outcome was the impact of vaping on skin microcirculatory blood flow as assessed by transcutaneous gas tensions and endothelial -dependent vs. -independent microcirculatory skin vasoreactivity. Secondary outcomes included continuous hemodynamic parameters, as well as biomarkers of acute lung injury (club cell protein 16 (CC16)) and oxidative stress. (ClinicalTrials.gov identifier, NCT03036644)

Design and method: Twenty-three young tobacco smokers were exposed to 25 puffs of a PG/GLY mix (50:50) vaporized at 60 watts, or sham-vaping, in a randomized placebo-controlled single-blind crossover design.

Results: E-cigarettes vaping decreased transcutaneous oxygen tension during 60 minutes with the nadir reached at 30 minutes after exposure (mean \pm SEM) (mmHg, 84 ± 2 to 70 ± 4 ; $p < 0.001$; Figure 1.A). Vaping increased heart rate (bpm, 59 ± 2 to 69 ± 3 ($p < 0.001$; Figure 1.B)) as well as systolic (mm Hg, 109 ± 2 to 120 ± 4 ($p = 0.003$; Figure 1.C)) and diastolic (mm Hg, 67 ± 1 to 75 ± 2 ($p < 0.001$; Figure 1.D)) blood pressure during the vaporization. In contrast, vaping did not impair skin microvascular function, assessed by local heating ($p > 0.2$) and iontophoresis of acetylcholine ($p > 0.1$; Figure 1.E) and sodium nitroprusside ($p > 0.8$; Figure 1.F). E-cigarettes increased CC16 in the serum (median [IQR]) (mg.L⁻¹, 4.6 [3.6–6.75] to 5.65 [4.5–7.4]; $p = 0.003$) and in the urine (ng.mg⁻¹, 7.875 [2–73.8] to 10.42 [3.2–56.9]; $p = 0.032$), induced small airways bronchoconstriction, as reflected by the rise of forced expiratory flow-25% (L.s-1, 2.5 [1.7–2.6] to 2 [1.4–2.4]; $p = 0.001$) and forced mid-expiratory flow rate (L.s-1, 4.2 [3.5–5.4] to 3.7 [3.1–4.9]; $p = 0.001$) but did not modify plasma myeloperoxidase ($p > 0.6$) and its oxidation protein products ($p > 0.8$), and superoxide anion production in human umbilical vein endothelial cells ($p > 0.1$).



Conclusions: Intense nicotine free e-cigarettes vaping decreases transcutaneous oxygenation, increases lung injury markers and small airways resistances but does not exert deleterious effects on microvascular endothelial function and oxidative stress.

DIETARY SODIUM-INDUCED CHANGES IN THE MICROCIRCULATORY SYSTEM OF THE SKIN ARE ASSOCIATED WITH BLOOD PRESSURE RESPONSE IN HEALTHY MALES

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Objective: Studies indicate that not only the kidney but also the skin microcirculation might be pivotal for a sodium-sensitive blood pressure (BP) response. While high sodium diet (HSD) is associated with reduced density of blood capillaries, animal studies showed an increment of skin lymphatic capillaries in both amount and size. We investigated sodium-induced changes in both lymphatic and blood skin microcirculation of healthy males in relation to blood pressure (BP).

Design and method: We performed a randomized crossover study in healthy males. All subjects pursued an 8-day low sodium diet (LSD: < 50 mmol Na⁺/day) and HSD (>200 mmol Na⁺/day). Diet order was randomized and time in-between diets was 1–2 weeks. After each diet, BP measurements and skin biopsies were obtained. Endothelia of blood (CD31) and lymphatic capillaries (D2–40) were identified through immunohistochemistry.

Results: Overall (n = 12, mean age 22 years), there was no BP increase after HSD vs. LSD (mean arterial pressure (SD): 78 (5) vs. 78 (5), p = 0.66). HSD increased lymphatic cross sectional surface area (p = 0.01). No differences in lymphatic or blood capillary density were observed. There was a correlation between lymphatic and blood capillary density after LSD but not after HSD (fig 1a). Differences in mean arterial pressure between LSD and HSD correlated with changes in blood capillary density (fig 1b), but not with lymphatic capillary density or cross sectional surface area.

Conclusions: HSD is associated with skin lymphangiogenesis and a loss of correlation between the lymphatic and blood microcirculation. Blood microcirculatory changes correlate with BP response, possibly playing a role in sodium-sensitive hypertension development

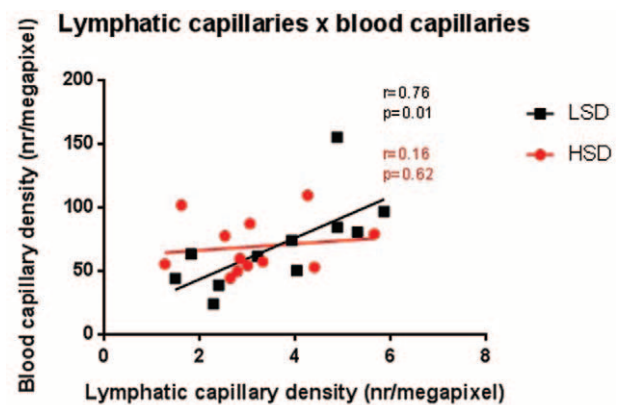


Fig 1A. Correlation between lymphatic capillary density and blood capillary density after low sodium diet (LSD) and high sodium diet (HSD). Densities are expressed as the number of lymphatic/blood capillaries per megapixel (= 1.000.000 pixels).

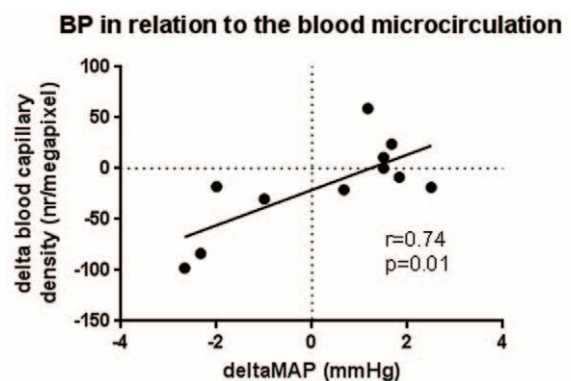


Fig 1B. Absolute differences in mean arterial pressure (MAP) between high sodium diet (HSD) and low sodium diet (LSD) in relation to absolute differences in blood capillary density between HSD and LSD.