

# ORAL SESSION

## ORAL SESSION 1A:

## CARDIOVASCULAR RISK FACTORS

### PREDICTIVE POWER OF 24-HOUR AMBULATORY PULSE PRESSURE COMPONENTS FOR CARDIOVASCULAR MORTALITY IN DIFFERENT AGE AND HEART RATE STRATA DERIVED FROM DATA OF DUBLIN OUTCOME STUDY

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**Objective:** It has been previously shown that average pulse pressure (PP), the systolic-diastolic blood pressure (BP) difference, measured with 24-hour ambulatory BP monitoring (24hABPM), can be expressed as a sum of two components: 'elastic' PP (ePP) and 'stiffening' PP (stPP) associated, respectively, with arterial stiffness (at the diastolic pressure) and its pressure dependence. The study objective was to determine PP, ePP and stPP ('PP variables') and assess their prognostic value in a large cohort of previously untreated subjects stratified by age and pulse rate (PR).

**Design and method:** The study included untreated subjects assessed for hypertension in Dublin, Ireland, in whom 24hABPM records of adequate quality were obtained. The PP components were determined from the linear relationship between systolic- and diastolic BP using a model based on the nonlinear pressure-volume relationship in arteries that expresses stiffness-pressure relationship. Predictive power for cardiovascular (CV) mortality was expressed by hazard ratio (HR) determined using Cox regression models applied separately to PP and ePP & stPP (combined), adjusted for age, sex, BMI, smoking status, diabetes, previous CV disease, 24 h mean arterial pressure (MAP) and MAP dipping, and for the age and PR strata shown in the Table.

**Results:** Of the 11,291 subjects included (age  $54.4 \pm 14.5$ , 47% male) 566 CV deaths occurred during the follow-up period (mean 5.8 years). Mean  $\pm$  SD of PP, ePP and stPP were, respectively,  $56.6 \pm 12.4$ ,  $49.0 \pm 9.8$ , and  $7.6 \pm 6.9$  mmHg, and ePP and stPP were uncorrelated ( $r = 0.075$ ). Table shows that the predictive power of ePP increased progressively with ageing, mainly for low PR. For age  $\geq 65$  years ePP had greater predictive power than PP and stPP, especially for low PR. In contrast, for age  $< 50$  and high PR, PP and stPP were stronger predictors than ePP, and for low PR none of PP variables had significant predictive power.

**Conclusions:** PP components derived from 24hABPM may have greater predictive power for CV death than PP itself in elderly subjects. Studies investigating occurrence of an independent association of PP components with additional fatalities are required in order to demonstrate the specificity of these new measures.

		<50 years (N=4052, 49 deaths)			50-65 years (N=4443, 161 deaths)			$\geq 65$ years (N=2796, 356 deaths)		
PP Variables →		PP	ePP	stPP	PP	ePP	stPP	PP	ePP	stPP
	HR	0.81	0.81	0.94	1.33	1.33	1.06	1.22	1.43	0.92
PR $\leq 70$ bpm	95%CI	0.4-1.6	0.4-1.5	0.5-1.6	1.0-1.7	1.1-1.6	0.8-1.3	1.0-1.4	1.2-1.7	0.8-1.1
	p-value	NS	NS	NS	0.02	0.008	NS	0.02	$3 \cdot 10^{-4}$	NS
PR $> 70$ bpm	HR	1.33	1.17	1.32	1.15	1.18	1.0	1.19	1.22	1.01
	95%CI	1.1-1.6	0.9-1.5	1.0-1.7	0.9-1.4	1.0-1.4	0.8-1.2	1.0-1.4	1.0-1.4	0.9-1.2
	p-value	0.006	NS	0.04	NS	NS	NS	0.05	0.01	NS

Hazard ratio (HR per 1SD change), 95%CI, Confidence Intervals, NS for p-value $>0.05$

### ASSOCIATION OF RETINAL VESSEL CALIBERS AND LONGITUDINAL CHANGES IN ARTERIAL STIFFNESS: THE NAGAHAMA STUDY

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**Objective:** Morphological change in retinal vessel calibers has been reported as a marker of cardiovascular risk, but its association with arterial stiffening, a possible factor relating retinal vessel sings and cardiovascular outcomes, is not clear. The study aim was to clarify the relationship between retinal small vessel calibers and longitudinal change in large arterial stiffness in a sample of the general population.

**Design and method:** The study included 6,720 Japanese participants ( $52.1 \pm 12.8$  years). Central retinal arteriolar equivalent (CRAE) and venular equivalent (CRVE) were measured by fundus photography. Arterial stiffness was evaluated by brachial-to-ankle pulse wave velocity (baPWV) at baseline and at 5 years.

**Results:** The overall change in baPWV (d-baPWV) during mean follow-up  $1,814 \pm 136$  days was  $41 \pm 131$  cm/sec ( $3.4 \pm 9.9$  % of baseline), and was significantly larger in men ( $52 \pm 147$  cm/sec) than in women ( $36 \pm 122$  cm/sec,  $p < 0.001$ ).  $\delta$ -baPWV was significantly increased in individuals with narrower CRAE (quartiles: Q1,  $4.3 \pm 10.6$ %; Q2,  $3.3 \pm 10.0$ %; Q3,  $3.1 \pm 9.3$ %; Q4,  $3.1 \pm 9.7$ %,  $p = 0.001$ ), while no significant association was observed with CRVE. Although several factors also significantly differ among the CRAE quartiles, multivariate analysis identified CRAE as a significant inverse determinant of  $\delta$ -baPWV ( $\beta = -0.033$ ,  $p = 0.006$ ) independent of the possible covariates including age ( $\beta = 0.433$ ,  $p < 0.001$ ), male sex ( $\beta = 0.050$ ,  $p < 0.001$ ), BMI ( $\beta = 0.028$ ,  $p = 0.024$ ), mean BP ( $\beta = 0.059$ ,  $p < 0.001$ ), and baseline baPWV ( $\beta = -0.438$ ,  $p < 0.001$ ). The association of CRAE with  $\delta$ -baPWV remained significant in a model further adjusted for CRVE ( $\beta = -0.040$ ,  $p = 0.002$ ). Further, the association between CRAE and  $\delta$ -baPWV was prominent in a middle-aged (age Q2,  $\beta = -0.078$ ,  $p = 0.002$ ), but not younger (Q1,  $p = 0.232$ ) or older (Q3,  $p = 0.427$ ; Q4,  $p = 0.542$ ) participants.

**Conclusions:** Narrower CRAE in middle-age was associated with the long-term risk of arteriosclerosis in a general population sample.

### MORTALITY RATES IN HYPERTENSIVE SUBJECTS WITH PERIPHERAL ARTERIAL DISEASE: DETECTION OF A J-CURVE PHENOMENON

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**Objective:** Determination of asymptomatic organ damage is important in cardiovascular risk stratification, and has a great impact on the treatment of hypertension. The measurement of the ankle-brachial index (ABI) is an accepted method for the detection of asymptomatic peripheral arterial disease (PAD). Abnormal ABI is accepted as a marker of cardiovascular risk that predicts adverse cardiovascular outcomes.

**Purpose:** The assessment of mortality rates during the follow-up period of the ERV program in hypertensive patients with ABI  $\leq 0.9$ .

**Design and method:** The Hungarian ERV program is a large-scale, multicenter, observational study with a cross-sectional and a longitudinal part. The first period of the study was conducted from April 2007 to September 2008 in 55 hypertension outpatient clinics in Hungary and the prospective phase was ended in April 2014. In all patients ABI was measured and cardiovascular outcomes were collected in the 5 years follow-up period.

**Results:** In the 21892 enrolled hypertensive patients (50–75 years of age), the prevalence of PAD (ABI  $\leq 0.9$ ) was 14.4 %. In 9.4% of the subjects high ABI ( $> 1.3$ ) was measured.

Among these hypertensive subjects the five years cumulative death ratio in both gender was twice as high in PAD patients compared to those without PAD (17.4% vs 7.4% in men,  $p < 0.001$ ; 9.8% vs 4.2% in women,  $p < 0.001$ ). The cumulative death ratio was significantly higher in patients with high ABI, as well. The relative risk of cumulative death was higher in case of low ABI compared to patients with normal ABI values both in men (RR:2.32;  $p < 0.001$ ) and in women (RR:2.32;  $p < 0.001$ ).

In hypertensive PAD patients mortality increased in both genders in patients with systolic blood pressure below 120 mmHg and above 160 mmHg compared to systolic blood pressure 130–139 mmHg ( $p < 0.001$  and  $p < 0.01$ ) and in men below diastolic pressure 70 mmHg and above 90 mmHg compared to diastolic blood pressure 80–89 mmHg ( $p < 0.001$  and  $p < 0.01$ ).

**Conclusions:** Low ABI is a strong predictor of mortality in hypertensive patients. In hypertensive PAD patients, the J-curve shape phenomenon between blood pressure and mortality was firstly described in our analysis.

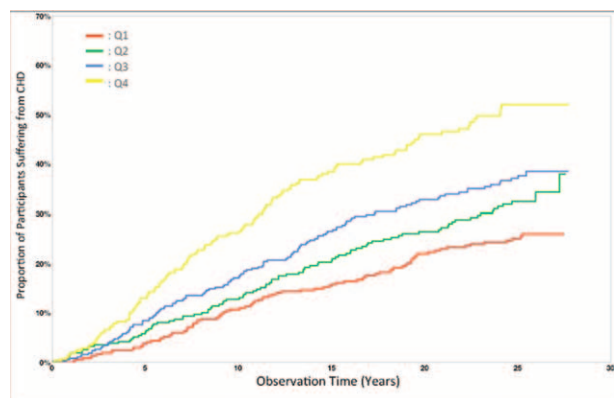
### EXERCISE SYSTOLIC BLOOD PRESSURE AND QUARTILE-BASED RISK OF CORONARY HEART DISEASE IN HEALTHY MEN DURING 28 YEARS OF FOLLOW-UP

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**Objective:** There is increasing evidence regarding exercise blood pressure as a predictor for later cardiovascular disease in apparently healthy individuals. We aimed to investigate the association between exercise systolic blood pressure and risk of coronary heart disease (CHD) in healthy men after two consecutive bicycle exercise tests seven years apart.

**Design and method:** 1999 presumably healthy men underwent thorough medical examination and were considered free of any chronic disease or long-term pharmacological treatment. After seven years, 1392 men were still considered healthy after the same examination, and able to complete a six-minute bicycle exercise test at 100 W workload at both visits. Exercise blood pressure was measured auscultatory at both visits, at rest and every two minutes during the test. Peak measurement during the test at the second visit was used in a Cox regression analysis, adjusted for age, systolic blood pressure at rest at first visit, serum cholesterol, smoking status, family history of CHD and physical fitness. Participants were divided in quartiles of peak systolic blood pressure at 100 W (Q1: 100–160 mmHg, Q2: 165–175 mmHg, Q3: 180–195 mmHg, Q4: >= 200 mmHg), and followed for up to 28 years after the second visit.

**Results:** There were 452 events of the combined endpoint of angina pectoris, non-fatal myocardial infarction and CHD mortality. Unadjusted, there was a significant increase in risk of CHD with increasing exercise systolic blood pressure (figure). In the multiple-adjusted analysis, there was a significantly increased risk of CHD in both Q3 and Q4 compared to Q1, hazard ratios (95 % confidence interval, p-value) 1.33 (1.00–1.78, 0.05) and 1.70 (1.24–2.35, 0.001), respectively.



**Conclusions:** There is increased long-term risk of coronary heart disease with blood pressure above 180 mmHg at moderate workload during bicycle exercise in middle-aged Caucasian men who were healthy during a seven-year period. The results are consistent after adjustment for the classical cardiovascular risk factors, family history of CHD and physical fitness.

### MASKED HYPERTENSION INCIDENCE: RISK FACTORS IN A PROSPECTIVE COHORT STUDY

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**Objective:** Masked hypertension affects approximately 10 to 20% of the general population and is associated with a higher risk of cardiovascular diseases. No previous prospective study has examined risk factors associated with masked hypertension incidence. The aim of this study was to examine risk factors associated with masked hypertension incidence in a prospective cohort from Quebec City, Canada.

**Design and method:** This is a dynamic cohort study using two pooled longitudinal samples of initially normotensive participants (Year 0 – Year 3; Year 3 – Year 5). The study sample was composed of 1,836 participants. At each time, blood pressure (BP) was measured using Spacelabs 90207. Manual BP was defined as the mean of the first three readings taken at rest. Ambulatory BP was defined as the mean of the next readings recorded every 15 minutes during daytime working hours. Risk factors of masked hypertension incidence were examined using cross-lagged generalized estimating equations.

**Results:** After mutual adjustment, masked hypertension incidence was associated with male gender (RR = 1.53, 95% CI: 1.19–1.96), age (RR40–49 = 1.55, 95% CI: 1.14–2.10; RR ≥ 50 = 1.48, 95% CI: 1.05–2.09), body mass index (RR > 27 = 1.45, 95% CI: 1.12–1.87), smoking status (RR = 1.49, 95% CI: 1.07–2.08) and alcohol intake (RR > 6/week = 1.46, 95% CI: 1.06–2.00).

**Conclusions:** Findings point toward sociodemographic and lifestyle related risk factors associated with masked hypertension incidence. These factors should be considered in screening efforts of individuals at risk for developing masked hypertension.

### RELATIONSHIPS BETWEEN SERUM URIC ACID AND BLOOD PRESSURE, METABOLIC VARIABLES AND CARDIOVASCULAR RISK PROFILE IN TREATED HYPERTENSIVE PATIENTS FROM CENTRAL AND EASTERN EUROPEAN COUNTRIES: RESULTS OF THE BP-CARE STUDY

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**Objective:** Limited information is available on the association between serum uric acid (SUA) and metabolic syndrome, diabetes mellitus, renal failure, blood pressure (BP) control and cardiovascular (CV) risk profile in treated hypertensives of eastern European countries.

**Design and method:** The BP-CARE study examined BP control and CV risk profile in about 8000 treated hypertensive patients followed by non-specialist or specialist physicians in Albania, Belarus, Bosnia, Czech Republic, Latvia, Romania, Serbia, Slovakia and Ukraine. In 3220 of them measurements included, along with clinic BP, 24-hour BP, metabolic and renal function variables, SUA values.

**Results:** 51% were males, while mean age (±SD) was 60.0 ± 10.9 yrs, clinic BP 147.3 ± 18/87.8 ± 10 mmHg, 24 hour BP 137.3 ± 19/81.3 ± 10 mmHg and SUA values 5.68 ± 1.9 mg/dl, with a normal distribution in the population. SUA was significantly higher in males than females (5.99 ± 1.9 vs 5.34 ± 1.9 mg/dl, P < 0.0001) and progressively and significantly greater from the low to the medium, high and very high risk patients (4.87 ± 1.38 vs 5.85 ± 2.00, P < 0.0001, ESH CV risk categories). Significant differences were also found between diabetic and non-diabetic patients (5.92 ± 2.2 vs 5.58 ± 1.8, P < 0.0001), patients with and without metabolic syndrome (5.92 ± 2.1 vs 5.43 ± 1.7, P < 0.0001) and from stage 1 to stage 5 renal insufficiency (from 5.87 ± 2.0 to 10.48 ± 3.4, P < 0.0001). No significant difference in SUA was found between patients treated and non-treated with diuretic or angiotensin II blockers or in those under antihypertensive drug combination vs monotherapy. No difference in SUA was also found when analyzing the data in relation to clinic or 24-hour BP control.

**Conclusions:** These data provide evidence that similarly to what described in western Europe, in central and eastern European countries SUA values are closely related to metabolic alterations, including diabetes mellitus, to renal insufficiency and CV risk profile. At variance from other studies, however, no relationship was found with BP control.

### ELECTRONIC CIGARETTE SMOKING EXERTS AN UNFAVOURABLE EFFECT ON AORTIC HEMODYNAMICS AND WAVE REFLECTIONS

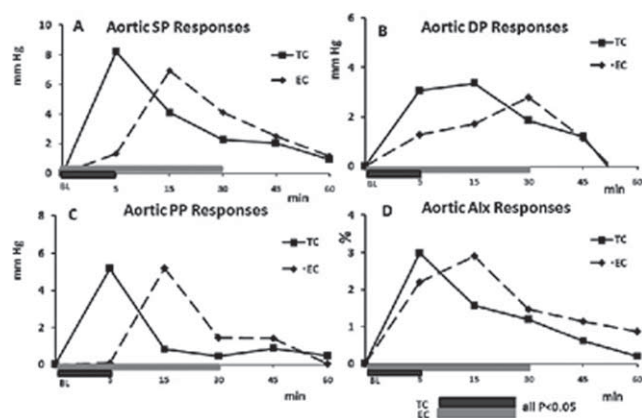
D. Terentes-Printzios, N. Ioakeimidis, C. Vlachopoulos, M. Abdelrassoul, C. Georgakopoulos, I. Gourgouli, K. Aznaouridis, E. Solomou, D. Tousoulis. *First Department of Cardiology, Hippokraton Hospital, Athens Medical School, Athens, GREECE*

**Objective:** We investigated the acute effect of electronic cigarette (EC) smoking on the aortic pressure waveform amplification. We also sought to compare the effect of EC and combustible cigarette (TC) smoking on aortic haemodynamics.

**Design and method:** We studied 24 smokers (age: 30 ± 8 years) on 3 separate occasions: a) tobacco cigarette (nicotine content, 1.2 mg) over 5 minutes, b) EC

(18 mg E-liquid) for a period of 30 minutes, and c) nothing (sham procedure) for 60 minutes. Smoking EC for 30 min (15 puffs) was chosen to mimic the common pattern of EC smoking. All participants were asked to fill in the Fagerstrom Test for Nicotine Dependence (FTND) that is a standard instrument for assessing the intensity of nicotine dependence.

**Results:** The mean (SD) FTND score of the study population was 3.6 (2.5). Of them, nine were highly nicotine dependent (FTND core > 5). There were no significant differences in all baseline measurements between high and low nicotine dependence smokers. Both TC and EC smoking caused a significant increase in brachial pressures and heart rate (HR), and the differences in blood pressure (BP) and HR responses between the two smoking forms were not significant. The aortic pressures also increased significantly after smoking both TC and EC, with the greatest changes seen in the first 5 minutes after TC smoking and 15 minutes EC smoking (figures 1A-C, all  $P < 0.05$ ). Although AIx, decreased in both two smoking forms, by applying a correction factor for changes in HR, the AIx increased significantly after TC (by 3.0 % at 5 minutes,  $P < 0.05$ ) and EC (by 2.9% at 15 minutes,  $P < 0.05$ ) (figure 1D).



**Conclusions:** Electronic cigarette smoking exerts an unfavourable and comparable to that of TC smoking acute effect on aortic pressure waveform amplification. Due to the prognostic role of aortic hemodynamics on cardiovascular disease risk, EC could still be considered a hazardous smoking method.

#### RISK OF CARDIOVASCULAR DISEASE IN TREATED AND UNTREATED INDIVIDUALS WITH HYPERTENSION: THE ISFAHAN COHORT STUDY

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**Objective:** It is not clear whether controlling blood pressure (BP) through antihypertensive treatment can eliminate the attributable risk of cardiovascular disease (CVD). We aimed to evaluate the residual risk of CVD in treated individuals with hypertension.

**Design and method:** We used the data from the Isfahan Cohort Study, a population-based prospective study of Iranian adults aged 35 years or older at baseline. Of a total 6504, 5432 participants free of a CVD history at baseline with at least one follow-up were included. Participants were stratified to five different BP categories based on baseline BP (cutoffs of systolic/diastolic BP at 120/80 and 140/90 mmHg) and treatment status (yes/no). Cox proportional hazard regression was used to predict the hazard ratio (HR) for CVD events and its corresponding 95% confidence interval (CI).

**Results:** During a median 10.9 years and 49,439 person-years of follow-up, a total of 706 incident CVD events were recorded comprising 563 cases of coronary heart disease (CHD) and 143 stroke. Successfully treated individuals were at higher risk of CVD (HR 1.93, 95% CI 1.28–2.90) and CVD mortality (HR 2.64, 95% CI 1.29–5.40) than the group with optimal BP in a multivariable model. Further adjusting for treatment duration and BP attenuated but did not eliminate

the CVD (HR 1.65, 95% CI 1.08–2.52) and CVD mortality (HR 2.17, 95% CI 1.03–4.57) risk. A stronger association was found for CHD (HR 2.58, 95% CI 1.66–4.02) but not for stroke (HR 0.46, 95% CI 0.14–1.56). Both men (HR 2.45, 95% CI 1.27–4.74) and women (HR 1.62, 95% CI 0.95–2.77) with controlled BP had a higher risk of cardiovascular events, although not significant in women. In untreated individuals, the risk of CVD started at 120/80 mmHg (HR 1.38, 95% CI 1.09–1.75) and escalated in individuals with values from 130/85 mmHg to less than 140/90 mmHg (HR 1.94, 95% CI 1.29–2.92).

**Conclusions:** A substantial residual risk of CHD remains despite treatment which could not be explained by usual confounders and BP itself. Hence, despite undeniable benefits of lowering BP, treatment may not totally counterbalance the risk of CVD at the population level.

#### IMPACT OF EXERCISE BLOOD PRESSURE ON STROKE RISK IN PHYSICALLY FIT AND UNFIT MEN. RESULTS FROM 35 YEARS FOLLOW-UP OF HEALTHY MIDDLE-AGED MEN

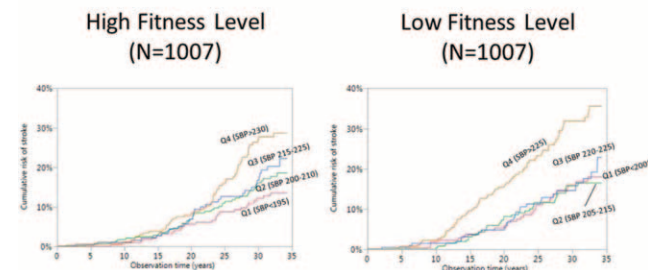
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**Objective:** Resting blood pressure is one of the major risk factors for stroke. Our group recently showed that maximal blood pressure during exercise testing is a strong predictor of stroke in this cohort, independently of resting blood pressure. In the present study we investigate if maximal systolic blood pressure's ability to predict stroke is influenced by a person's level of cardiorespiratory fitness.

**Design and method:** The study enrolled 2014 healthy men aged 40–59 years between 1972–1975. The baseline examination included a maximal exercise test and the men were followed for a total of 35 years. Data on first-time stroke were collected from follow-up visits, hospital medical records from all national hospitals, and the national Cause of Death Registry. For data analyses, we grouped the men according to high or low fitness level (above/below median, values adjusted for age) and further for quartiles of maximal blood pressure. Multi-adjusted Cox regression analyses (including adjustment for resting blood pressure) were used to estimate risks for stroke.

**Results:** During a median follow-up of time 31.9 years 316 first-time strokes occurred. There were no losses to follow-up. Fitness levels correlated positively with maximal systolic blood pressure. Among men with high fitness level, the highest quartile of maximal blood pressure had a higher risk of stroke than the lowest quartile (hazard ratio 1.75, confidence interval 1.06–2.94,  $p = 0.03$ ). Among men with low fitness level, the highest quartile of maximal systolic blood pressure had a non-significantly higher risk of stroke than the lowest quartile (hazard ratio 1.50, confidence interval 0.91–2.63,  $p = 0.11$ ). When resting systolic blood pressure was omitted from the models, maximal systolic blood pressure predicted stroke significantly in both fit and unfit men.

Figure. Quartiles of maximal systolic blood pressure (mmHg) and stroke risk. SBP=systolic blood pressure.



**Conclusions:** In healthy middle-aged men, maximal systolic blood pressure predicted stroke in men with high cardiorespiratory fitness, independently of resting systolic blood pressure. In men with low cardiorespiratory fitness the association was not significant, but there was no evidence of a qualitative different effect in this subgroup, and further research is needed to assess if maximal blood pressure has a predictive value for stroke in men, independently of fitness levels.

#### CARDIOVASCULAR RISK IN HYPERTENSIVE PATIENTS INCLUDED IN THE IBERICAN STUDY

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**Objective:** The general objectives of IBERICAN are to determine the prevalence and incidence of cardiovascular risk factors in Spain, as well as cardiovascular events. The objective of the present work is to know the cardiovascular risk of hypertensive patients included in the IBERICAN Study.

**Design and method:** IBERICAN is a longitudinal, observational, and multicenter study in which patients from 18 to 85 years of age are included in primary care consultations in Spain. The cohort obtained will be followed annually for at least 5 years. The final estimated sample is 7,000 patients. The baseline characteristics of the first 5,944 patients included are presented. Cardiovascular risk factors (diabetes, obesity, dyslipidemia, smoking, sedentary lifestyle) and cardiovascular disease (ischemic heart disease, stroke, heart failure, peripheral arterial disease) have been analysed to estimate the cardiovascular risk according to the SCORE for low risk countries.

**Results:** 2,873 patients have hypertension (48.3%), their average age was  $64.7 \pm 12$  years, 49.7% women, hypertension evolution time was  $9.7 \pm 6$  years, BMI  $31.1 \pm 8.9$  kg/m<sup>2</sup>. The prevalence of risk factors in this population is: dyslipidemia 65.8%; obesity 47.2%; sedentary lifestyle 35.4%, diabetes 30.7 and smoker 13.4%. The cardiovascular disease was in 23.8% of the patients: ischemic heart disease 10.4%; peripheral arterial disease 7%; heart failure 5.6%, and stroke 5.5%. The degree of control of blood pressure was: 56.7%. The distribution of hypertensive patients according to the risk category was: low risk 6.2%; moderate 25.8%; high 19.5% and very high risk 48.5%. 68% of hypertensive patients are at high or very high risk.

**Conclusions:** The population of hypertensive patients in the IBERICAN study has a high prevalence of cardiovascular risk factors and cardiovascular disease. The level of risk is very high in almost half of the hypertensive and two out of three are high or very high risk.

#### A RETROSPECTIVE STUDY ON THE TAILORING OF SCORE CHARTS IN A SPECIALIZED TERTIARY HYPERTENSION UNIT

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**Objective:** The use of Systematic Coronary Risk Evaluation (SCORE) charts for low risk countries is recommended for estimating the individual 10-year risks of fatal cardiovascular events in France. These charts were estimated from 12 European cohort studies in 2003. The objective was to compare SCORE predictions to a 10-year risk of fatal cardiovascular disease obtained from Kaplan-Meier in a population of French patients attending in a specialized Tertiary Hypertension Unit (THU) or Paris area during the 2000–2014 period.

Table 1: SCORE accuracy among patients in primary prevention

	Total n=8114		Men n=4235		Women n=3879	
SCORE risk groups [95%CI]	n		n		n	
<1%	0.2% [0-0.3]	4231	0.2% [0-0.5]	1668	0.1% [0-0.3]	2563
1-5%	0.5% [0.2-0.9]	2523	0.7% [0.2-1.1]	1664	0.2% [0-0.7]	859
5-10%	1.4% [0.4-2.4]	747	1.5% [0.3-2.7]	518	1.1% [0.2-2.6]	229
>10%	9.3% [6.2-12.3]	522	7.2% [3.7-10.5]	328	12.9% [6.8-18.5]	194

CI: Confidence Interval

**Design and method:** We retrospectively included all consecutive patients attending for a first outpatient visit of the THU between 07/2000 and 12/2014 in this monocentric cohort study. We excluded foreign-born patients. Vital status and causes of deaths were retrieved respectively from the national person identification database and national causes of death database. Risk of fatal cardiovascular disease at 10 years was calculated for each patient using the SCORE model. A Kaplan-Meier model was then fitted to estimate risk of fatal cardiovascular disease at 10 years for each SCORE prediction groups (<1, 1–5, 5–10, >10%) for patients in primary prevention.

**Results:** A total of 8114 patients in primary prevention were included. Their characteristics at the first outpatient visit: median age: 50 years; women: 48%; current smoker: 16.8%; median office SBP: 141 mmHg; median cholesterol levels: 5.25 mmol/l. SCORE risk of fatal cardiovascular disease of 1–5 and 5–10% at 10 years overestimated the actual risk obtained from Kaplan-Meier estimators for both men and women (Table 1).

**Conclusions:** SCORE charts overestimate the risk of fatal cardiovascular disease at 10 years for French hypertensive patients attending a THU and thus are not adapted for day-to-day practice. There is a need to fit a specific model for this population and for other subgroups.

#### EFFECT OF ELECTRONIC CIGARETTE SMOKING ON BLOOD PRESSURE IN HYPERTENSIVE PATIENTS. EVALUATION BY NON-INVASIVE CONTINUOUS AMBULATORY BLOOD PRESSURE MEASUREMENT

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**Objective:** The electronic cigarettes (EC) is a device that heats a liquid containing nicotine and flavors into an aerosol for inhalation. There is some evidence from controlled trials that electronic cigarette (EC) may help to stop smoking long-term. However, a large proportion of smokers who successfully quit cigarette smoking continue to use EC for unlimited time, switching from an addiction to another. There is a clear similarity between the detrimental vascular effects of EC and conventional cigarette. Little is known about the acute influence on blood pressure (BP) of nicotine inhalation by EC and its duration of action in hypertensive subjects. Aim of this study was to evaluate the magnitude and time-course of BP changes during EC smoking.

**Design and method:** This is a randomized, cross-over and placebo controlled study. We evaluated 30 mild-to-moderate hypertensive patients on pharmacological treatment and adequate BP control (<140/90 mmHg). Patients (22 males, mean age  $54 \pm 21$  years) were former smokers, who quit tobacco cigarette in favor of EC at least 6 months before. BP and heart rate (HR) were measured by continuous non-invasive ambulatory BP and ECG monitoring (SOMNOtouch NIBP).

BP and HR were monitored during a 30 minute rest in the sitting position; during other 30 minutes after smoking EC (inhalation equivalent to 0.8 mg of nicotine of a regular cigarette) or placebo EC (same device, same flavor but no nicotine in the solution).

**Results:** EC vaping was accompanied by significant increase blood pressure, which lasted about 30 minutes (average  $28 \pm 11$  minutes). Compared to placebo the EC smoking increased systolic BP by  $9.6 \pm 4.1$  mmHg, diastolic BP by  $7.1 \pm 3.9$  mmHg and heart rate by  $16.4 \pm 13$  beat per minute. All the differences resulted statistically significant (Student's t test  $P < 0.05$ ).

**Conclusions:** Under these experimental conditions, EC smoking caused a statistically significant increase in BP and HR in hypertensive patients. This effect seems also clinically relevant since the duration of BP increase was relatively long (28 minutes) and the daily number of inhalations, in EC smokers, is usually high (>20).

# ORAL SESSION

## ORAL SESSION 1B: BLOOD PRESSURE MEASUREMENT

### TELEMONITORING AND/OR SELF-MONITORING OF BLOOD PRESSURE IN HYPERTENSION (TASMINH4): A RANDOMISED CONTROLLED TRIAL

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**Objective:** Previous studies evaluating titration of antihypertensive medication using self-monitoring have contradictory findings and the precise place of telemonitoring over self-monitoring alone is unclear. The TASMINH4 trial aimed to assess the efficacy of self-monitored blood pressure, with or without telemonitoring, for antihypertensive titration in primary care, compared to usual care.

**Design and method:** Randomised controlled trial in 142 UK General Practices including hypertensive patients, aged over 35, with blood pressure > 140/90mmHg who were willing to self-monitor their blood pressure. Randomisation (1:1:1 basis) to medication titration using self-monitored blood pressure, self-monitored blood pressure with telemonitoring or usual care (clinic blood pressure). Neither participants nor investigators were masked to group assignment. The primary end point was difference in systolic blood pressure between intervention and control taking into account baseline covariates and primary analysis was for complete cases without imputation. Trial registration: ISRCTN 83571366

**Results:** 1182 participants were randomised to antihypertensive titration using self-monitoring (395), telemonitoring (393) or clinic blood pressure (394) of whom 1003 (85%) were included in the primary analysis. After 12 months, systolic blood pressure was significantly lower in both self-monitoring groups (self-monitoring 137.0mmHg, telemonitoring 136.0mmHg) compared to usual care (140.4mmHg): adjusted mean differences vs usual care: telemonitoring -4.7mmHg (95% confidence interval -7.0, -2.4) and self-monitoring alone -3.5mmHg (-5.8, -1.2) with no significant difference between self-monitoring groups (-1.2mmHg (-3.5, 1.2)) [see Table]. Results were similar in sensitivity analyses including multiple imputation and were consistent in pre-specified sub-groups for age, gender, blood pressure target, deprivation and history of cardiovascular disease.

TABLE MEAN SYSTOLIC BLOOD PRESSURE AT BASELINE, 6 MONTHS AND 12 MONTHS FOR EACH GROUP

	Baseline	6 Months	12 Months	Adjusted Mean difference (6m) vs usual care	Adjusted Mean difference (12m) vs usual care
<b>Systolic Blood Pressure Mean (sd) (N) (mmHg)</b>					
Telemonitoring	153.2 (14.3) (389)	139.0 (16.77) (338)	136.0 (16.13) (327)	-3.7 (-5.9; -1.5) *	-4.70 (-7.0; -2.4) *
Self-Monitoring	152.9 (13.6) (391)	140.4 (15.73) (349)	137.0 (16.7) (328)	-2.1 (-4.3; 0.1)	-3.5 (-5.8; -1.2) *
Usual Care	153.1 (14.0) (393)	142.5 (15.4) (358)	140.4 (16.5) (348)		

\*Level of significance ≤ 0.027

**Conclusions:** Self-monitoring, with or without telemonitoring, when used by General Practitioners to titrate antihypertensive medication in individuals with poorly controlled blood pressure, leads to significantly lower blood pressure than titration guided by clinic readings. With most GPs and many patients using self-monitoring, it could become the cornerstone of hypertension management in primary care.

### PROGNOSTIC POWER OF MORNING HOME BLOOD PRESSURE IN VERY ELDERLY CLINICAL POPULATION

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**Objective:** Home blood pressure (BP) has been a stronger association with cardiovascular disease risk than clinic BP. However, the data are sparse about the impact of home BP for cardiovascular outcome in very elderly clinical population.

**Design and method:** We assessed the data from the J-HOP (Japan Morning Surge-Home Blood Pressure) study, which was a nationwide practice-based study that included 4,310 Japanese with a history of and/or risk factors for cardiovascular disease. A total of 4,310 patients, 349 of whom were aged > 80 years, were analyzed. Home BP measures were taken twice daily (morning and evening) over 14 days at baseline.

**Results:** Average age was 82.8 years (range 80–96 years). Average morning and evening BP levels were  $146 \pm 19/73 \pm 10$  mmHg and  $134 \pm 17/68 \pm 9$  mmHg, respectively. Twenty-two cardiovascular events (sudden death, fatal and nonfatal stroke, angina pectoris requiring coronary intervention, and acute myocardial infarction) occurred during follow-up (1205 person-years). Cox hazard analysis showed that morning systolic BP (SBP) increase was associated with cardiovascular events after adjusted for age, gender, body mass index, total-cholesterol, high-density-lipoprotein cholesterol, diabetes, past history of cardiovascular disease, use of antihypertensive drug and statin, and clinic SBP (Hazard ratio [HR] per 1SD, 1.68; 95% confidence interval [CI], 1.08–2.63;  $P = 0.021$ ), while this association was not found in evening SBP (HR per 1SD, 1.52; 95%CI, [0.94–2.45];  $P = 0.085$ ). Both morning and evening diastolic BP was not associated with cardiovascular events.

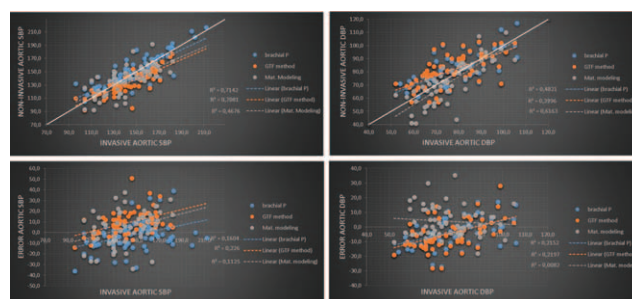
**Conclusions:** Morning home SBP was associated with cardiovascular events in very elderly clinical population.

### COMPARISON OF NON-INVASIVE TECHNIQUES FOR AORTIC PRESSURE APPRAISAL AGAINST INVASIVE PRESSURE MEASURES

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**Objective:** In term of prognostic value, aortic blood pressure may be superior compared to the brachial pressure. A non-invasive technique for the computation of aortic pressure from peripheral information through the use of the generalized transfer function (GTF) is the most-used in clinical research. However, the dispersed and biased appraisal of aortic pressure obtained through this technique might hamper the scientific results obtained in population studies. Low-order, patient-specific whole-body mathematical models might help to bridge brachial to aortic pressure waveforms.

The object of the present investigation was to compare (i) GTF method, (ii) a patient-specific 1D-0D mathematical model, and (iii) brachial blood pressure in the appraisal of aortic pressure measured through catheter.



**Design and method:** One-hundred patients referred to diagnostic coronary angiography were included. Brachial pressure and tonometric radial waveform were quantified simultaneously to invasive aortic pressure, which was quantified with a calibrated, fluid-filled catheter. End-systolic and end-diastolic left ventricular volumes and carotid-femoral pulse wave velocity were measured immediately prior to the invasive procedure and were used to set the mathematical model.

**Results:** Systolic aortic pressure was underestimated ( $9.4 \pm 11$  mmHg,  $R^2 = 0.71$ ) while diastolic aortic pressure was overestimated ( $4.5 \pm 10.2$  mmHg,  $R^2 = 0.4$ ) by the GTF method. Mathematical model underestimated systolic ( $4 \pm 16.5$  mmHg,  $R^2 = 0.47$ ) and diastolic ( $3.9 \pm 10.4$  mmHg,  $R^2 = 0.62$ ) aortic pressure values. Oscillometric brachial pressure overestimated systolic ( $2.4 \pm 12.6$  mmHg,  $R^2 = 0.71$ ) and diastolic ( $3.7 \pm 9.8$  mmHg,  $R^2 = 0.48$ ) aortic pressure. Both brachial pressure and GTF methods presented a trend for higher systolic and diastolic pressure overestimation for higher aortic pressure, while mathematical modeling did not.

**Conclusions:** Despite oscillometric brachial pressures overestimate aortic pressure extremes its predictions correlate with invasive pressure similarly to both the widely-used GTF method and the subject specific, multiscale mathematical model.

#### IMPACT OF AMERICAN VS CANADIAN STYLE BLOOD PRESSURE MEASUREMENT ON BLOOD PRESSURE CLASSIFICATION ACCORDING TO THE 2017 ACC/AHA TASK FORCE HYPERTENSION GUIDELINES

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**Objective:** Due to the new ACC/AHA task force hypertension guidelines (ACC/AHA), concerns have been raised that the lower cut-off values of blood pressure (BP) categories will lead to a relevant increase of hypertension prevalence. However, not only the cut-off values were changed, but also office blood pressure measurement (BPM) technique was redefined. Our aim was to study the differences in systolic BP classification based on BPM techniques recommended by the American and Canadian guidelines (CHEP).

**Design and method:** In this cross-sectional, single-centre trial, 1000 adult subjects were recruited. After five minutes of rest, four sequential standard office BPM were performed at two-minute intervals in a quiet room and in sitting position. Based on the ACC/AHA, we calculated the mean of the first and second systolic BPM (sBPM). Based on the CHEP, we calculated the mean of the second and third sBPM. A systolic BP (sBP) < 120 mmHg was regarded as normal, 120–129 mmHg as elevated and > 129 as hypertensive, as per ACC/AHA definition. BP differences were calculated using a related-samples Wilcoxon Signed Rank Test.

Figure 1: Related-Samples Wilcoxon Signed Rank Test showing the differences between sBP.

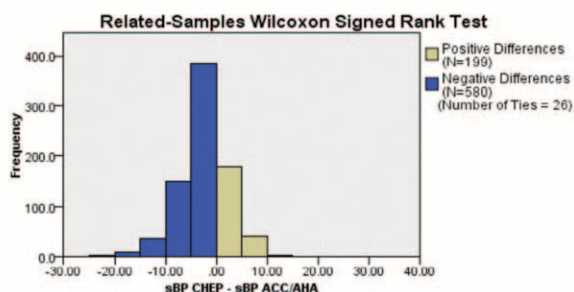
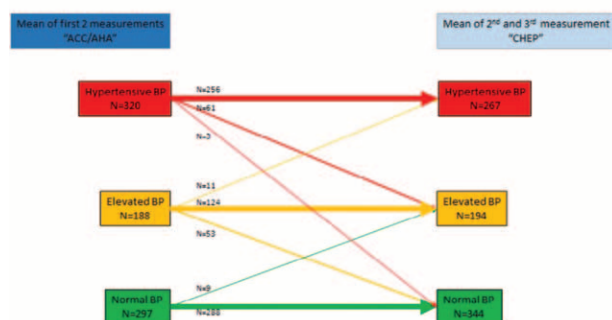


Figure 2: sBP category reclassification based on two different BPM techniques



**Results:** Complete measurements were available in 805 subjects. 195 patients were excluded due to incomplete measurements. Median sBP was 126 (114.5–

138) mmHg in ACC/AHA technique and 123 (112.5–135) mmHg in CHEP technique ( $p$ -value < 0.005), with 199 (24.7%) subjects showing a higher BP value with CHEP technique and 580 (72.0%) subjects with the ACC/AHA technique. 26 subjects had the same sBP with both techniques (Figure 1). Applying both BPM techniques during one BPM session, lead to disagreement regarding sBP classification in 20% of cases. Comparing CHEP and AHA/ACC technique 344 (43%) vs. 297 (37%) subjects were classified as normal BP, 194 (24%) vs. 188 (23%) as elevated BP and 267 (33%) vs. 320 (40%) as hypertensive BP (Figure 2).

**Conclusions:** There are significant differences in sBP values and classification depending on the guideline regarding BPM technique applied. 20% of hypertensive patients based on ACC/AHA would be reclassified to a lower BP category by applying CHEP.

#### RISK OF NEW ONSET METABOLIC SYNDROME ASSOCIATED WITH SELECTIVE AND COMBINED ELEVATION IN OFFICE, HOME AND AMBULATORY BLOOD PRESSURE

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**Objective:** In the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study, clinical, metabolic variables as well as office, home, and ambulatory blood pressure (BP) values were measured contemporaneously at baseline and after a ten-year period of follow-up, which allowed us to assess the value of selective and combined elevation of these BPs in predicting new onset metabolic syndrome (MetS).

**Design and method:** The present analysis included 1,182 participants without MetS at baseline, as defined by the APT III criteria. Based on office, 24-hour ambulatory BP and home values, subjects were divided into 4 groups: normal, with coat hypertension (WCH), masked hypertension (MH); and sustained hypertension (SH).

**Results:** As compared to subjects with in-office and out-of-office BP normality a greater age- and gender-adjusted incidence of new onset MetS was observed in WCH (OR = 2.03, CI:1.21–3.41,  $p = 0.007$ ), MH (OR = 2.55, CI:1.26–5.17;  $p = 0.009$ ) and SH (OR = 2.28, CI:1.43–3.99,  $p = 0.0009$ ) when out-of-office BP was defined by ambulatory criteria. This was not the same when out-of-office BP was based on home criteria, as only the WCH group showed a significant greater OR risk (2.16, CI: 1.28–3.63,  $p = 0.003$ ).

**Conclusions:** Our study provides evidence that isolated or combined BP elevations when identified by office/ambulatory measurements, carry an increase in risk of new onset MetS, while classifying the population by combining office/home BPs only WCH is associated with a greater risk of incident MetS. In a clinical perspective, a comprehensive evaluation of BP status based on office/ambulatory measurements may substantially improve the risk stratification of new onset MetS and to activate measures for its prevention

#### FIXED-DOSE COMBINATION THERAPY DECREASED PREVALENCE OF MASKED UNCONTROLLED HYPERTENSION (MUCH) IN VERY HIGH RISK PATIENTS

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**Objective:** Several authors found masked hypertension (MH) and masked uncontrolled hypertension (MUCH) to be independent predictors of target organ damages and to be associated with CV events. Variable prevalence of MUCH was reported; importantly it was highest in subjects with high risk (diabetics (DM2), chronic kidney disease (CKD), previous CV events etc.). There is no information on the effect of treatment on CV outcomes in MUCH. Our aim was to analyze clinical characteristics of MUCH and impact of fixed dose combination (FDC) in a group of very high risk patients.

**Design and method:** A total of 912 patients (age  $73 \pm 9.5$  years; 46% men) were followed for 6 months in outpatient settings. Of total, 32% had uncomplicated hypertension (HT), 35% were DM2, 52% had coronary heart disease (CHD) and



26% atrial fibrillation (AFib). At baseline, all were on two antihypertensive drugs and additional therapy depending on co-morbidities. Office BP was measured using Omron M6 device following ESH/ESC guidelines, ABPM (Mobilograph) was performed basal and in MUCH patients third antihypertensive drug was added as a fixed dose combination (FDC). Second ABPM was done 3–6 months later. MUCH was defined as office BP < 140/90 mmHg and 24-h ABP > 130/80 mmHg and/or awake ABP > 135/85 mmHg and/or sleep ABP > 120/70 mmHg. Glomerular filtration rate (GFR) was estimated using CKD-Epi equation, and albuminuria was determined from the 24-hour sample. CKD was defined as eGFR < 60 ml/min/1.73m<sup>2</sup>.

**Results:** At basal MUCH was found in 22% of patients, and out of them 54.5%, 41%, 35.5% and 10% had DM2, CKD, Afib and CHD, respectively. At the end of follow-up, following therapy modification MUCH was found in only 73 patients (8%). All of them were DM2 patients with albuminuria > 200 mg/dU and eGFR < 40 ml/min. They were older (68 ± 8 years), obese (BMI 38 ± 2.1 kg/m<sup>2</sup>) with duration of diabetes > 15 years. No gender difference was found.

**Conclusions:** High prevalence of MUCH in very high risk patients significantly decreased (22%–8%) with FDC therapy. True MUCH were older, obese patients with DM2 and CKD. Aiming to exclude MUCH ABPM should be part of routine work in all high risk patients.

#### GOVERNMENT EXPERT JOINT TWO YEARS INTERVENTION FOR HYPERTENSION AT A MULTI-ETHNIC RESOURCE-CONSTRICTION COUNTY NORTHWEST CHINA IS RELATED TO DECREASED STROKE MORTALITY

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**Objective:** Hypertension is common worldwide. Patterns of hypertension may vary in remote less developed areas. Xinjiang Northwest China is a multi-ethnic province with low income, low education and medical resource-constriction background, where hypertension is affecting up to 54.6% of adults of 30 years and older, characterized by lower treatment and control rates and higher prevalence and mortality of stroke. Therefore, we selected Emin county, a typical of above condition, to implement a government-expert joint comprehensive intervention for hypertension between January 2014 to December 2016. The aim is to raise awareness, treatment and control of hypertension, improve access to screening, and to decrease hospital admission and mortality to hypertension, cardiovascular diseases and stroke.

**Design and method:** Efforts were orchestrated from government, hypertension professionals, and general public. Medical staff education and door to door screening and education of population, establishment of hypertension department and BP measuring points, and an evidence- and condition-based 5 step anti-hypertensive treatment algorithm, and systemic management of hypertensive population were the main methods. Medical staff and public education was performed in four languages and materials were prepared in four language. Intervention outcome was evaluated by analyzing the data generated in 2014 and 2016.

**Results:** Cross-sectoral committee organized 102 seminars and training programs for medical staff and 540 times for population. 1 hypertension department and 184 BP measurement points were founded. Simultaneously with the intervention, 59405 subjects 15 years and older were invited to be screened, and 49497 subjects participated, with a 83.3% response rate. Awareness (64.4% vs 58%,  $P < 0.001$ ), treatment (44.6% vs 39%,  $P < 0.001$ ), and control (14.7% vs 10%,  $P < 0.001$ ) of hypertension were improved at 2016. Hospital admission rates due to hypertension (10.14 vs 8.39%), CVD (4.02 vs 2.60%) and stroke (3.72 vs 3.10%) were decreased. More importantly, mortality due to stroke (23.0 vs 14.0%) was decreased after two years of intervention.

**Conclusions:** With government-expert joint effort, it was possible to achieve higher hypertension awareness and treatment, to decrease hospital admission due to hypertension, CVD and stroke and mortality due to stroke within a short time in resource-constriction area.

#### PATTERNS OF HYPERTENSION IN RENAL TRANSPLANT PATIENTS EVALUATED WITH 24H AMBULATORY BLOOD PRESSURE MONITORING

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**Objective:** Hypertension (HTN) is particularly frequent in renal transplant recipients (RTR) and substantially contributes to the high cardiovascular risk of those patients. However, prevalence of the different patterns of hypertension in

KTR using 24 h ambulatory blood pressure monitoring (ABPM) along with their determining factor are lacking. The aim of our study was to describe the epidemiology of hypertension in RTR, based on ambulatory blood pressure monitoring (ABPM).

**Design and method:** In this cross-sectional study, prevalent RTR were proposed systematic blood pressure work-up consisting of ABPM, office blood pressure (3 consecutive blood pressure measurements performed by a nurse after 5 minutes of quiet rest) and detection of orthostatic hypotension. Optimal target was defined as BP < 130/80 mmHg, resistant HTN defined as BP above the target despite the use of at least 3 antihypertensive drugs including one diuretic. Orthostatic hypotension was defined as an orthostatic reduction in BP of at least 15 mmHg.

**Results:** 211 RTR (mean age of 61 years, 65% of male, 26% diabetic, 93% under CNI-based treatment, with post-transplant time ranging from 0.3 to 30 years) underwent ABPM. 89% of them were receiving antihypertensive treatment (2.2 different drugs on average including angiotensin renin blockers for 58%). Mean ABPM was 132/76 mmHg not different from the mean office BP (131/72 mmHg). Proportion of RTR with optimal BP was 43% and 46% after ABPM and office BP evaluation, respectively (NS). Prevalence of resistant hypertension was around 20% irrespective of the BP measurement technique. White coat and masked hypertension were present in 15% and 18% of RTR, respectively. Orthostatic hypotension was detected in 19% of the patients. In multivariate analysis, RTR age, albuminuria and CKD stages 3b and below were independent factors associated to uncontrolled/resistant hypertension.

**Conclusions:** Our findings suggest that ABPM does not confer significant advantage over a well formalized office BP measurement in order to characterize BP profile of RTR. While prevalence of resistant hypertension seems to be lower than in the general and native CKD populations, our data suggest that orthostatic hypotension is frequent and needs to be systematically detected.

#### RISK OF DEVELOPING SUSTAINED HYPERTENSION IN ISOLATED SYSTOLIC HYPERTENSION OF THE YOUNG IDENTIFIED WITH AMBULATORY BLOOD PRESSURE MONITORING

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**Objective:** Whether isolated systolic hypertension of the young (ISHY) is at increased risk of adverse outcome and should be treated is still debated. Previous data indicate that one of the main determinants of ISHY is a pronounced white-coat effect. The aim of the present study was to examine the risk of developing hypertension needing treatment (HT) in subjects with ISHY diagnosed with ambulatory blood pressure monitoring (ABPM).

**Design and method:** Methods: Among 1206, 18-to-45-year-old, participants from the HARVEST study, we identified 269 subjects with normotension (NT), 209 with ISHY, 277 with isolated diastolic hypertension (IDH) and 451 with systolic-diastolic hypertension (SDH). The 97 mmHg partition value was used to distinguish between subjects with high ( $\geq 97$  mmHg) and low 24 h mean BP. The risk of HT, defined according to available International guidelines, was evaluated in multivariable Cox analysis adjusting for several confounders.

**Results:** Compared to the other hypertension subtypes, ISHY participants were younger, more frequently males and more active in sports. They had lower office and 24 h heart rate, lower cholesterol and higher left ventricular stroke volume than the other three groups. During an 11.5-year follow-up, 65.1% of participants developed HT. In multivariate Cox analysis, using the NT group as a reference, the risk of incident HT was 1.29 (1.03–1.61) in IDH and 1.87 (1.53–2.28) in SDH participants, while in ISHY group the risk was not significantly different from that in NT being 1.12 (95%CI, 0.87–1.45). When the ISHY participants were divided according to their 24 h mean BP, only one third showed a high mean BP. The 140 ISHY participants with low mean BP had no increase in risk of HT (0.98, 0.72–1.33), whereas those with high 24 h mean BP had a significant increase in risk (1.74, 1.31–2.30).

**Conclusions:** Subjects with ISHY identified with ABPM are at low risk of developing hypertension needing treatment later in life. The risk is increased only in the minority of ISHY subjects with high 24 h mean BP.

#### NEW BP GOAL OF 130/80 MMHG MAKES NO DIFFERENCE IN IDENTIFYING HYPERTENSIVE TARGET ORGAN DAMAGE: THE NORTHERN SHANGHAI STUDY

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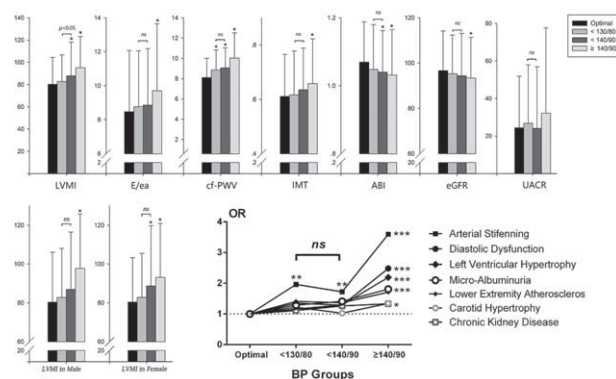
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**Objective:** High blood pressure (BP) promotes the development of hypertensive target organ damage (TOD). As the BP goal of 130/80 mmHg is now under debated, whether the thresholds of 130/80 mmHg and 140/90 mmHg differs in the patterns of TOD remains unclear. This analysis is focusing on the relationships between different BP groups and TOD.

**Design and method:** This analysis is nested in Northern Shanghai Study (NSS, Clinicaltrials.gov NCT02368938), participants prospectively recruited from June 2014 to June 2017 [n = 2098, 45.52% men, aged  $71.3 \pm 6.1$  years]. Preclinical TODs including arterial stiffening, left ventricular hypertrophy, left ventricular diastolic dysfunction, micro-albuminuria, chronic kidney disease, carotid hypertrophy and lower-extremity atherosclerosis were assessed in all the participants. Other clinical information was obtained by standard questionnaire. Participants were categorized into four groups according to BP (group1: < 120/80, group2: < 130/80, group3: < 140/90 and group4: over 140/90). Hypertensive target organ damages among four groups were compared. We fitted logistic regression models to assess the odds of different BP groups, compared with optimal BP group (<120/80).

**Results:** LVMI in group2 is significantly lower than group3 ( $p < 0.05$ ). However, after stratified by gender, group2 and group3 showed no significant differences in LVMI. Group2 and group3 showed no significant differences in other TOD

including E/ea, cf-PWV, IMT, ABI, eGFR and UACR. In multivariate logistic regression models, group2 and group3 showed no significant differences in odds risk of all the TOD, as compared with optimal BP group (<120/80 mmHg).



**Conclusions:** Compared with 140/90 mmHg, the BP goal of 130/80 mm Hg makes no difference in identifying hypertensive target organ damage.



# ORAL SESSION

## ORAL SESSION 1C: DIABETES

### EARLY VASCULAR PARAMETERS IN THE MICRO- AND MACROCIRCULATION IN TYPE 2 DIABETES

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**Objective:** Diabetes converts from a metabolic disorder into a predominantly vascular disease, once its duration extends over several years or/and when additional cardiovascular risk factors such as hypertension coexist. In a large cross-sectional analysis we analyzed various vascular parameters in the renal, retinal and systemic circulation, with the goal to identify which vascular parameter of early organ damage is the earliest that can be clinically detected.

**Design and method:** In 111 patients with type 2 diabetes (T2DM) (off any anti-diabetic medication for at least 4 weeks) and 54 subjects without T2DM we assessed urinary albumin creatinine ratio (urinary albumin creatinine ratio [UACR], early morning spot urine) and estimated glomerular filtration rate (eGFR), retinal capillary flow (RCF), intercapillary distance (ICD) as parameters of capillary rarefaction, wall-to-lumen ratio (WLR) of the retinal arterioles [all assessed by Scanning Laser Doppler Flowmetry], and central systolic pressure (cSBP) and central pulse pressure (cPP) [measured by pulse wave analysis, Syphymocor] both reflecting vascular stiffness of large arteries.

**Results:** Compared to subjects without T2DM, patients with T2DM (duration: mean 63.9 ± 56.4, range 1–271 months) were older (59.8 ± 7.3 vs. 43.4 ± 12.9 years,  $p < 0.001$ ), more females (33.3 vs 20.4 %,  $p < 0.001$ ) but 24-hour systolic and diastolic blood pressure did not differ between the two groups (129.3 ± 11.4 / 78.9 ± 8.3 vs. 130.4 ± 10.8 / 77.4 ± 5.6 mmHg). The analysis adjusted for age, gender and cardiovascular risk factors showed that ICD, cPP were significantly higher and eGFR was significantly lower in patients with T2DM than in subjects without T2DM.

	Non-T2DM-subjects (n=54)	Patients with T2DM (n= 111)	Unadjusted p-value	Age-gender-adjusted p-value	Adjusted p-value (potential confounders)
<b>Retinal parameters</b>					
ICD (μm)	20.8 ± 3.5	23.9 ± 5.1	<0.001	<0.001	0.001
RCF (AU)	310.4 ± 55.1	297.8 ± 72.9	0.15	0.35	0.72
WLR (-)	0.35 ± 0.08	0.38 ± 0.11	0.04	0.67	0.90
<b>Renal parameters</b>					
eGFR (ml/min/1.73m <sup>2</sup> )	95.9 ± 17.3	91.7 ± 9.9	0.10	<0.001	<0.001
UACR (mg/g)	7.9 ± 7.5	21.3 ± 86.6	<0.001	0.55	0.91
<b>Vascular stiffness parameters of large arteries</b>					
cSBP (mmHg)	106.7 ± 12.4	119.5 ± 12.9	<0.001	0.37	0.81
cPP (mmHg)	34.8 ± 10.6	41.8 ± 11.7	0.001	0.31	<0.001

**Conclusions:** These data suggest that at similar blood pressure capillary rarefaction in the retinal circulation (ICD), eGFR in the renal circulation and central pulse pressure (cPP) of large arteries are earlier detectable than vascular remodeling of the micro- (WLR, RCF, UACR) and macrocirculation (cSPB) in patients with T2DM.

### BLOOD PRESSURE AND ARTERIAL STIFFNESS: EFFECTS OF CANAGLIFLOZIN VERSUS PERINDOPRIL IN DIABETIC PATIENTS WITH ESSENTIAL HYPERTENSION

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**Objective:** Introduction: Hypertension control is a priority target for the reduction of cardiovascular and renal risks. In type 2 Diabetes, the blood pressure (BP) reduction has an important impact in decreasing macro and microvascular complications. Sodium-glucose co-transporter-2 (SGLT2), a newly developed oral anti-diabetic drug family is able to inhibit SGLT2, decrease glucose plasma levels, BP and weight. Arterial stiffness is an established risk factor for cardiovascular events and mortality. Treatment of hypertension improves arterial stiffness and SGLT2 have shown to reduce blood pressure and ameliorates pulse wave velocity

**Aims:** To evaluate, in patients with type 2 diabetes and hypertension, pretreated with amlodipine, the effects of Canagliflozin, compared with Perindopril, an ACEI, after 6 months treatment on central blood pressure and carotid-femoral pulse wave velocity (c-fPWV).

**Design and method:** Thirty type 2 diabetic patients with hypertension, pretreated with amlodipine 10 mg daily and metformin 750–2000 mg daily, were randomized and a third medication was added; either canagliflozin 300 mg daily (n = 15, 9female, mean age: 63 ± 8 y) or perindopril 10 mg daily (n = 15, 5females, mean age 59 ± 4 y), for 6 months.

Ambulatory blood pressure monitoring (ABPM) with Mobil-O-Graph device was assessed at baseline, and after 3 and 6 months of treatment. In addition, in all individuals before and after 6 months of treatment, the c-f PWV was measured by tonometry.

**Results:** Both treatments significantly reduced either the office or ABPM systolic, diastolic and central systolic blood pressures. Similarly, in both groups, c-f PWV was improved after 6 months of treatment.

Canagliflozin plus amlodipine significantly reduced HbA1C (8.1 ± 0.5% to 7.0 ± 0.4%;  $p < 0.05$ ) after 6 months of treatment. Perindopril plus amlodipine failed to change HbA1C. In the same way, only canagliflozin significantly reduced uric acid and 24h urinary sodium after 6 months treatment.

Other security laboratory parameters, including GOT, GPT, bilirubin failed to show any change.

**Conclusions:** Canagliflozin reduced ambulatory BP and central BP in diabetics patients. In addition, arterial stiffness was improved in a similar way to perindopril. These two conditions might be important for the cardiovascular protection effects of SGLT2 inhibitors

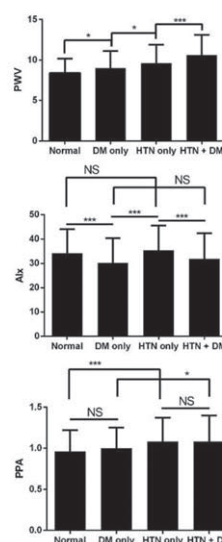
### COMPARISON OF ARTERIAL STIFFNESS PARAMETERS IN HYPERTENSIVE AND TYPE-2 DIABETIC PATIENTS: THE NORTHERN SHANGHAI STUDY

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**Objective:** Both hypertension and diabetes are powerful risk factors of cardiovascular disease, however, their contribution to arterial stiffness is different. This study was designed to compare different arterial stiffness parameters among hypertensive and type-2 diabetic patients in a community-based elderly cohort.

Figure 1. Comparison between populations according to the presence of diabetes or

hypertension



All participants were divided into four groups (without hypertension and without diabetes, without hypertension and with diabetes, with hypertension and without diabetes, with hypertension and with diabetes). HTN: hypertension. DM: diabetes. PPA, pulse pressure amplification; PWV, pulse wave velocity; AIx, augmentation index.

\*P: P values are adjusted for age, gender, BMI, mean blood pressure, heart rate, LDL-C, and use of insulin. P values: \* <0.05, \*\*\* <0.001, NS not significant.

The results suggested that PWV was associated with both DM and HTN. AIx was associated with DM but not HTN, and PPA was associated with HTN but not DM.

**Design and method:** 2,098 (aged 70.3 ± 5.6 years) participants were recruited till June 2017. All participants were divided into 4 groups: I. without hypertension

and without diabetes (normal group), II. without hypertension and with diabetes (DM group), III. with hypertension and without diabetes (HTN group), and IV. with hypertension and with diabetes (DM+HTN group). Three arterial stiffness parameters were measured with validated devices, including carotid-femoral pulse wave velocity (PWV), augmentation index (AIx), and pulse pressure amplification (PPA).

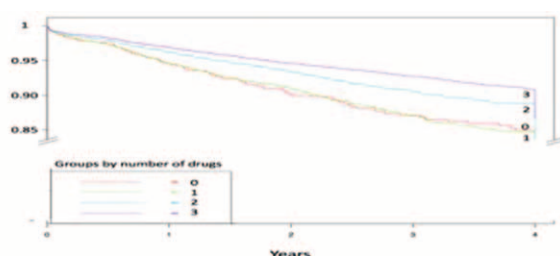
**Results:** The body mass index (BMI) was significantly lower in normal group than in the other 3 groups ( $P < 0.02$ ). Mean age, current smoker rate, physical activity, and education level were similar among 4 groups ( $P > 0.22$ ). Spearman correlation analysis showed that arterial stiffness parameters significantly correlated with age, mean blood pressure and heart rate. Generalized linear model with Tukey adjustment was applied to pairwise compare arterial stiffness parameters. Potential confounders including age, gender, BMI, mean blood pressure, heart rate, LDL-C, and use of insulin were adjusted in the model. Compared with normal group, PWV in the other 3 groups were significantly higher ( $P < 0.01$ ), and PWV in DM+HTN group was significantly higher than DM group and HTN group ( $P < 0.001$ ). The AIx in DM group and in DM+HTN group were significantly lower than in normal group ( $P < 0.001$ ), while AIx in HTN group and normal group were similar ( $P = 0.49$ ). As for PPA, they did not differ between participants with diabetes and without diabetes (with/without hypertension,  $P = 0.99$  and  $P = 0.12$ , respectively), while PPA in patients with hypertension were significantly higher than those without hypertension ( $P < 0.001$ ).

**Conclusions:** In the community-based elderly cohort, PWV is associated with both DM and HTN. AIx is associated with DM but not HTN, and PPA is associated with HTN but not DM. This result may improve the cardiovascular risk assessment in the future.

#### IMPACT ON MORTALITY OF THE GAP IN THE USE OF CARDIOVASCULAR PREVENTING DRUGS IN DIABETES: A POPULATION STUDY

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**Objective:** Diabetes is a condition of high cardiovascular risk and 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 class of drugs. The objective of the SATURNO study was to assess in diabetic subjects 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 data from Electronic Health Records (EHR).



NUMBER DRUGS	SUBJECTS	CASES	HR (CI 95%) Model 1	HR (CI 95%) Model 2	HR (CI 95%) Model 3
0	1630	154	Ref.	Ref.	Ref.
1	6478	592	.96 (0.8,1.15)	0.93 (0.77,1.12)	0.97 (0.8,1.17)
2	12667	848	0.75 (0.63,0.89)	0.71 (0.59,0.86)	0.79 (0.63,0.98)
3	17977	917	.66 (0.55,0.79)	.62 (0.5,0.76)	0.72 (0.56,0.95)

**Design and method:** Subjects and methods: Patients with diabetes and a diagnosis of stroke, TIA, MI or REV after January 1st, 2011 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 register during an observational period of 1.7+1.5 years. The survival analysis models were adjusted for group (group 0, group 1, group 2, group 3), age (continuous), gender (male, female), systolic blood pressure (continuous), LDL-cholesterol (continuous), HDL-cholesterol (continuous) and diabetes treatment (yes, no). We further adjusted for hypertension treatment (yes, no) and hypertension (yes, no) (Model 2) and for dyslipidemia treatment (yes, no) and dyslipidemia (yes, no) (Model 3). R

**Results:** A total of 38752 patients (61% men, mean age 73 yr) were included, 22502 with stroke or TIA, MI 11692 and REV 4363. The number of subjects in each group, the number of subjects and 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 in diabetic subjects.

#### ISOLATED SYSTOLIC HYPERTENSION VERSUS COMBINED SYSTOLIC-DIASTOLIC HYPERTENSION AS PREDICTORS OF NEW-ONSET DIABETES MELLITUS: DATA FROM A GREEK 8-YEARS-FOLLOW-UP STUDY

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**Objective:** The aim of the study was to compare the predictive role of isolated systolic hypertension (ISH) and combined systolic-diastolic hypertension for the incidence of new-onset diabetes mellitus (NOD) in essential hypertensive patients.

**Design and method:** We followed up 1435 non-diabetic essential hypertensives with office systolic blood pressure (BP)  $\geq 140$  mmHg [mean age 57 years, 730 males, office BP = 153/92 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 for estimation of metabolic profile. Patients with baseline ISH exhibited office systolic BP  $\geq 140$  mmHg and office diastolic BP  $< 90$  mmHg, while those with systolic-diastolic hypertension had office systolic BP  $\geq 140$  mmHg and office diastolic BP  $\geq 90$  mmHg. Moreover, NOD was defined if at one or more of the follow-up visits a previously non-diabetic patient reported being on insulin or an oral hypoglycemic drug or if casual plasma glucose concentration  $\geq 200$  mg/dl or fasting glucose concentration  $\geq 126$  mg/dl or 2-h post load glucose  $\geq 200$  mg/dl during an oral glucose tolerance test.

**Results:** The incidence of NOD over the follow-up period was 4.2% ( $n = 60$ ). Patients with ISH ( $n = 460$ ) compared to those with systolic-diastolic hypertension ( $n = 975$ ) were older ( $65 \pm 11$  vs  $54 \pm 10$  years,  $p < 0.0001$ ), had at baseline lower waist circumference ( $94.5 \pm 11$  vs  $99 \pm 13$  cm,  $p < 0.0001$ ), office systolic BP ( $149 \pm 12$  vs  $155 \pm 13$  mmHg,  $p < 0.0001$ ), office diastolic BP ( $80 \pm 8$  vs  $98 \pm 6$  mmHg,  $p < 0.0001$ ), while did not differ regarding left ventricular mass index, glucose and lipid levels ( $p = \text{NS}$  for all). Univariate Cox regression analysis revealed that baseline ISH (hazard ratio = 2.143,  $p = 0.016$ ) and systolic-diastolic hypertension (hazard ratio = 1.272,  $p = 0.029$ ) predicted NOD. However, in multivariate Cox regression model, age (hazard ratio = 1.039,  $p < 0.001$ ), baseline glucose levels (hazard ratio 1.011,  $p = 0.016$ ), waist circumference (hazard ratio = 1.067,  $p < 0.001$ ) and ISH (hazard ratio = 1.651,  $p = 0.029$ ) but not systolic-diastolic hypertension were independent predictors of NOD.

**Conclusions:** ISH but not systolic-diastolic hypertension exhibits independent prognostic value for NOD. These findings support that ISH constitutes a hypertensive phenotype of increased metabolic risk needing careful evaluation and treatment.

#### CYSTATIN C IS ASSOCIATED WITH THE PRESENCE OF CAROTID ATHEROSCLEROSIS IN PATIENTS WITH DIABETES TYPE 2 AND CHRONIC KIDNEY DISEASE

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**Objective:** Cystatin C has been proposed as a novel marker of renal function and as a predictor of the severity of coronary atherosclerosis and future cardiovascular events. The aim was to evaluate the possible role of chronic kidney disease and particularly CysC on the characteristics of carotid atherosclerosis in patients with type 2 diabetes (DT2).

**Design and method:** We investigated 195 patients both sexes with DT2 aged  $56.54 \pm 4.17$  years. Control group included 84 healthy subjects the same age. The intima-media thickness (IMT) was measured as the distance between the lumen-intima interface and the media-adventitia interface. Atherosclerotic plaque was defined as a focal structure encroaching into the arterial lumen of 0.5 mm or 50% of the surrounding IMT value. Total plaque area (TPA) was calculated as the sum of all plaque areas. GFR was estimated using the modification of diet in renal disease (MDRD) equation.

**Results:** Patients were divided into 2 groups by CysC levels tertiles. Patients in the high CysC tertile ( $n = 76$ ) had significantly higher mean carotid IMT

( $0.88 \pm 0.12$  mm vs.  $0.76 \pm 0.07$  mm,  $P = 0.03$ ), and TPA ( $4.69 \pm 2.03$  mm<sup>2</sup> vs.  $2.71 \pm 0.57$  mm<sup>2</sup>,  $P = 0.02$ ) compared to patients in the lower tertiles ( $n = 119$ ). CysC levels demonstrated significant positive correlation with the mean carotid IMT ( $r = 0.35$ ,  $P = 0.011$ ).

In multivariate analyses adjusted for cardiovascular risk factors, the association between CysC and IMT remained significant ( $P = 0.037$ ). In contrast, neither serum creatinine nor estimated GFR were associated with IMT ( $P = 0.17$ ).

**Conclusions:** Our study demonstrated a significant association of increased CysC levels with characteristics of carotid atherosclerosis in patients with type 2 diabetes and chronic kidney disease.

#### DETERMINANTS OF URINARY ALBUMIN EXCRETION IN NEWLY DIAGNOSED DIABETES MELLITUS

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**Objective:** Increased urinary albumin excretion (UAE) is a potent predictor of future cardiovascular disease that corresponds to a state of generalized microvascular dysfunction, even below the threshold values usually considered for microalbuminuria. This holds true in patients with hypertension and particularly in those with diabetes mellitus (DM), in whom it is associated with macrovascular disease. At the same time, both hypertension and DM are associated with large artery stiffening, while hypertension often coexists with DM. In the present study, we investigated whether an association exists between UAE and arterial stiffness in newly-diagnosed patients with DM, independent of blood pressure (BP) levels.

**Design and method:** Consecutive patients with newly-diagnosed DM were studied. All patients underwent office BP measurements and 24-hour ambulatory BP monitoring (Spacelabs 90207). Microalbuminuria was calculated from 24-hour urine samples. Arterial stiffness was evaluated with measurement of carotid-femoral pulse wave velocity (PWV) with applanation tonometry. Blood samples were drawn to estimate fasting glucose, glycated hemoglobin (HbA1c), lipid profile and renal function

**Results:** A total of 65 patients aged  $57 \pm 11$  years, 40 males and 25 females, with median DM duration of 2 months were included in the study. Fasting glucose was 121.5 (IR: 36) mg/dl and HbA1c 7.47 (IR: 2) %. The majority of patients (66.2%) had concomitant hypertension. In particular, 26 patients (40%) had a history of known hypertension with median duration of 8 (IR: 8) years, while 17 (26.2%) were simultaneously diagnosed with hypertension and DM. In our cohort, UAE was associated with fasting glucose ( $r = 0.294$ ,  $p = 0.040$ ),

HbA1c ( $r = 0.426$ ,  $p = 0.002$ ), creatinine ( $r = 0.308$ ,  $p = 0.035$ ), glomerular filtration rate ( $r = 0.442$ ,  $p = 0.002$ ), office systolic ( $r = 0.403$ ,  $p = 0.009$ ) and diastolic ( $r = 0.447$ ,  $p = 0.026$ ) BP and PWV ( $r = 0.308$ ,  $p = 0.031$ ). However, in the multivariate analysis adjusting for BP and other variables, HbA1c ( $\beta = 0.351$ ,  $p = 0.015$ ) was the only significant predictor of UAE, whereas the association between UAE and PWV no longer remained significant.

**Conclusions:** In newly-diagnosed patients with DM, hyperglycemia is an independent predictor of UAE, emphasizing the need for early and effective glycemic control. The observed association between UAE and arterial stiffening seems to be mediated by hyperglycemia and increased BP.

#### NON-PROTEINURIC DIABETIC NEPHROPATHY IS THE MAIN CAUSE OF CHRONIC KIDNEY DISEASE

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**Objective:** Diabetic nephropathy traditionally produces significant proteinuria prior to the development of renal impairment. However, this clinical paradigm has recently been questioned. The current study evaluated the impact of diabetes mellitus on the prevalence of renal disease in general population.

**Design and method:** Data from of the HERMEX survey, an observational, cross sectional, population based study were used. The final sample included 2,813 subjects (mean age 51.2 years, 53.5% female). Four hundred patients have diabetes. Urinary albumin excretion (UAE) rate was analyzed and glomerular filtration rate (GFR) was estimated using the CKD-EPI formula.

**Results:** Among participants without diabetes, 2.9%(2.2–3.6) had a GFR < 60 ml/min. Prevalence of abnormal UAE in population without diabetes was 3.3% (2.6–4.0). The global prevalence of renal disease was 5.6%(4.8–6.6). Prevalence of GFR < 60 ml/min in subjects with diabetes was 8.8%(6.4–11.9) ( $p < 0.001$ , Chi-square test). Prevalence of abnormal UAE in population with diabetes was 14.1%(7.7–19.8) ( $p < 0.001$ , Chi-square test). CKD prevalence was 20.3%(16.6–24.6) ( $p < 0.001$ , Chi-square test). The logistic regression analysis showed a positive independent association of CKD with age, high blood pressure and albuminuria. No significant relationship was found with diabetes mellitus

**Conclusions:** : CKD is more prevalent in population with diabetes. Nevertheless, most of patients with diabetes and CKD have no albuminuria. An increased cardiovascular burden seems to produce this clinical presentation.



# ORAL SESSION

## ORAL SESSION 2A:

## BLOOD PRESSURE VARIABILITY

### REDUCED BLOOD PRESSURE VARIABILITY AS A PREDICTOR OF CARDIAC EVENTS AFTER MYOCARDIAL INFARCTION: A 6 MONTHS FOLLOW-UP STUDY

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**Objective:** The impact of blood pressure variability (BPV) on cardiac function has been mainly examined through the prism of congestive heart failure and hypertension, but not in the setting of an acute coronary syndrome (ACS). The aim of this study is to determine the association between in-hospital short-term BPV and the development and aggravation of cardiac dysfunction in patients with acute myocardial infarction (AMI).

**Design and method:** A total population of 57 AMI patients [74.5% male; mean age: 67.56 years; 75.4% hypertensives] underwent 24hr ambulatory BP measurement during hospitalization. At 6 months a follow-up was scheduled for each patient in order to collect data on hospitalizations for heart failure (HF), but also to assess the overall cardiovascular outcome. The latter was defined as the composite end-point of hospitalizations for heart failure (n = 8), decline in ejection fraction (EF%) compared to the in-hospital value (n = 11), deterioration of NYHA class (n = 3) and new onset of heart failure symptoms (n = 2). In-hospital BPV was assessed using standard deviation (SD) and average real variability (ARV). The study population was divided into a STEMI group (n = 24) and a non-STEMI (n = 33) one.

**Results:** BPV was not associated with hospitalizations for HF. However, when the composite end-point was assessed, ARV of systolic BP demonstrated a significant negative association [B = -0.430; odds ratio, 0.651; CI, 0.473–0.895 (P = 0.008)] in the total population. A relatively significant predictive role of ARV was shown after splitting the population into the STEMI [B = -0.531; odds ratio, 0.588; CI, 0.339–1.019 (P = 0.058)] and non-STEMI group [B = -0.4; odds ratio, 0.670; CI, 0.443–1.014 (P = 0.058)]. Multinomial logistic regression analysis of incidence of cardiovascular events highlighted systolic BP ARV as the only independent predictor during a 6-month follow-up [B = -0.508; odds ratio, 0.602; CI, 0.407–0.891 (P = 0.011)] regardless the ACS type.

**Conclusions:** In the setting of ACS, reduced in-hospital systolic BP ARV was associated with cardiovascular morbidity during the 6 months of follow-up. This finding could be attributed to a dysautonomic state of the cardiovascular system related to the pathophysiology of ACS, linking BP regulation mechanisms to worse overall outcome in this high risk setting.

### NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO ARE INDEPENDENT PREDICTORS FOR BLOOD PRESSURE VARIABILITY

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**Objective:** Hypertension is a major risk factor for cardiovascular diseases. Ambulatory blood pressure monitoring is used for detection, follow-up of hypertensive patients and also demonstrates the diurnal variability of the blood pressure. Decreased blood pressure variability is associated with hypertensive target organ damage and higher risk for cardiovascular events. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are also related to inflammation and increased cardiovascular risk. The purpose of the study is to investigate the relationship between NLR and PLR with non-dipper status of hypertensive and normotensive patients.

**Design and method:** A total of 482 patients were evaluated retrospectively. Patients with previous hypertension diagnosis, acute coronary syndrome, serious valve regurgitation or stenosis, coronary artery disease, echocardiographic findings of

reduced left ventricular ejection fraction (LVEF < 55%), congenital heart diseases, abnormal kidney function, chronic liver disorders, chronic inflammatory disease, patients who had a recent history of acute infection were excluded.

**Results:** Mean age of the study population was 50.1 ± 15.5 years, 38.1% were male. Four groups were formed according to hypertension diagnosis, dipper and non-dipper patterns. Group 1 was consisted of 165 patients with hypertensive and non-dipper status; group 2 was consisted of 88 patients with hypertensive and dipper status; group 3 was consisted of 123 patients with normotensive and non-dipper status; and group 4 was consisted of 91 patients with normotensive and dipper status. Neutrophil lymphocyte ratio was statistically different among groups (p = 0.000). Group 1 had significantly higher values compared to Group 2 (p = 0.001), Group 3 (0.002) and Group 4 (p = 0.023). In hypertensive patient group, PLR values of Group 1 was significantly higher than Group 2 (p = 0.002). Pearson correlation analysis showed that NLR and PLR were correlated with BP variability between night and day (r = -0.188, p = 0.000 for NLR and r = -0.182 and p = 0.000 for PLR). Regression analysis showed NLR (p = 0.040), PLR (p = 0.021), age (p = 0.006) and hypertension (p = 0.000) were independent predictors of BP variability.

Table 1. Comparison of the baseline characteristics and laboratory results of the study groups.

Variables	Group 1 (n=180)	Group 2 (n=88)	Group 3 (n=123)	Group 4 (n=91)	P
Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Men, %	68 (41.2%)	50 (56.8%)	34 (27.6%)	26 (28.6%)	0.000
Age, years	52.5 ± 15.0	48.7 ± 14.6	49.1 ± 16.2	44.3 ± 15.2	0.001
LVEF, %	58.0 ± 2.3	57.6 ± 1.7	57.9 ± 2.5	58.2 ± 2.3	0.507
FBG, mg/dL	101.6 ± 32.8	103.6 ± 31.6	98.2 ± 26.5	97.6 ± 40.1	0.590
BUN, mg/dL	14.4 ± 4.6	13.7 ± 4.5	13.6 ± 5.2	12.9 ± 4.2	0.180
Creatinine, mg/dL	0.8 ± 0.2	0.8 ± 0.2	0.7 ± 0.1	0.7 ± 0.1	0.070
HDL-C, mg/dL	50.1 ± 12.8	51.7 ± 14.3	53.2 ± 11.6	52.9 ± 12.1	0.433
LDL-C, mg/dL	128.2 ± 38.3	129.2 ± 27.3	121.0 ± 33.6	125.4 ± 45.6	0.050
Triglyceride, mg/dL	172.7 ± 109.0	138.9 ± 48.2	134.6 ± 79.1	138.5 ± 71.6	0.019
Hb, g/dL	14.1 ± 1.8	14.7 ± 1.8	13.6 ± 1.8	13.8 ± 1.7	0.000
WBC, x10 <sup>3</sup> /mm <sup>3</sup>	8.3 ± 2.3	8.2 ± 2.1	7.7 ± 1.9	7.8 ± 2.0	0.048
Neutrophils, x10 <sup>3</sup> /mm <sup>3</sup>	5.5 ± 3.5	4.7 ± 1.7	4.5 ± 1.6	4.7 ± 1.7	0.006
Lymphocytes, x10 <sup>3</sup> /mm <sup>3</sup>	2.3 ± 0.7	2.6 ± 0.8	2.4 ± 0.8	2.3 ± 0.6	0.006
Eosinophils, x10 <sup>3</sup> /mm <sup>3</sup>	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	0.092
Platelets, x10 <sup>3</sup> /mm <sup>3</sup>	280.0 ± 77.6	270.9 ± 65.3	277.8 ± 67.9	268.1 ± 54.5	0.549
RDW, fL	43.0 ± 29.9	40.6 ± 3.4	41.0 ± 4.7	40.4 ± 4.0	0.648
MPV, fL	11.1 ± 7.1	11.6 ± 9.2	11.2 ± 8.4	10.4 ± 0.9	0.756
PDW, fL	12.4 ± 2.9	12.4 ± 2.5	12.2 ± 2.1	12.2 ± 2.1	0.752
NLR	2.696 ± 1.918	1.933 ± 0.916	2.357 ± 0.066	2.177 ± 1.154	0.000
PLR	133.3 ± 49.9	112.2 ± 45.4	133.5 ± 90.3	121.7 ± 33.5	0.008

Abbreviations: BUN, blood urea nitrogen; FBG, fasting plasma glucose; Hb, hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; MPV, mean platelet volume; NLR, neutrophil/lymphocyte ratio; PDW, platelet distribution width; PLR, platelet/lymphocyte ratio; RDW, red cell distribution width; WBC, white blood cell.

Table 2. Comparison of white blood cell parameters between Group 1-2 and Group 3-4.

Variables	p value of Group 1 compared to Group 2	p value of Group 3 compared to Group 4
WBC	0.657	0.759
Neutrophils	0.056	0.578
Lymphocytes	0.001	0.595
Eosinophils	0.349	0.226
Platelets	0.377	0.285
RDW	0.478	0.408
MPV	0.637	0.357
PDW	0.965	0.998
NLR	0.000	0.564
PLR	0.002	0.454

Abbreviations: MPV, mean platelet volume; NLR, neutrophil/lymphocyte ratio; PDW, platelet distribution width; PLR, platelet/lymphocyte ratio; WBC, white blood cell.

**Conclusions:** In conclusion NLR and PLR can be used as easily accessible and inexpensive markers for non-dipper status especially in hypertensive patients.

### SHORT-TERM BLOOD PRESSURE VARIABILITY PREDICTS CARDIOVASCULAR EVENTS AND ALL-CAUSE MORTALITY IN HEMODIALYSIS PATIENTS

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**Objective:** Long-term office BP variability in hemodialysis patients is associated with increased risk of cardiovascular events and mortality. However, the association of the main hemodynamic culprit in dialysis, i.e. interdialytic BP fluctuations, with outcomes has not been investigated. This study examines the prognostic role of short-term BP variability (BPV) for cardiovascular events and all-cause mortality in this population.

**Design and method:** 227 hemodialysis patients underwent 44-hour ambulatory monitoring during a standard interval and followed-up for  $30.17 \pm 17.70$  months. We calculated standard deviation (SD), weighted SD (wSD), coefficient of variation (CV), and average real variability (ARV) of BP with validated formulas. The primary end-point was first occurrence of all-cause death, non-fatal myocardial infarction or non-fatal stroke. Secondary end-points were: (i)all-cause mortality; (ii)cardiovascular mortality; (iii)a combination of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, resuscitation after cardiac arrest, coronary revascularization or hospitalization for heart failure.

**Results:** Cumulative freedom from the primary end-point was similar for quartiles of predialysis SBP and 44hour-SBP, but was progressively longer for increasing quartiles of 44hour-SBP-SD ( $p = 0.014$ ), wSD ( $p = 0.007$ ), CV ( $p = 0.031$ ) and ARV (83.9%, 71.9%, 70.2% and 43.9% for quartiles 1 to 4 respectively;  $p < 0.001$ ), a finding that was similar for the composite cardiovascular outcome. Higher quartiles of 44hour-SBP-ARV were significantly associated with higher future risk for all studied outcomes. Among diastolic BPV indices, 44hour-DBP-CV and 44hour-DBP-ARV were associated with increased risk for the composite cardiovascular outcome. In Cox regression analysis all SBP-BPV indices were related to the primary end-point, independently of SBP levels (ARV: HR: 1.118, 95%CI: 1.055–1.185, per mmHg increase).

**Conclusions:** Increased BPV during the interdialytic interval is associated with higher risk of death and cardiovascular events in hemodialysis, whereas ambulatory BP levels per se are not. Short-term BPV could be a major player promoting the adverse cardiovascular profile of these individuals.

#### PROGNOSTIC SIGNIFICANCE OF VISIT-TO-VISIT VARIABILITY, MEAN AND MAXIMUM BLOOD PRESSURE IN TREATED HYPERTENSIVE PATIENTS WITH HIGH CARDIOVASCULAR RISK

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**Objective:** Associating the visit-to-visit variability (VTV) of systolic BP (SBP), mean and maximum SBP with cardiovascular disease (CVD) and mortality outcomes in treated hypertensive patients with high CV risk.

**Design and method:** This prospective study included 142 hypertensive patients (65% females), with high CV risk defined with ESH score, mean age  $63.1 \pm 8$  years, in the beginning, the office blood pressure was 155.5 mmHg. Each participant was followed over a period of time of 6.2 years and BP measurements 6 or more visits; follow-up for CVD or mortality outcomes. The VTV of SBP was defined as the standard deviation (SD), coefficient variation (CV) and across SBP measurements obtained at 6 or more visits conducted.

**Results:** SD SBP was  $14.5 \pm 4$ , CV SBP  $10.1 \pm 3$ , mean SBP  $145.8 \pm 14$  and max SBP  $166.1 \pm 17$  mmHg. During the follow-up period, the incidence of non-fatal and fatal CV events was 19.7%, CV mortality 7%, and total mortality 9.9%. The effects of SD, CV, mean and maximum SBP on study outcomes were estimated by using a Cox proportional hazards model, unadjusted (model 1), with adjustment for age, sex, number of antihypertensive-drugs, and DM (model 2), or with additional adjustment for current smoking, heart rate, total cholesterol, triglycerides and body mass index (model 3). Mean, SD, CV, and maximum SBP were analyzed as continuous variables with hazard ratios (HRs) and 95% confidence intervals (CIs) shown per increase of 1 mmHg for each parameter. Total and CV mortality risk were significantly and positively associated with mean SBP during the measurement period (HR:1.043, 95%CI 1.01–1.077,  $P = 0.011$ ); (HR:1.047, 95%CI 1.09–1.086,  $P = 0.014$ ), while associations between total and CV mortality risk and SD, CV and maximum SBP were not statistically significant. Major CV events risk were positively associated with mean (HR:1.038, 95%CI 1.016–1.061,  $p < 0.001$ ); SD (HR: 1.108, 95%CI 1.025–1.198,  $P = 0.010$ ; CV (HR: 1.172, 95%CI 1.029–1.334,  $P = 0.017$ ); and maximum SBP (HR: 1.032, 95%CI 1.010–1.054,  $P = 0.004$ ); (model 1). These associations remained essentially unchanged after adjustments for other factors (models 2 and 3).

**Conclusions:** In our study VTV has been associated with cardiovascular disease but not with mortality.

#### TREATMENT WITH SGLT-2 INHIBITORS IN PATIENTS WITH DIABETES MELLITUS AND ESSENTIAL HYPERTENSION – DYNAMIC OF BLOOD PRESSURE VISIT-TO-VISIT VARIABILITY

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**Objective:** Aim of study was to elucidate possible dynamic of blood pressure (BP) level and BP visit-to-visit variability in patient with essential hypertension(EH) and diabetes mellitus (DM).

**Design and method:** We included in to the study 26 patients with EH. and DM. (13 male and 13 women, mean age  $62.5 \pm 7.98$  years). Mean BMI. was  $27.4 \pm 4.12$  kg/m<sup>2</sup>, mean GFR.  $69.4 \pm 11.87$  ml/min/1.73 m<sup>2</sup>. Patients were treated with DM. and EH. in accordance with the current recommendations. At the enrollment visit they receive  $2.4 \pm 1.12$  oral hypoglycemic agents in general, 6 patients were treated with insulin. All patients had insufficient glycemic control when enrolled in the study. 13 patients were additionally received empagliflozin 10 mg OD. and 13 patients – dapagliflozin 10 mg OD. The participants had their office BP. measured during the 12-month follow-up (6 months before treatment with SGLT-2 inhibitors and 6 months after the beginning of treatment). All patients received antihypertensive therapy, 71% of patients had good BP. control. Antihypertension treatment was stable during the study. Blood pressure variability calculation was performed per data of electronic ambulatory cards. We defined systolic and diastolic visit-to-visit variability of BP. using average real variability.

**Results:** Mean systolic BP at the inclusion into the study was  $130.3 \pm 8.47$  mm Hg, diastolic BP –  $79.6 \pm 6.33$  mm Hg. Mean systolic BP variability was  $9.41 \pm 1.83$  mm Hg, diastolic BP variability –  $6.64 \pm 0.51$  mm Hg. After the 6 months of treatment with SGLT-2 inhibitors glycemic control was better. Only 1 patient continued to take insulin. At the end of study patients received  $1.8 \pm 0.83$  oral hypoglycemic agents. Systolic blood pressure decreased by  $5.2 \pm 10.18$  mm Hg ( $p = 0.020$ ) and diastolic - by  $2.7 \pm 6.11$  mm Hg ( $p = 0.037$ ). BP variability decreased by  $4.5 \pm 6.45$  mm Hg for systolic ( $p < 0.001$ ) and  $0.8 \pm 1.79$  mm Hg ( $p = 0.056$ ) for diastolic BP. The dynamics of BP was not different when treated with different hypoglycemic drugs.

**Conclusions:** Therapy with SGLT-2 inhibitors improves blood pressure control and decrease BP visit-to-visit variability in patients with EH and DM.

#### PROGNOSTIC IMPLICATIONS OF VISIT-TO-VISIT BLOOD PRESSURE VARIABILITY IN THE PATIENTS WITH HEART FAILURE

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**Objective:** The prognostic value of that visit-to-visit blood pressure variability (BPV) has not yet been validated in heart failure (HF) patients.

**Design and method:** We evaluated the patients hospitalized for acute decompensated HF who registered in the Korean Acute Heart Failure (KorAHF) Registry. Of the 5,627 patients, 900 patients with atrial fibrillation were excluded. The average BP and BPV, as determined by the standard deviation (SD) and coefficient of variation (CV) of systolic and diastolic BP, were recorded at the time of discharge and in outpatient clinic at 3 months, 6 months and 12 months after discharge. The cardiovascular outcome was defined as a composite of death and rehospitalization with aggravated HF.

**Results:** A total of 3,727 patients (1703 females) were analyzed. Mean age was  $67.4 \pm 15.3$ . Average BP was  $132.1 \pm 31.5/78.1 \pm 18.8$  mmHg at admission and  $115.2 \pm 18.2/71.1 \pm 11.5$  mmHg at discharge. Average BP was  $117.0 \pm 16.0/68.0 \pm 9.3$  mmHg and visit-to-visit BPV was  $12.6 \pm 7.8/8.5 \pm 5.2$  mmHg by SD and  $10.7 \pm 6.4/12.6 \pm 7.8$  % by CV. After a mean follow up duration of  $138.3 \pm 77.0$  days, 250 patients (6.7%) died and 625 patients (16.8%) were rehospitalization with aggravated HF. The patients with clinical event showed significantly lower SBP ( $114.4 \pm 16.8$  vs.  $117.7 \pm 15.7$ ,  $P < 0.001$ ) and DBP ( $66.1 \pm 9.0$  vs.  $68.5 \pm 9.3$ ,  $P < 0.001$ ), but systolic BPV ( $12.4 \pm 8.1$  vs.  $12.6 \pm 7.8$  by SD,  $10.9 \pm 6.8$  vs.  $10.7 \pm 6.3$  by CV) and diastolic BPV ( $9.0 \pm 5.6$  vs.  $8.4 \pm 5.2$  by SD,  $13.7 \pm 9.2$  vs.  $12.3 \pm 7.3$  by CV) were comparable between two groups. In multiple regression analysis, average SBP and DBP was independent predictor

of clinical outcomes, but systolic BPV and diastolic BPV did not predict clinical event. In survival analysis, there was also no association between systolic/diastolic BPV and the composite clinical outcomes.

**Conclusions:** In contrast with other clinical entity, these findings suggest that visit-to-visit BPV is not associated with clinical outcomes in heart failure patients.

### FIVE CONSECUTIVE OFFICE BLOOD PRESSURE MEASUREMENTS VERSUS CURRENT PRACTICE. HOW AGE, GENDER, DIABETES AND HYPERTENSION AFFECT BLOOD PRESSURE

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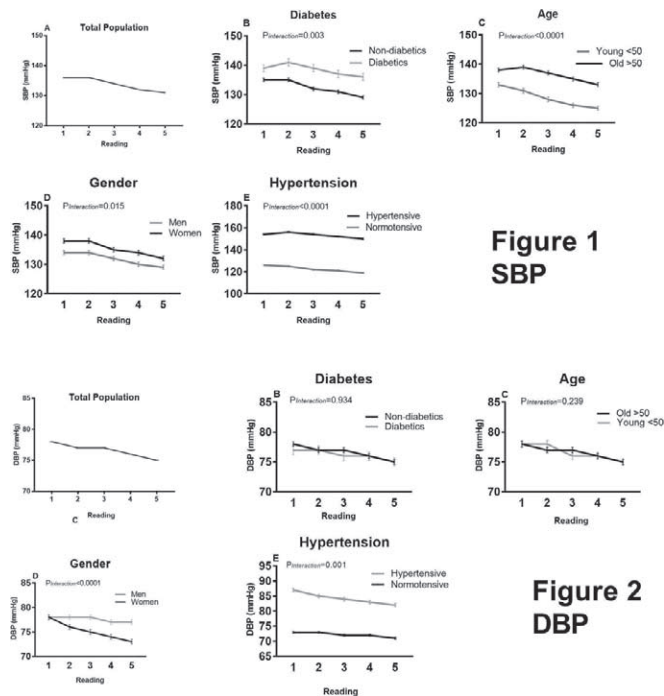
**Objective:** Recently, new data from trials conducted on hypertension have been surging, leading to changes in the management of patients with arterial hypertension, and subsequently giving rise to modifications of practice guidelines. Yet, there is no consensus on the number of readings that should be considered to measure the accurate BP. The study aimed to determine the impact of age, gender, diabetes mellitus and hypertension on the systolic (SBP) and diastolic blood pressure (DBP) variability patterns in cardiac patients. Moreover, we highlighted the variability that occurs in percentage of patients diagnosed with hypertension according to different current guidelines V's using mean of 5 consecutive BP readings.

**Methods:** 1389 cardiac patients (median age, 54 (18, 87 y)) presenting at Al-hyatt Heart and Vascular Center were studied. Five consecutive blood pressure measurements were taken, with one-minute interval. High SBP and DBP were classified according to the mean of the 5 readings as SBP > 140 and DBP > 90 mmHg according to different guidelines and SBP > 130 and DBP > 80 as per to new AHA/ACC cutoffs. Young subjects were defined as those < 50y of age. A decrease in BP over 5 readings were defined as a difference between BP-reading 5 (R5) and R1 of -1 mmHg or more, while an increase was defined as R5-R1 ≥ 1 mmHg.

**Result:** Number of patients diagnosed with hypertension varied among different guidelines and protocols, we found that this number was significantly altered when comparing different guidelines to the mean of five BP readings as follows: 560 (40.3%) patient as per to ESC ( $P < 0.001$ ), 518 (37.3%) patient as per to CHEP ( $p < 0.001$ ), 862 (62%) patients according to new AHA/ACC ( $p < 0.001$ ). SBP decreased from R1 to R5 in 66% of patients by a mean of 6 mmHg. The decrease was greater in younger subjects (8 mmHg) compared to older patients

(4 mmHg,  $P < 0.001$ ). Sex, age, DM and hypertension significantly affected the SBP pattern. DBP declined in 55% of the population (mean decrease = 3 mmHg). Only hypertension and gender, but not DM or age affected the DBP pattern. The second reading of the SBP was notably higher than the other readings in hypertensive patients, diabetic patients, and older individuals with an average of 3–5 mmHg.

**Conclusion:** Subject characteristics such as age, gender, DM and HTN have an impact on blood pressure which might alter the diagnosis of hypertension. The study suggests that relying on the average of 5 BP measurements is more appropriate as the second reading often shows the greatest divergence based on subject characteristics and because 5 readings reflects an individual's daily life blood pressure variability more closely.





# ORAL SESSION

## ORAL SESSION 2B:

## ATRIAL FIBRILLATION AND HEART FAILURE

### ISOLATED SYSTOLIC HYPERTENSION VERSUS COMBINED SYSTOLIC-DIASTOLIC HYPERTENSION AS PREDICTORS OF ATRIAL FIBRILLATION: DATA FROM A GREEK 8-YEAR-FOLLOW-UP STUDY

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**Objective:** The aim of the present study was to compare the predictive role of isolated systolic hypertension (ISH) and combined systolic-diastolic hypertension for the incidence of atrial fibrillation (AF) in essential hypertension.

**Design and method:** We followed up 1605 essential hypertensives with office systolic blood pressure (BP)  $\geq$  140 mmHg [mean age 58.1 years, 842 males, office BP = 153/92 mmHg] for a mean period of 8 years. Patients with baseline ISH exhibited office systolic BP  $\geq$  140 mmHg and office diastolic BP  $<$  90 mmHg, while those with systolic-diastolic hypertension had office systolic BP  $\geq$  140 mmHg and office diastolic BP  $\geq$  90 mmHg. Moreover, new-onset AF was defined as hospitalization for AF or compatible electrocardiographic tracings.

**Results:** The incidence of new-onset AF over the follow-up period was 3.4% (n = 55). Patients with ISH (n = 510) compared to those with systolic-diastolic hypertension (n = 1095) were older ( $65 \pm 10$  vs  $55 \pm 11$  years,  $p < 0.0001$ ), had at baseline lower office systolic BP ( $149 \pm 10$  vs  $155 \pm 13$  mmHg,  $p < 0.0001$ ) and office diastolic BP ( $80 \pm 5$  vs  $98 \pm 7$  mmHg,  $p < 0.0001$ ), while did not differ regarding left ventricular mass index ( $p = \text{NS}$ ). Univariate Cox regression analysis revealed that baseline ISH (hazard ratio = 4.612,  $p = 0.013$ ) and systolic-diastolic hypertension (hazard ratio = 1.794,  $p = 0.036$ ) predicted new-onset AF. However, in multivariate Cox regression model, age (hazard ratio = 1.078,  $p < 0.001$ ), left atrium diameter (hazard ratio = 1.102,  $p < 0.001$ ) and ISH (hazard ratio = 1.551,  $p = 0.035$ ) but not systolic-diastolic hypertension turned out to be independent predictors of new-onset AF episodes.

**Conclusions:** In hypertensive patients, ISH but not systolic-diastolic hypertension exhibits independent prognostic value for AF. These findings support that ISH constitutes a hypertensive phenotype of increased risk for AF needing careful management.

### ELECTROANATOMICAL MAPPING OF ATRIAL FIBRILLATION, EPICARDIAL FAT AND ATRIAL FIBROSIS IN PATIENTS WITH METABOLIC SYNDROME

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**Objective:** Epicardial fat may influence upon remodeling of the heart which can be the cause of atrial fibrillation (AFib). Study objective - to evaluate the epicardial fat thickness (EFT) and to reveal the possible relationship of this parameter with galectin-3 (Gal-3) as markers of fibrosis in patients with AFib and metabolic syndrome (MetS).

**Design and method:** 100 patients 35–65 y.o. with MetS (IDF,2005) including 50 patients with paroxysmal (n = 28) and persistent (n = 22) AFib were examined. The control group was 50 persons without metabolic disorders. The examination includes: medical history, echocardiography, serum levels of Gal-3 (Enzyme immunoassay). The EFT was measured with echocardiography. 25 patients with paroxysmal AFib were treated with radiofrequency ablation with vein isolation. Ablation procedure was performed with the system of electroanatomical mapping CARTO 3 (Biosense Webster Inc, USA) and contact force monitoring catheter (SmartTouch). After ablation, we analyzed the clinical data and the effectiveness of therapy during follow-up (12 months).

**Results:** The epicardial fat thickness was more than 2 fold greater in the MetS compared with the control group ( $4.7 \pm 1.3$  and  $2.4 \pm 0.9$  mm;  $p < 0.001$ ). Gal-3 in patients with MetS with AFib was more than 2 fold higher than in healthy control ( $0.72$  [0.44;1.36] and  $0.32$  [0.28;0.42] ng/ml;  $p < 0.001$ ). Correlation analysis was showed a strong positive correlation between EFT and volume of the left atrium ( $r = 0.61$ ;  $p < 0.001$ ). In patients with MetS and AFib with EFT more than 3.5 mm the risk of AFib is 3.9 folds higher (OR = 3.92, 95%CI 1.98–7.78,  $p < 0.001$ ). Positive correlation between EFT and Gal-3 was revealed ( $r = 0.61$ ;  $p < 0.001$ ). After prospective study, we registered recurrent paroxysms of AFib in 29 patients. EFT was greater in patients with recurrent paroxysms of AFib than in patients without paroxysms of AFib ( $4.5 \pm 1.5$  and  $2.8 \pm 1.5$  mm,  $p = 0.001$ ). The multivariate regression analysis demonstrated that EFT is an independent predictor of non-effective of radiofrequency ablation therapy of AFib (OR = 1.47, 95%CI 1.02–2.04,  $p = 0.014$ ).

**Conclusions:** Greater thickness of epicardial fat is associated with higher levels of galectin-3 and with higher risk of non-effectiveness of radiofrequency ablation. Left atrium fibrosis degree correlates with epicardial fat thickness and it can influence on remodeling of the heart. Greater thickness of epicardial fat

### THE EFFECT OF SOCIAL FACTORS ON THE PREVALENCE OF ATRIAL FIBRILLATION IN HYPERTENSIVE PATIENTS

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**Objective:** Atrial fibrillation (AF) is a common arrhythmia in hypertensive patients. Several conditions are deemed to be associated with AF. This study examined the effect of social factors (sex, age, obesity, smoking, alcohol consumption and marital status) on AF prevalence in a large cohort of hypertensive patients.

**Design and method:** The study comprised 30785 hypertensives (52.4% men,  $58.8 \pm 12.9$  years,  $165.2 \pm 10.6/99.1 \pm 9.8$  mmHg). Sex, age (years), smoking status (current, former, never), alcohol consumption (rare, light, moderate, heavy), and marital status (married, single, divorced) were recorded. Body mass index (BMI, kg/m<sup>2</sup>), body surface area (BSA, m<sup>2</sup>), waist-to-hip ratio (WHR), waist-to-stature ratio (WSR) and sphericity index (SI = BMI/BSA, kg/m<sup>4</sup>) were calculated.

**Results:** Sinus rhythm (SR) was prevalent in 90.1%, paroxysmal AF (PAF) in 5.5% and sustained AF (SAF) in 4.4% of patients. In SR, PAF, SAF groups, men were 52.1%, 52.7%, 57.3% and women were 47.9%, 47.3%, 42.7%, respectively ( $p$  for trend  $< 0.01$ ). In SR, PAF, SAF male and female subgroups, mean age was 56.1, 65.9, 73.2 and 59.1, 68.5, 75.1, mean BMI 28.04, 28.71, 30.07 and 29.19, 31.32, 30.67, mean WHR 0.919, 0.942, 0.968 and 0.845, 0.889, 0.896, mean WSR 0.574, 0.600, 0.635 and 0.562, 0.603, 0.614, mean SI 13.99, 14.34 14.96 and 16.39, 17.33, 17.58, current smokers were 38.3%, 26.5% 26.3% and 29.7%, 20.0%, 25.0% of patients, former smokers 14.4%, 29.4% 35.1% and 7.8%, 12.9%, 20.8% of patients, light alcohol consumption was present in 56.7%, 46.6% 23.8% and 38.0%, 65.1%, 53.5% of patients, moderate alcohol consumption in 14.9%, 42.2%, 56.4% and 3.1%, 25.3%, 21.4% of patients, heavy alcohol consumption in 3.0%, 9.9%, 18.3% and 0.4%, 1.4%, 4.6% of patients, married were 82.1%, 87.4% 90.4% and 86.6%, 81.4%, 90.9% of patients, single 13.7%, 8.2%, 4.0% and 9.4%, 14.0%, 4.5% of patients and divorced 4.2%, 4.4%, 5.6% and 4.0%, 4.6%, 4.6% of patients, respectively (in men all  $p$  for trend  $< 0.01$ , in women  $p$  for trend  $< 0.01$  only for age, WHR, WSR, SI, former smoking, heavy alcohol consumption).

**Conclusions:** All the examined social factors (sex, age, obesity, smoking, alcohol consumption and marital status) are associated with AF prevalence in hypertensive patients, especially in men.

### OPPORTUNISTIC SCREENING FOR ATRIAL FIBRILLATION IN THE PHARMACIES: A POPULATION BASED OBSERVATIONAL STUDY

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**Objective:** Opportunistic screening outside medical clinics using easily available devices measuring blood pressure while simultaneously detecting irregular pulse

could be potentially useful to identify patients with asymptomatic or unknown atrial fibrillation, thus reducing the burden of cardiovascular events, primarily systemic thromboembolism (NICE medical technology guidance 13, 2015). We performed a cross-sectional observational study aimed at evaluate the prevalence of atrial fibrillation and associated clinical conditions in adults older than 50 years living in the province of Verona.

**Design and method:** All the citizens aged 50 or more were invited through an information campaign to reach their pharmacy to have their blood pressure and heart rate monitored with the Microlife Afib® device, which utilises an algorithm to calculate the irregularity of interval times between heartbeats and identify atrial fibrillation. Pharmacists collected for 6 months also anthropometric and demographic data of the participants, along with information concerning their personal history of cardiovascular disease and the use of anti-hypertensive and anti-thrombotic agents. All those who were positive to the screening for atrial fibrillation were referred to their medical doctor.

**Results:** A total number of 3109 citizens took part in the study; 1605 of them were hypertensive, 297 diabetic and 372 obese. Positive for atrial fibrillation were 99 subjects (56 males). Only 44 of them had a previous diagnosis of atrial fibrillation and were receiving anticoagulation agents (77%) or aspirin (7%). Although subject positive to the screening were hypertensive, diabetic or obese in the same proportion of the negative ones, they had in a larger proportion a previous stroke (7% versus 2%,  $P < 0.01$ ).

**Conclusions:** Aim of our investigation was to obtain epidemiological data concerning the prevalence of atrial fibrillation, to identify previously non-detected cases and to promote consciousness in the population concerning the risk factors and the clinical consequences of atrial fibrillation. The results of our study indicate that opportunistic screening for atrial fibrillation in the pharmacies is feasible and allows identify a large number of subjects with silent, non-previously diagnosed atrial fibrillation, and is potentially useful in large-scale projects aimed at the prevention of cardiovascular mortality.

#### **AUTOMATED VERSUS AUSCULTATORY OR INTRA-ARTERIAL BLOOD PRESSURE MEASUREMENT IN ATRIAL FIBRILLATION: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Objective:** The cuff-based measurement of blood pressure (BP) in atrial fibrillation (AF) is considered as difficult and uncertain and the accuracy of automated BP monitors in AF is regarded questionable.

**Design and method:** A systematic PubMed search was conducted for identifying studies comparing automated (oscillometric or automated auscultatory) BP measurements versus manual auscultatory (mercury or aneroid sphygmomanometers) or intra-arterial BP measurements in patients with sustained AF.

**Results:** Fifteen articles including 13 non-invasive studies ( $N = 877$ ; 5 home, 2 ambulatory, 4 office BP monitors) and 4 invasive studies ( $N = 179$ ; 2 office, 2 home monitors) were included in meta-analyses. There was a significant heterogeneity in the validation procedure used for comparing BP measurements in different studies. Meta-analysis of non-invasive studies showed pooled correlation coefficients between auscultatory and automated BP measurements to be stronger for systolic (SBP) than diastolic BP (DBP) ( $r$  0.87 versus 0.76,  $p < 0.05$ ). Automated BP measurements were slightly higher than auscultatory measurements (pooled average SBP difference 0.5 mmHg, 95% confidence intervals [CI] -0.9, 1.9; DBP 1.5 mmHg, 95% CI -0.6, 3.6). Meta-analysis of invasive studies showed automated SBP to be lower than intra-arterial SBP measurements (pooled difference -4.2 mmHg, 95% CI -8.4, -0.02), whereas automated DBP was higher (6.1 mmHg, 95% CI: 3.8, 8.4).

**Conclusions:** There is significant heterogeneity in the non-invasive validation studies of automated BP monitors in AF. The current evidence suggests acceptable agreement of automated with auscultatory BP measurements, which is further supported by limited invasive studies showing similar relationship as in sinus rhythm. There seems to be a consistent trend towards more accurate measurement of systolic BP and overestimation of diastolic BP, which however is less important in AF patients who are usually elderly with systolic hypertension.

#### **HIGH SYSTOLIC BLOOD PRESSURE IS ASSOCIATED WITH INCIDENT LATENT HEART FAILURE: THE SUIA STUDY**

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**Objective:** Preventing organ dysfunction is essential for the extension of the healthy life expectancy among the high prevalence of longevity populations, but there are few epidemiological studies on heart failure (HF) for residents other than Westerners. We hypothesized that high systolic blood pressure (BP) affects the risk of subsequent latent HF in a general Japanese population.

**Design and method:** We prospectively followed-up 2,760 participants (average age  $66.7 \pm 10.4$  years) initially free of latent HF for incident latent HF in the Suita Study. B-type natriuretic peptide (BNP) was measured by the CLEIA method. Latent HF was defined as  $\text{BNP} \geq 100$  pg/mL or HF medication from medical records. Each subject's health status and BNP were checked in biannual medical examinations, and annual questionnaires were also completed by all subjects. BP was measured twice in the sitting position after resting for  $> 5$  min. The values' mean was used for the analysis. The endpoint of the follow-up period for incident latent HF was whichever of the following occurred first: the date of the first diagnosis of latent HF,  $\text{BNP} \geq 100$  pg/mL, or HF medication. We analyzed Cox proportional hazard ratios (HRs) and 95% confidence intervals (CIs) for incident latent HF after adjusting for cardiovascular risk factors.

**Results:** In 16,856 person-years of follow-up, 270 incident latent HF events occurred. The age- and sex-adjusted HRs (95% CI) for incident latent HF were 1.92 (1.24–2.99) in grade II or III systolic hypertension ( $\geq 160$  mmHg) and 1.99 (1.30–3.06) in high pulse pressure  $> 60$  mmHg, compared with optimal systolic BP ( $< 120$  mmHg) and low pulse pressure  $< 40$  mmHg, respectively. The multivariable-adjusted HR (95%CI) for incident latent HF was 2.17 (1.37–3.44), compared with optimal systolic BP. The age- and sex- and multivariable-adjusted HRs (95%CI) for incident latent HF were 1.34 (1.05–1.72) and 1.09 (0.83–1.43) in antihypertensive drug use, respectively. No association between diastolic BP and incident latent HF was observed.

**Conclusions:** Our findings are the first to show that grade II or III systolic hypertension is a robust predictive marker of incident latent HF in a general Japanese population.

#### **ZINC-ALPHA 2 GLYCOPROTEIN FACILITATES CATECHOLAMINE-INDUCED LIPOLYSIS IN HUMAN ADIPOCYTES THROUGH A CATALASE-LIKE EFFECT: FOCUS ON CARDIAC CACHEXIA**

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**Objective:** Cardiac cachexia development in heart failure is characterized by fat mass loss and elevated levels of circulating fatty acid (FA). Zinc alpha 2 glycoprotein (ZAG) has been demonstrated to induce lipolysis in vivo in rodents and in cardiac cachexia. We investigate ZAG mechanisms of action in human adipocytes obtained from healthy subjects (CTR), heart failure non cachectic patients (HF-nCX) and cardiac cachectic patients (HFCX).

**Design and method:** Two sets of experiments have been performed: in the first pilot study 6 CTR, 4 HF-nCX and 3 HFCX subjects have been enrolled. Subcutaneous adipose tissue sample has been obtained during dermatological surgical procedure or at the moment of ICD or PM generator change. Isolate mature adipocytes were incubated with ZAG 25 ug/mL. H2O2 release in culture medium was evaluate before and after 1 and 2 hours of ZAG-incubation. Adipocytes have been also incubated with Norepinephrine (NE) 10–5 M, H2O2 10–4 M and 10–5 M and BRL44408 10–5 M (Selective alpha2A-adrenoceptor antagonist). Infranant glycerol was measured as an index of lipolysis. In the second set of experiments 16 CTR, 19 HF-nCX and 12 HFCX patients have been enrolled. Adipocytes were incubated with ZAG 25 ug/mL, Benzylamine (BZ) 1 mM and Tyramine (TY) 1 mM in different combination and H2O2 production was measured.

**Results:** ZAG did not increased lipolysis but co-incubation with noradrenaline resulted in higher glycerol release in HFCX vs noradrenaline alone ( $+60\%$ ,  $p < 0.05$ ). ZAG reduced H2O2 release from adipocytes to a greater extent in HFCX ( $+65\%$ ,  $p < 0.05$ ) within the first hour of incubation. H2O2 incubation with adipocytes did not reduce glycerol release in the three group, nor reduced the NE-mediated lipolysis. H2O2 blunted the BRL44408-induced lipolysis when co-incubated with NE. A greater release of H2O2 from HFCX in basal condition and after incubation with BZ and TY was observed. ZAG reduced BZ-related H2O2 production in all the three groups, whereas TY did not.

**Conclusions:** ZAG has a facilitating role in NE-induced lipolysis that could be linked to an antioxidant, reducing H2O2 levels especially in HFCX patients. ZAG reduced BZ-related semi-carbazide sensitive-oxidase H2O2 generation suggesting an involvement of this enzyme in its action.

# ORAL SESSION

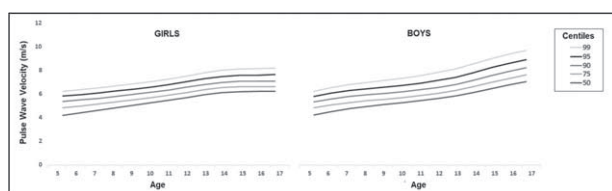
## ORAL SESSION 3A:

## CHILDREN AND ADOLESCENTS

### REFERENCE VALUES FOR AORTIC PULSE WAVE VELOCITY IN PORTUGUESE CHILDREN AND ADOLESCENTS – AN UPDATE FROM THE PORTUGUESE VASCULAR PHENOTYPE IN CHILDREN AND ADOLESCENTS COHORT

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**Objective:** Carotid-femoral pulse wave velocity (PWV) is the gold-standard method to estimate aortic stiffness, and has been clearly associated with cardiovascular risk in different clinical subsets. Still, its use in clinical practice is still limited in some specific groups, particularly in pediatrics, due to the absence of reference values for this population. This subanalysis of the PORT-VASPh Cohort aimed to propose reference values in Portuguese children and adolescents, based on a statistical definition that considers the fundamental physiological role of aging in arterial stiffness.



**Design and method:** The PORT-VASPh cohort has 953 children and adolescents enrolled, age ranging from 5 to 17 years. The overall health profile for each participant was defined based on three clinical evaluations, in which blood pressure (BP) was measured under standard conditions over the brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. For the proposal of reference values for PWV, data were collected from 758 healthy and normotensive participants included in the cohort, 60% males and 40% females, with a mean age of  $11.95 \pm 2.87$  years (ranging from 5 to 17 years) and a body mass index (BMI) of  $18.56 \pm 2.98$  kg/m<sup>2</sup>. Carotid-femoral PWV was measured to all participants with the Complior SP device, complying with the methodological recommendations. All participants were evaluated by the same clinician.

**Results:** Gender-specific percentile tables, accounting for age, were obtained, as depicted in Figure 1. Mean PWV was  $6.08 \pm 0.90$  m/s, and was higher in boys as compared with girls ( $6.19 \pm 0.90$  m/s versus  $5.91 \pm 0.86$  m/s, respectively;  $p < 0.0001$ ). A significant correlation of PWV with age, BMI, systolic and diastolic BP and family history of hypertension was identified.

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

### HYPERTENSION IN HIGH SCHOOL STUDENTS: GENETIC AND ENVIRONMENTAL FACTORS (HYGEF STUDY)

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**Objective:** To evaluate the impact of gene pathways (ADDs, Endogenous Ouabain genetic polymorphisms) in the transition from normotension to hypertension HT

we perform a large epidemiological study in 3 regions of Italy (Milan, Mi, Lombardy, Livorno, Li, Tuscany, and Grottaglie, Gt, Puglia) among young (age < 18) high school students.

**Design and method:** During two consecutive medical visits, we collected the anthropometric data and blood pressure values and a spot urine, saliva sample was taken for the DNA study.

**Results:** Preliminary results obtained on 2,635 boys (f 1,501, m 1,134, age  $16.80 \pm 1.83$  years) show a regional difference both for estimated urinary Na<sup>+</sup> (Li  $171.5 \pm 2.1$ , Mi  $178.7 \pm 2.8$ , Pt.  $196.4 \pm 2.5$  mEq/24 h,  $p < 0.001$ ), although SBP values were higher in Tuscany (Li  $121.1 \pm 0.36$ , vs Mi  $118.9 \pm 0.4$ , Gt  $118.4 \pm 0.41$  mmHg). SBP throughout the sample was significantly correlated with BMI ( $r = 0.324$ ,  $p < 0.0001$ ), and with Ur.Na<sup>+</sup> ( $r = 0.138$ ,  $p < 0.0001$ ). In the analysis of the genotypes, removed environmental factors, the Lanosterol Synthase (LSS) polymorphism, the enzyme involved in the synthesis of Endogenous Ouabain (EO) and cholesterol, was associated with increased DBP values (LSS AA  $69.2 \pm 0.67$ , LSS AC  $68.3 \pm 0.32$ , LSS CC  $66.7 \pm 0.3$  mmHg,  $p < 0.0001$ ). Carriers of both mutated variants of ADD1 and ADD2 (ADD1GT/ADD2 CT,  $n = 167$ ) showed greater ( $p = 0.015$ ) urinary excretion ( $192.9 \pm 4.26$  mEq/24 h) than subjects with genetic variants ADD1 GG/ADD2 CC ( $n = 826$ ) ( $185.2 \pm 1.9$  mEq/24 h). The Na/K urinary ratio was increased in the boys carrying LSS AA/CYP1A1 CC  $4.04 \pm 0.41$  vs. LSS GG/CYP1A1 AA  $3.19 \pm 0.35$  mEq/L, suggesting an interaction between EO and aldosterone.

**Conclusions:** The results obtained in this young population confirm the role of the Adducin-EO genetic network and allow to identify interactions between environmental factors (different eating habits) and the genetic polymorphisms linked to hypertension. RF-funded study: PE-2011-02346988

### PERFORMANCE OF 4 DEFINITIONS OF CHILDHOOD ELEVATED BLOOD PRESSURE IN PREDICTING SUBCLINICAL CARDIOVASCULAR OUTCOMES IN ADULTHOOD

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**Objective:** Childhood elevated blood pressure (BP) is a public health problem worldwide. Subclinical cardiovascular disease (CVD) may already be present in children with elevated BP. Children with elevated BP were likely to have hypertension as adults, and childhood elevated BP was associated with increased risk of early onset subclinical CVD in adulthood. Therefore, accurate early identification of children with elevated BP is the central aspect in the primordial prevention of CVD. In adults, the definition of hypertension is based mainly on the association of BP levels with adverse cardiovascular outcomes. However, there is no evidence relating childhood BP levels to cardiovascular outcomes. Given that the upper limits of BP ranges in children were not ideal, the BP percentiles, rather than absolute levels, were used to define childhood elevated BP. As a result, the definition of childhood elevated BP was based on the BP distribution and, to some extent, arbitrary.

We aimed to compare the ability of the pediatric BP standards issued by the US Fourth Report, the recently proposed US, Chinese, and international standards to predict adult hypertension and subclinical cardiovascular disease (CVD).

**Design and method:** 2296 children were randomly selected from Beijing at baseline. The follow-up survey was conducted among 1177 adults. Subclinical adult CVD was assessed using the carotid-femoral pulse wave velocity (cf-PWV), carotid intima-media thickness (CIMT), and left ventricular mass index (LVMI).

**Results:** The prevalence of pediatric elevated BP was significantly higher according to the Chinese standards vs the Fourth Report, the updated US standards, and the international standards (18.7% vs 14.2%, 17.5%, and 18.0%, respectively; all  $P$ s < .001). Children identified as elevated BP using any of the 4 standards were more likely to have adult hypertension, high cfPWV, and high LVMI than children without elevated BP. However, only the Chinese and updated US standards can predict the increased risk of adult high CIMT.

**Conclusions:** Our results indicated that the Chinese standards performed equally or better compared with 3 other standards in predicting adult hypertension and subclinical CVD.



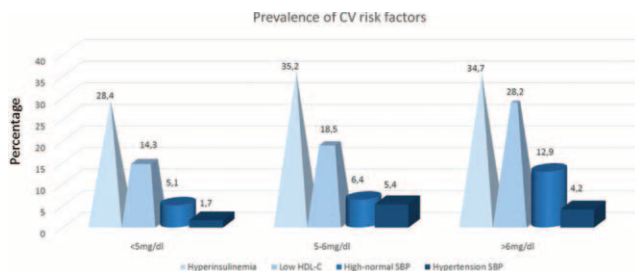
## URIC ACID IS ASSOCIATED WITH CARDIOMETABOLIC RISK FACTORS IN OVERWEIGHT AND OBESE CHILDREN AND ADOLESCENTS

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**Objective:** This study examined the association of serum uric acid (UA) with levels of cardiometabolic risk factors in overweight and moderate obese children and adolescents.

**Design and method:** Three hundred and thirty three Caucasians of both sexes (149 females), of European origin, from 5 to 18 years of age (mean age 11.4 ± 2.6) were included. Overweight and obesity were defined based on the extended international body mass index cut-offs. The subjects were divided into 3 groups according to serum UA: < 5 mg/dl n = 118 subjects (35%); UA 5–6 mg/dl n = 130 subjects (39%) or UA > 6 mg/dl n = 85 subjects (26%). Fasting blood was obtained and uric acid, glucose, insulin, and lipid profile, were measured. Likewise office BP and 24-hour ABPM were assessed. Hyperinsulinemia was defined from norms for pubertal stage. Abnormal fasting lipids were defined from normative data (Daniels et al, 2008). Subjects were qualified as normotensive, high-normal or hypertensive according to the ESH criteria (Lurbe et al, 2016).

**Results:** There were significant differences among groups regarding, BMI, waist, fasting insulin, office SBP and night-time SBP increasing progressively across the serum UA groups. Controlling by age and sex, uric acid was significantly correlated with BMI ( $r = 0.27$ ,  $p = 0.000$ ), waist ( $r = 0.33$ ;  $p = 0.000$ ), birth weight ( $r = -0.11$ ;  $p = 0.05$ ), office SBP ( $r = 0.21$ ;  $p = 0.000$ ), daytime SBP ( $r = 0.16$ ;  $p = 0.03$ ), nighttime SBP ( $r = 0.24$ ;  $p = 0.000$ ), insulin ( $r = 0.25$ ;  $p = 0.000$ ), and Log Triglycerides ( $r = -0.137$ ;  $p = 0.019$ ). In a multiple regression analysis sex, waist, birth weight, SBP (office, daytime and nighttime), were independent determinants of uric acid when age, BMI, HDL-C and insulin were included ( $R^2 = 0.29$ ). The prevalence of hyperinsulinemia, low HDL-C, high-normal BP, and hypertension in each UA group are shown in the Figure.



**Conclusions:** In overweight and moderate obese children and adolescents there is a trend toward greater prevalence of cardiometabolic risk factors as the uric acid values rose. The role of hyperuricemia and its association with cardiometabolic risk factors should receive more attention, beginning in early childhood.

## EFFECTS OF MODERATE INTERVAL TRAINING ON MEASURES OF HEART RATE VARIABILITY, PULSE WAVE VELOCITY AND SYSTOLIC BLOOD PRESSURE IN ELEMENTARY SCHOOL CHILDREN

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**Objective:** Assessment of heart rate variability (HRV) is increasingly used to evaluate dynamic features of cardiovascular (cv) control mechanisms and offers unique insight into autonomic cv modulation in health and disease outcomes. Regular exercise is known to positively influence hemodynamics and various cv risk factors. The present study aimed to evaluate the efficacy of a nine-month moderate interval-training program on HRV, pulse wave velocity (PWV) and systolic blood pressure in elementary school children.

**Design and method:** 68 students ( $8.6 \pm 0.5$  years, 49% girls, BMI  $17.9 \pm 2.5$  kg/m<sup>2</sup>), were randomized into intervention (IG) (n = 34) and control (CG) (n = 34) group. Both IG and CG had regular physical education classes (PE) (3 × 45 min/week). During a nine-month intervention period, the IG received an additional exercise intervention program (2 × 45 min/week). This evaluated exercise program was carried out by trained instructors and comprised an “intense joyful-movement” program equivalent to a moderate interval training. Measures of HRV, PWV, and systolic blood pressure were obtained before and after the intervention program.

**Results:** IG showed positive modifications of HRV, PWV and systolic blood pressure. After the intervention, HF-Power increased from  $35.0 \pm 2.1\%$  to  $42.6 \pm 2.37\%$  ( $p < 0.001$ ), and the Low-Power decreased from  $48.4 \pm 1.6\%$  to  $44.7 \pm 1.8\%$  ( $p = 0.025$ ) in the IG. In the IG and CG the HF-Power ( $p < 0.001$ ) and LF-Power ( $p = 0.003$ ) evolved differently during the intervention period. The LF/HF ratio change was different in both groups ( $p < 0.020$ ). The IG showed a reduction of the mean value from  $1.6 \pm 0.2\%$  to  $1.3 \pm 0.1\%$ , while the LF/HF-ratio of the CG increased from  $1.2 \pm 0.1\%$  to  $1.5 \pm 0.2\%$ . The PWV decreased from  $4.80$  m/s to  $4.56$  m/s in the IG, while the PWV in the CG increased from  $4.56$  m/s to  $4.66$  m/s ( $p < 0.001$ ). The peripheral ( $p < 0.001$ ) and central ( $p = 0.052$ ) systolic blood pressure also evolved in favor of the IG.

**Conclusions:** Among elementary school children additional moderate intensity interval-training program had favorable effects on hemodynamic parameters and on measures of cardiac autonomic control due to increasing cardiac vagal activity. Exercise time should be increased as early as possible to positively influence cardiac autonomic function and potentially reduce cardiovascular morbidity in later life.

## RELATION BETWEEN DIETARY HABITS AND ANTHROPOMETRIC AND VASCULAR PARAMETERS IN CHILDREN ATTENDING THE PRIMARY SCHOOL

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**Objective:** Since childhood, unhealthy dietary habits could trigger the onset of cardiovascular risk factors, such as obesity and hypertension. Aim of this school-based study was to identify the possible relation between dietary patterns, physical activity and anthropometric, hemodynamic (blood pressure, BP; pulse wave velocity, PWV) and gluco-lipid parameters.

**Design and method:** A validated Food Frequency Questionnaire (FFQ) and a validated questionnaire assessing the degree of physical activity (PAQ-C) were administered to children attending the 3rd and 4th class of 4 primary schools. Children responded with the aid of their parents and a dedicated dietitian. From FFQ, composed by 15 categories for a total of 61 foods, nutritional content in term of energy and macro-nutrients intake was extrapolated. Also dietary patterns obtained by Principal Component Analysis (PCA) were identified. Metabolic Equivalent of Task (MET) were computed for each child from IPAQ.

**Results:** Three hundred and nine children between 8 and 11 years participated (74.8% response rate) of whose 302 (97.7%) children compiled the FFQ. Significant correlations were found between: “junk food” intake and BMI ( $r_s = 0.141$ ,  $p < 0.05$ ), diastolic BP ( $r_s = 0.114$ ,  $p < 0.05$ ); PWV ( $r_s = 0.155$ ,  $p < 0.001$ ), triglycerides ( $r_s = 0.150$ ,  $p < 0.05$ ); meat intake and diastolic BP ( $r_s = 0.124$ ,  $p < 0.05$ ); vegetables intake and Z-score of diastolic BP ( $r_s = -0.115$ ,  $p < 0.05$ ); “animal fats” intake and cholesterol ( $r_s = 0.165$ ,  $p < 0.05$ ). PCA identifies three dietary patterns: one characterized by junk food, meat, sweet, cereals and tubers; one composed by fruits, vegetables and fish and legumes and one characterized by eggs. No significant correlation was found between physical activity and the analyzed parameters.

**Conclusions:** The significant correlation between some categories of food and anthropometric, vascular and gluco-lipid parameters in 8–11y children suggests that it is important to begin early with policies to prevent the onset of overt cardiovascular risk factors.

## DETERMINANTS OF AORTIC PULSE WAVE VELOCITY IN PORTUGUESE CHILDREN AND ADOLESCENTS – AN UPDATE OF THE PORTUGUESE VASCULAR PHENOTYPE IN CHILDREN AND ADOLESCENTS (PORT-VASPH) COHORT

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**Objective:** The PORT-VASPh Cohort was designed to contribute to a better understanding of vascular function in children and adolescents, mostly focusing PWV and other complementary aspects of arterial hemodynamics. This analysis is aimed at identifying the main determinants of PWV in this population.

Table 1. Multivariable Linear Regression

	PWV (m/s)		
	$\beta$	IC 95%	p
Age	0.196	0.177-0.216	<0.001
Gender	-0.098	-0.194-0.002	0.046
MBP (mmHg)	0.009	0.006-0.013	<0.001
BMI (Kg/m <sup>2</sup> )	0.013	0.004-0.031	0.128
Family history of CVD	0.326	0.156-0.496	<0.001

**Design and method:** The PORT-VASPh cohort is a prospective and observational study, with 953 children and adolescents enrolled, 40% females, age ranging from 5 to 17 years (mean age:  $12.08 \pm 2.92$  years), mean body mass index

(BMI) of  $18.96 \pm 3.26$  kg/m<sup>2</sup>. The overall health profile for each participant was defined based on three clinical evaluations, in which blood pressure (BP) was measured under standard conditions over the brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. Carotid-femoral PWV was measured to all participants at the third clinical evaluation, with the Complior SP device, complying with the methodological recommendations. All participants were evaluated by the same experienced clinician.

**Results:** Mean PWV was  $6.20 \pm 0.95$  m/s, and was higher in males compared with females ( $6.31 \pm 0.97$  m/s versus  $6.02 \pm 0.89$ , respectively;  $p < 0.0001$ ). PWV was also significantly higher in hypertensives (Ht), in overweight participants and in those with a family history of cardiovascular disease. The determinants of PWV were assessed through linear regression. In a univariable analysis, age, gender, BMI, mean blood pressure (MBP), and family history of cardiovascular disease (CVD) were significantly associated with PWV. In a multivariable model, BMI lost its association with PWV. All the remaining variables maintained a significant association with PWV, as depicted in table 1.

**Conclusions:** In children and adolescents, aortic PWV is strongly influenced by age, gender, BP and genetics, in line with the available evidences in adult populations. Further studies are needed towards a thorough understanding of the arterial dynamics at these ages.

# ORAL SESSION

## ORAL SESSION 3B:

## EXPERIMENTAL HYPERTENSION AND PHARMACOLOGY

### G PROTEIN-COUPLED ESTROGEN RECEPTORS: NOVEL THERAPEUTIC TARGETS IN ALDOSTERONE/SALT-INDUCED HYPERTENSION?

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**Objective:** Some effects of aldosterone may be modulated by the G protein-coupled estrogen receptor 1 (GPER). Furthermore, the GPER agonist, G-1, can exert T cell-mediated anti-inflammatory actions, acutely lower blood pressure (BP), and reduce post-stroke infarct injury.

**Design and method:** Here we tested in mice the effects of G-1 (0.03 mg/kg/d s.c.) and G-15 (GPER antagonist; 0.3 mg/kg/d s.c.) on BP (using tail-cuff plethysmography) over 14 d in two models of hypertension: 1) aldosterone/salt (0.72 mg/kg/d s.c. + 0.9 % NaCl for drinking) and 2) angiotensin II (0.7 mg/kg/d s.c.); and also assessed sex differences, and the role of lymphocytes and endogenous estrogen (in ovariectomised females) in those effects. All groups were  $n = 8$ .

**Results:** In male C57Bl6 mice, the aldosterone/salt-induced increase in BP (~25 mmHg) was attenuated by ~50 % with co-administration of G-1 ( $P < 0.05$ ). G-15 did not alter aldosterone/salt-induced hypertension in male C57Bl6 but prevented the anti-hypertensive effect of G-1. Moreover, whereas aldosterone/salt alone had no effect on BP in female C57Bl6 mice for  $> 7$  d, co-administration of G-15 with aldosterone/salt resulted in a prompt increase of ~20 mmHg by d 7 ( $P < 0.05$ ). In contrast, ovariectomised females resembled males in their BP profile in response to aldosterone/salt. There was virtually no effect of aldosterone/salt on BP in either male or female RAG1-deficient (RAG KO) mice, but this could be rescued by adoptive transfer of T cells from C57Bl6 into RAG KO ( $P < 0.05$ ). Neither G-1 nor G-15 had any effect on angiotensin II-induced hypertension in male C57Bl6 mice. T cells, as well as B cells, macrophages and neutrophils in spleen and kidneys were found to have high expression of GPER.

**Conclusions:** The findings suggest that aldosterone/salt-induced hypertension is strictly T lymphocyte-dependent and is markedly suppressed by GPER activation on these cells by endogenous estrogen or by administration of G-1.

### ACUTE AND CHRONIC EFFECTS OF CHIOS MASTIC GUM ON BLOOD PRESSURE IN A RODENT MODEL OF 2-KIDNEY 1-CLIP HYPERTENSION

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**Objective:** Chios mastic gum (CMG), a Greek plant resin, has been studied for its protective role against endothelial and vascular inflammation by suppressing oxidative stress and downregulating the expression of pro-inflammatory mediators. We sought to investigate the effect of CMG administration on blood pressure (BP) and hypertension-induced target organ damage.

**Design and method:** 16-week-old male Wistar rats were allocated into 3 groups: Control group; 2-kidney, 1-clip (2K1C) group; CMG group which was treated with CMG (40 mg/kg body weight /day) for 2-weeks after the establishment of hypertension.

**Results:** Acute CMG administration led to a decrease in systolic, diastolic and mean arterial BP (153 vs 188 mmHg, 108 vs 141 mmHg and 122 vs 156 mmHg for CMG and 2K1C groups, respectively), while these hemodynamic effects were sustained throughout the 2-week administration period (136 vs 194 mmHg, 100 vs 141 mmHg and 112 vs 159 mmHg for CMG and 2K1C groups, respectively). CMG also attenuated target organ damage as proposed by amelioration of biomechanical properties of the aorta –including cross-sectional area (CSA), aortic

wall stiffness and thickness–, reversal of myocardial small vessel hypertrophy and maintenance of serum albumin levels. Furthermore, CMG administration was associated with decreased interleukin-6 (IL-6) and C-reactive protein (CRP) levels. The BP lowering effects of CMG are likely to be mediated by the decrease in renin serum levels. Regression analysis showed that the amelioration of organ damage was BP-lowering dependent and was not correlated with direct effects of renin or with its anti-inflammatory properties.

**Conclusions:** Our results indicate an anti-hypertensive effect of CMG via down-regulation of renin excretion and suppression of the inflammatory cascade associated with alleviation of target organ damage. These observations provide substantial evidence for the potentially beneficial role of CMG in treating hypertension, yet clinical translation studies are further required.

### UNILATERAL OCCLUSION OF THE CAROTID ARTERY MAY BE AN INDEPENDENT PATHOGENETIC MECHANISM OF PULMONARY HYPERTENSION

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**Objective:** To determine changes in NO-mediated dilatation of pulmonary arteries (PA) and contribution of soluble guanylate cyclase (sGC) -dependent and -independent mechanisms and to evaluate morphological characteristics of PA in rats with unilateral carotid bodies ischemia.

**Design and method:** Ligations of left common carotid artery (CCA) or external carotid artery (ECA) were performed on white rats to stop the blood flow in carotid bodies. A month later, inhibition of NO-mediated dilatation of isolated PA was evaluated using sGC blocker (ODQ) and K<sup>+</sup>-channels antagonists (glibenclamide for K<sup>+</sup>ATP channels and tetraethylammonium (TEA) for K<sup>+</sup>v-channels). Sodium nitroprusside (SNP) was used as a donor of NO. Phosphodiesterase V blocker (Zaprinast) was used for evaluation of sGC-dependent vasodilation. Morphological characteristics of small PA, relative mass of right ventricle (RV) and systolic pressure (SBP) in RV were evaluated.

**Results:** ODQ blocked dilatation in rats with unilateral ischemia of the carotid body more effectively than in control group ( $p < 0.05$ ). There was no difference in PA relaxation in response to Zaprinast between the experimental and the control groups. TEA reduced PA relaxation with SNP at concentrations from 10–9 to 10–7 M in the control group and at concentrations from 10–10 to 10–8 M in the experimental group ( $p < 0.05$ ). Glibenclamide significantly inhibited relaxation in the control group but it had no effect on NO-mediated dilatation in the experimental group. There were structural changes in PA of the rats with unilateral ligation of CCA or ECA: area of the media increased by 20% and 50% respectively ( $p < 0.05$ ). The number of layers of smooth muscle and relative mass of RV did not change, but SBP in RV increased by 19.5% ( $p < 0.05$ ).

**Conclusions:** We suspect a mechanism associated with carotid bodies which can be a sufficient stimulus for pulmonary hypertension development. Moderate hypertrophy of PA was found in experimental groups, so this did not reflect on the mass of RV but increased SBP in RV. Hypertrophy of PA increased the contribution of sGC. This may be the result of the decreased contribution of independent from sGC mechanism which is the direct activation of K<sup>+</sup>-channels by NO.

### GLOBAL DELETION OF MICRORNA-181A RESULTS IN ELEVATED BLOOD PRESSURE IN MICE

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**Objective:** MicroRNA-181a (miR-181a) is down-regulated in both human hypertensive subjects and genetically hypertensive mice (BPH/2J). We have previously shown miR-181a can bind to and regulate renin mRNA levels. Therefore, it is proposed that miR-181a may exert post-transcriptional control over the renin-angiotensin system via up-regulation of renin expression, thus increasing blood pressure (BP).

**Aims:** To determine the role of the miR-181a1 gene in BP regulation and renin expression in CRISPR/Cas9 miR-181a-1 knock out (KO) mice.



**Design and method:** Twelve-week-old wild-type (WT, n = 6), BPH/2J (n = 6) and miR-181a1 heterozygous (n = 6) and homozygous (n = 8) KO mice were implanted with radio-telemetry probes to measure BP, heart rate and activity. The cardiovascular response to aversive stress, as well as angiotensin-converting enzyme (ACE) inhibition and ganglionic blockade were recorded. Renal renin mRNA and miR-181a expression were assessed using real-time PCR.

**Results:** Mean arterial pressure (MAP) was 8 mmHg higher in homozygous KO compared to WT mice during the active (P < 0.001) but not the inactive period (P = 0.22). Similarly, systolic BP was 7.2 mmHg greater in homozygous KO mice during the active period only (P = 0.02). However, diastolic BP was 13% greater in homozygous KO mice during the active period (mean difference 12.7 mmHg, P < 0.001) and 11% greater during the inactive period (mean difference 8.9 mmHg, P = 0.02), when compared to WT mice. Heterozygous KO mice had similar MAP, systolic and diastolic BP to WT mice (all P = 1.0). WT, homozygous or heterozygous KO mice showed no difference in the pressor response to aversive stress or depressor response to ACE inhibition and ganglionic blockade (active period). Compared to WT mice, miR-181a levels were 12-fold lower in homozygous KO mice (P < 0.001) and this was associated with higher renal renin expression (fold change +2.2, P = 0.06).

**Conclusions:** Homozygous KO mice have elevated BP which appears to be driven primarily by increased diastolic BP. We propose that the elevated BP seen in these mice is due to an increase in renin expression mediated by a lack of regulation by miR-181a. This microRNA may be a target for future therapies to lower BP.

#### OSTEONECTIN AND A DISINTEGRIN AND METALLOPROTEINASE WITH THROMBOSPONDIN TYPE 1 MOTIF (ADAMTS1) INDUCE FIBROSIS IN DEOXYCORTICOSTERONE-SALT HYPERTENSIVE RAT KIDNEY

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**Objective:** Osteonectin (secreted protein acidic and rich in cysteine:SPARC) and a disintegrin and metalloproteinase with thrombospondin type 1 motif (ADAMTS1), both of which regulate various cell function in development and tissue formation, promote collagen deposition in some tissues. We reported a positive correlation between ADAMTS1 and fibrillar collagen deposition in deoxycorticosterone acetate (DOCA)-salt hypertensive rats (ESH2017). This study investigated; 1) the roles of osteonectin and ADAMTS1 in renal fibrosis, and 2) the contribution of renin-angiotensin system in the regulation of osteonectin and ADAMTS1 in DOCA-salt hypertensive rats.

**Design and method:** Uninephrectomized rats (n = 5–6/group) were treated with DOCA (40 mg/kg/week, s.c.) and 1% NaCl (in drinking water) for 0, 1, 2, or 3 weeks with/without losartan (30 mg/kg/day, p.o.). Blood pressure, proteinuria, and plasma creatinine levels were measured. Fibrillar collagens were detected by Masson's trichrome staining. The protein levels of osteopontin, collagen I, TGF- $\beta$ , osteonectin, ADAMTS1, and angiotensin converting enzyme (ACE) were examined by Western blotting. We also measured the ACE and NADPH oxidase activity.

**Results:** Blood pressure showed time-dependent increases from 2 weeks, and the levels of proteinuria and plasma creatinine increased from 2 weeks. Fibrillar collagen deposition occurred from 2 weeks with an additional increase in 3 weeks. The collagen I protein, in particular collagen I with larger molecular weight (140kDa, 210kDa), increased in 3 weeks, while 70kDa Western bands showed no differences among groups, suggesting that post-translational collagen processing, not production, were stimulated in hypertensive rats. The expression of osteopontin, TGF- $\beta$ , and ACE and the activity of ACE and NADPH oxidase were upregulated in accordance with blood pressure elevation. Latent ADAMTS1 increased in 1 week, and active forms increased in 3 weeks, which were decreased by losartan treatment. Osteonectin levels elevated from 1 week and reversed to the control levels at 3 weeks.

**Conclusions:** Osteonectin (SPARC) may induce renal inflammation and fibrosis through ADAMTS1 upregulation in hypertensive rats. Further investigation to show that osteonectin and subsequent ADAMTS1 upregulation is placed in the upstream of fibrosis and downstream of renin-angiotensin system will be needed.

#### PREDICTION OF BLOOD PRESSURE-LOWERING EFFICACY OF ANTIHYPERTENSIVE TREATMENT DEPENDING ON INDIVIDUAL PATIENT CHARACTERISTICS: INITIAL MODEL

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**Objective:** Hypertension is highly prevalent in population, while comorbidity and concomitant medications can result in individual treatment risk and benefit. Evidence from clinical trials comes from limited, "purified" population and therefore can be poorly translated into real-world setting. The main objective of this study was to create a model for prediction of blood pressure response for beta-blockers depending on individual patients characteristics based on a real-world clinical data of hypertensive patients.

**Design and method:** For real-world efficacy data we used 89000 electronic medical records of patients referred to specialized cardiology clinic due to uncontrolled HTN during the period of January 2010 - December 2016. We extracted data on established risk factors, target organ damage and concomitant metabolic (diabetes, obesity) and cardiovascular diseases (coronary artery disease, heart failure) and used them as individual characteristics that may contribute to treatment response. Antihypertensive efficacy of beta-blockers was determined as more than 10 mmHg decrease of blood pressure level on follow-up visit (within 1–3 months from initial visit with prescription, standard dose, stable doses of all other antihypertensives). We adapted the CART (Classification and Regression Tree) algorithm for building effective personalized antihypertensive treatment rules decision tree. We evaluated model predictive power on the validation set using sensitivity and the specificity.

**Results:** According to the model, the most significant patient characteristics that affect the effectiveness of beta-blocker therapy were the level of systolic blood pressure (Gini index = 0.36), age (Gini index = 0.29), body mass index (Gini index = 0.18), family history (Gini index = 0.05), dyslipidemia (index Gini = 0.08), chronic heart failure (Gini index = 0.04). However, the model was characterized by high specificity (0.75) with low sensitivity (0.62). This means a strong ability of constructed decision trees to identify patients with ineffective treatment, however, obtained low sensitivity values mean failure to predict treatment effectiveness.

**Conclusions:** Our initial model confirmed that individual characteristics may predict treatment ineffectiveness of beta-blockers (lower blood pressure, age over 65 and obesity). However improvement of sensitivity of the model is needed for definitive conclusions.

#### INCREASED HEPATOCYTE GROWTH FACTOR IN MONOCROTALINE-INDUCED PULMONARY HYPERTENSION IN RATS

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**Objective:** Right-heart catheterization remains the only reliable diagnostic method of right ventricular damage in pulmonary hypertension (PH) and search for a specific biomarker still continues. The aim of this project is to evaluate the significance of plasma levels of hepatocyte growth factor (HGF) and related mRNA expressions in rat model of PH.

**Design and method:** To induce pulmonary hypertension, 12 weeks old male Wistar rats were subcutaneously injected with monocrotaline (60 mg/kg). They were divided into groups based on experiment duration (1, 2 and 4 weeks) and type of treatment (CON, MCT). Right ventricular pressure was measured in anesthetized rats during catheterisation. Samples of left ventricles (LV), right ventricles (RV), a. pulmonalis, lungs, liver were analysed by RT-qPCR. and plasma by ELISA.

**Results:** MCT-induced PH was characterized by significant progressive increase of right ventricular pressure (2-fold, p < 0.05), breathing frequency (by 40%, p < 0.05) and decrease of oxygen saturation (by 3%, p < 0.05). These were accompanied by increased RV and lungs weights (by 70%, p < 0.05) while weights of other measured organs remained unaffected. In the fourth week after PH induction in MCT group, RV as well as LV mRNA levels of HGF were significantly increased (by 60%, p < 0.05) and significantly reduced in a. pulmonalis, lungs and liver (by 20%, p < 0.05). This was accompanied by an identical pattern of MET receptor expression except for no change in a. pulmonalis and liver. Finally, plasma levels of HGF were significantly elevated (6-fold, p < 0.05) in MCT group when compared to controls after 2 as well as 4 weeks of PH induction.

**Conclusions:** During the progress of pulmonary hypertension, plasma levels of HGF rise and gene expression of HGF is enhanced selectively in heart ventricles. Consequently, the source of elevated levels of plasma HGF originates from the heart and therefore can present a potential specific biomarker of PH.

#### RENAL SYMPATHETIC NERVES AND INFLAMMATION IN HYPERTENSION: ASSESSING RENAL INFLAMMATION RESPONSE TO RENAL DENERVATION BY URINARY CYTOKINE EXCRETION IN DEOXYCORTICOSTERONE-SALT RAT

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**Objective:** Renal denervation (RDN) may be an effective treatment for hypertension; however, the mechanisms remain unknown. RDN mitigates hypertension in addition to the concomitant renal inflammation in the deoxycorticosterone (DOCA)-salt rat model. Renal inflammation is hypothesized to drive the hypertension, but the timing and relationship to mean arterial pressure (MAP) remain elusive. We aimed to elucidate the temporal inflammatory and MAP response to DOCA-salt through urinary cytokine excretion, and test its responsiveness to renal denervation. We hypothesized that (a) RDN would mitigate renal and urinary cytokine content, and (b) a decrease urinary cytokine would precede changes in MAP.

**Design and method:** 12 uninephrectomized male Sprague Dawley rats (300–325 g) received either surgical renal denervation (RDN; n = 6) or sham (Sham; n = 6). One week following, rats were administered DOCA (100 mg) and 0.9% saline for 21 days. Urine samples were collected weekly. Urinary and renal tissue cytokines (IL-1b, IL-2, IL-6, GRO/KC, MCP-1) were measured by multiplex assay. Temporal data analyzed by two-way ANOVA with Bonferroni post-hoc test ( $\alpha = 0.05$ ). All other data were analyzed by Student's t-test. Data presented as mean  $\pm$  SEM.

**Results:** MAP response to DOCA-salt was attenuated ( $*p < .05$ ) by RDN vs. Sham, where MAP significantly diverged at Days 14–21 (see Table). Similarly, all measured renal cytokines were markedly reduced ( $*p < .05$ ) in RDN vs. Sham - a reduction of 42–70% of Sham values (see Table). Urinary cytokine excretion on day 21 mirrored this effect, where each cytokine was lower ( $*p < .05$ ) in RDN vs. Sham – reduced by 44–84% Sham values (see Table). No difference was detected

between RDN and Sham urinary cytokine content on Days 0–7, and only urinary IL-1b and IL-2 were reduced ( $*p < .05$ ) at Day 14.

**Temporal MAP and Inflammatory Cytokine Responses (Renal, Urinary) to RDN**

Protocol Day	Sham	RDx	Sham	RDx	Sham	RDx	Sham	RDx
Treatment	Day 0	Day 7	Day 14	Day 21				
MAP (mmHg)	105 $\pm$ 2	96 $\pm$ 4	128 $\pm$ 5	124 $\pm$ 6	157 $\pm$ 4	*127 $\pm$ 8	166 $\pm$ 5	*136 $\pm$ 8
Urinary Content (pg/mg creatinine)	IL-1 $\beta$	78 $\pm$ 49	112 $\pm$ 40	152 $\pm$ 26	322 $\pm$ 120	631 $\pm$ 181	*277 $\pm$ 66	948 $\pm$ 258
	IL-2	100 $\pm$ 69	111 $\pm$ 39	134 $\pm$ 25	316 $\pm$ 124	611 $\pm$ 188	*296 $\pm$ 56	959 $\pm$ 122
	IL-6	856 $\pm$ 552	1044 $\pm$ 357	1304 $\pm$ 244	3171 $\pm$ 1076	4383 $\pm$ 1237	2671 $\pm$ 493	6423 $\pm$ 1405
	MCP-1	86 $\pm$ 52	96 $\pm$ 31	152 $\pm$ 33	249 $\pm$ 77	342 $\pm$ 93	319 $\pm$ 65	547 $\pm$ 124
	GRO/KC	47 $\pm$ 33	20 $\pm$ 2	32 $\pm$ 6	69 $\pm$ 18	98 $\pm$ 28	62 $\pm$ 9	205 $\pm$ 33
Renal Content (pg/mg protein)	IL-1 $\beta$	-	-	-	-	-	-	66 $\pm$ 3
	IL-2	-	-	-	-	-	-	9 $\pm$ 1
	IL-6	-	-	-	-	-	-	225 $\pm$ 18
	MCP-1	-	-	-	-	-	-	34 $\pm$ 4
	GRO/KC	-	-	-	-	-	-	20 $\pm$ 3

Data Presented as Mean $\pm$ SEM; n=6/group; \*p<.05 vs. time-matched Sham

**Conclusions:** In conclusion, these data support our hypothesis that urinary cytokines reflect renal inflammatory cytokine content, and both are abated by RDN. However, our second hypothesis was not supported, as differences in MAP appeared prior to a significant reduction of most urinary cytokines. With these findings, we hypothesize that hypertension may precede renal inflammation in this model. Further studies are necessary to elucidate the driving force for renal inflammation in this model.

# ORAL SESSION

## ORAL SESSION 3C:

## RESISTANT HYPERTENSION

### COST-EFFECTIVENESS OF RENAL DENERVATION THERAPY FOR TREATMENT RESISTANT HYPERTENSION: A BEST CASE SCENARIO

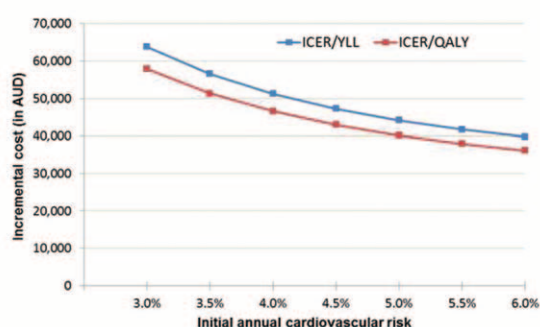
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**Objective:** In light of the current debate regarding the role of renal denervation (RDN) for the management of treatment-resistant hypertension (TRH), to determine the thresholds for cardiovascular risk and costs of RDN which would make the strategy cost-effective.

**Design and method:** A Markov model was constructed to simulate the onset of cardiovascular disease and death among a hypothetical cohort of 1000 TRH patients aged <65 years who either received standard treatment of care (SoC) or RDN plus SoC. The time horizon was 20 years. The effectiveness and cost-effectiveness of RDN were estimated relative to current SoC using decision analysis from the Australian public healthcare system perspective. The effect on lowering office blood pressure due to RDN was based on results observed in SIMPLICITY HTN-3 trial, and the expected subsequent change to cardiovascular risk was drawn from a published meta-regression. Cost data were drawn from published sources. An annual discount rate of 5% was applied to both costs and outcomes (years of life and quality-adjusted life-years, QALYs).

**Results:** Over a 20-year time horizon, the model predicted that at the current estimated costs of RDN (AUD 9531/€6573, 1€ = 1.45AUD), it would be cost-effective (incremental cost-effectiveness ratio at or below AUD 50,000 per year of life gained) only if targeted to patients whose absolute annual cardiovascular risk was at least 4.2% initially (approximately 21% over 5 years). With a 4.2% initial cardiovascular risk, the ICERs were AUD 49,519 (~€ 34,151, 1€ = 1.45 AUD) per life-year saved gained and AUD 44,987 (~€ 31,024) per QALY gained. If the costs of RDN were reduced to AUD 9000 and AUD 8500, cost-effectiveness would be achieved at annual risk thresholds of at least 3.8% and 3.5, respectively. Figure 1 showing the RDN effectiveness in terms of ICER value for treating TRH patients with different levels of initial cardiovascular risk.

Figure 1: Incremental cost-effectiveness ratio for RDN therapy compared to standard treatment for different levels of initial cardiovascular risk



**Conclusions:** At current costs and based on currently-observed effects on blood pressure, RDN is cost-effective only among patients at very high absolute cardiovascular risks. This sets parameters for the future health economic evaluation of next-generation RDN strategies currently being evaluated in clinical trials.

### DYNAMICS OF ASYMMETRIC DIMETHYLARGININE AFTER RENAL DENERVATION IN PATIENTS WITH RESISTANT HYPERTENSION

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**Objective:** The recent experimental and clinical studies evidence a potential bi-directional relationship between sympathetic activity and the endogenous circulating NO synthase inhibitor asymmetric dimethylarginine (ADMA). However, the data are controversial. The purpose of our study was to assess the change in ADMA level after renal sympathetic denervation (RSDN) in patients with resistant hypertension (RAH).

**Design and method:** We examined 19 patients (7 males) with verified RAH [mean age – 59 (28–70) years], who underwent the RSDN by standard protocol (Simplicity, Medtronic). ADMA level was measured by immune-enzyme assay (ADMA direct ELISA Kit, Immunodiagnostic AG, Bensheim, Germany, reference values 0.26–0.64 mcml/l) at baseline before the RSDN (the first patient was enrolled in 2013), <sup>6</sup>and 12 months after the operation (the last patient was examined in 2015). Statistical analysis was carried out using the program SPSS 17.0, the data are presented as median (25%;75%).

**Results:** At baseline ADMA was 0.81 (0.3; 1.98) mcml/l. The increased values were found in 1 male and 9 females (chi-square = 1.9; p = 0.2) without any gender differences compared to those with normal ADMA level. ADMA level remained unchanged at 6-month follow-up: 0.83 (0.35; 0.94) mcml/l (p = 0.91). Although it decreased by 12-month follow-up visit – 0.66 (0.23; 0.99) mcml/l, the changes were non-significant (p = 0.6, repeated measures, one-way ANOVA).

**Conclusions:** Half of RAH patients (53%) demonstrate increased ADMA indicating worse prognosis. Renal denervation failed to decrease ADMA level. However, small sample size and a trend toward improvement of endothelial function deserves further investigation in order to understand who may benefit from the RSDN procedure in the very high risk population with resistant hypertension.

### SPYRAL HTN-OFF MED TRIAL: CHANGES IN OFFICE AND AMBULATORY HEART RATE

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**Objective:** Heart rate (HR) is associated with cardiovascular outcomes in hypertensive high-risk vascular patients and heart failure. Recently, the randomized, sham-controlled SPYRAL HTN-OFF MED trial showed reduction of office and ambulatory blood pressure (BP) at 3 months post-renal denervation. The objective of the current analysis is to evaluate the effect of renal denervation on HR in an uncontrolled hypertensive population without medication.

**Design and method:** The SPYRAL HTN-OFF MED trial enrolled uncontrolled hypertensive patients who were drug naïve or removed from their antihypertensive medications. Patients were randomized 1:1 to renal denervation or sham control procedure. BP and HR were measured at baseline and 3 months post-procedure using ambulatory BP monitoring and in the office. For office BP and HR, each data point was an average of 3 measurements. Post-hoc analyses compared changes at 3 months in BP and HR for patients with baseline office HR above and below the median.

**Results:** At 3 months, average office, 24-hour, daytime and night-time HR were significantly reduced in the renal denervation group but not in the sham control group (Table 1). Also, the change in 24-hour HR at 3 months was significantly different between groups. Three-month changes in 24-hour systolic BP, diastolic BP and HR were significantly lower for renal denervation patients with higher baseline HR compared to those with lower baseline HR (Table 2). Similar trends were not seen in the sham control group.

**Conclusions:** In the SPYRAL HTN-OFF MED trial, significant reductions in HR were seen at 3 months in the renal denervation group but not in the sham



control group. Post-hoc analyses suggest patients with higher baseline HR could experience greater reductions in ambulatory HR and BP post-renal denervation.

Table 1: Baseline and 3-month changes in office and ambulatory HR for renal denervation and sham control groups. RDN: renal denervation; HR: heart rate

Parameter (bpm)	Renal denervation			Sham control			RDN vs. Sham p-value
	Baseline	Change at 3 months	p-value	Baseline	Change at 3 months	p-value	
Office HR	71.1 ± 11.0 (N=38)	-2.2 ± 6.0 (N=37)	0.036	73.4 ± 9.8 (N=42)	-1.3 ± 9.0 (N=41)	0.374	0.607
24-hour HR	72.3 ± 10.9 (N=37)	-2.5 ± 5.3 (N=35)	0.009	75.5 ± 11.5 (N=42)	-0.2 ± 4.1 (N=36)	0.825	0.042
Daytime HR	75.7 ± 11.6 (N=37)	-2.4 ± 5.5 (N=35)	0.014	79.1 ± 11.8 (N=42)	-0.4 ± 4.6 (N=36)	0.620	0.094
Night-time HR	66.4 ± 10.7 (N=38)	-2.2 ± 5.6 (N=36)	0.023	69.4 ± 12.2 (N=42)	0.4 ± 6.7 (N=38)	0.696	0.071

Table 2: Comparing patients with baseline office HR above and below the median; changes at 3 months in ambulatory SBP, DBP and HR. HR: heart rate; DBP: diastolic blood pressure; SBP: systolic blood pressure; Heart rate in beats per minute; blood pressure in mmHg

Parameter	Renal denervation			Sham control			P-value
	Baseline office HR < 71.7 bpm (N=21)	Baseline office HR ≥ 71.7 bpm (N=17)	P-value	Baseline office HR < 71.7 bpm (N=18)	Baseline office HR ≥ 71.7 bpm (N=24)	P-value	
24-hour SBP	-2.2 ± 11.3 (n=19)	-9.5 ± 7.5 (n=16)	0.034	-1.1 ± 11.9 (n=16)	-0.0 ± 8.7 (n=20)	0.751	
24-hour DBP	-2.0 ± 6.6 (n=19)	-8.2 ± 4.2 (n=16)	0.003	0.2 ± 6.1 (n=16)	-0.9 ± 4.8 (n=20)	0.542	
24-hour HR	-0.7 ± 4.5 (n=19)	-4.6 ± 5.5 (n=16)	0.027	1.3 ± 4.2 (n=16)	-1.3 ± 3.8 (n=20)	0.061	

## CONFIDENHTTM SYSTEM SAFETY AND PERFORMANCE OF DIAGNOSTIC ELECTRICAL MAPPING OF RENAL NERVES FOR RENAL SYMPATHETIC DENERVATION PROCEDURE

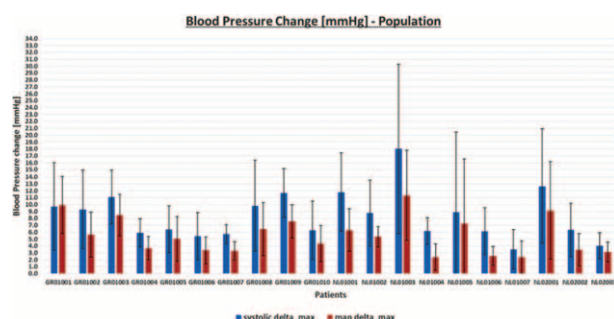
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**Objective:** Renal denervation procedures remains a so-called blind procedure. The objective of the present study is to assess the safety and feasibility of renal nerve stimulation using the ConfidenHTTM mapping system.

**Design and method:** The Confiden(HT) study is a prospective first-in-man multicenter study designed to assess the safety and feasibility of renal nerve mapping using the ConfidenHTÔ system in 20 hypertensive patients with an indication for coronary angiography or with a planned renal sympathetic denervation. The ConfidenHTÔ System consists of two main parts, a catheter and a console. The Console delivers electrical energy to the catheter using a multi-channel stimulator, and a real time intra-arterial Blood Pressure (BP) monitor, which records, analyzes and displays the stimulation outcome (BP and/or HR changes) during stimulation. The ConfidenHTÔ catheter is a non-occluding flexible catheter with expendable multi electrode design, compatible with an 8Fr guiding catheter and 0.014' guide wire, for a wide range of renal artery diameters.

The technology could help to improve RDN procedures by providing: (1) better patient selection of RDN responders and non-responders, and (2) intra-procedural guidance and feedback to optimize technical success rates. The primary performance endpoint was the change in blood pressure during stimulation.

20 patients (58 ± 11.5 years old, 156 ± 23 office systolic BP, 9/11 male/female respectively, and GFR of 78 ± 13 mL/min/1.73 m<sup>2</sup>) have been included. Most of procedures were performed under local anesthesia with mild conscious sedation.



**Results:** The system appeared safe in all 20 cases with no peri-procedural adverse events. Post stimulation there were no signs of angiographically visible spasms/thrombus or dissection in any of the treated arteries. A varying response to electrical stimulation was found among patients with a clear location dependent response along the artery (Hot and Cold spots). The increase in systolic BP and MAP ranged from 0 to 30 mmHg and 0 to 18 mmHg respectively.

**Conclusions:** Results suggest that renal nerve mapping using the ConfidenHTTM system technology is feasible and safe and offers promising diagnostic electrical renal nerve mapping opportunities in hypertensive patients which could help in optimizing the result of renal sympathetic denervation.

## MORE THAN 2-YEARS FOLLOW-UP OF RESISTANT HYPERTENSIVE PATIENTS WITH NEUROVASCULAR DECOMPRESSION OF THE BRAIN STEM ON THE LEFT SIDE

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**Objective:** In the background of resistant hypertension (RHT) the neurovascular pulsatile compression (NVPC) of the left rostral ventrolateral medulla may play a role. In these cases a neurosurgical decompression (NVD) decreased the blood pressure (BP) and the antihypertensive medication became more effective. The aim of this work was to compare BP values recorded at the farthest time from the time of the NVD, up to maximum 31 December 2016.

**Design and method:** Earlier we published first 2-year follow-up data of 9 operated patients. In this work we retrospectively collected these 9 patients data from the clinical center's patient management system. At the time of NVD, the mean age, BMI, and duration of HT, were 43.7 ± 3.0 years, 28.5 ± 1.6 kg/m<sup>2</sup> and 14.2 ± 3.1 years. We analyzed BP values recorded before NVD, and 24 months after NVD, and the last recorded ones.

**Results:** The types of NVPC showed by the MR-angiography were confirmed by the NVD in all patients. The NVDs were performed between 2000 and 2004. The mean follow-up time was 11 years (minimum 3 years, maximum 16 years). Both the systolic and the diastolic BP decreased significantly in all cases after the NVD and at the last record they were significantly lower than before the NVD. Last recorded BP values compared to the 24-month data also were lower (148/96 mm Hg vs. 135/81 mm Hg). In 5 cases the number of antihypertensives increased and the mean number of combinations was higher compared to 24-month data (5.7 vs. 6.7).

**Conclusions:** These results confirmed our previous opinion that in severe hypertension not responding to conventional therapy the NVD of the left side NVPC could guarantee a long-lasting BP reduction. Of course it could be not a direct effect of NVD but it may increase the sensitiveness for antihypertensive medication.

## EFFECTS OF DISTAL RENAL DENERVATION VERSUS CONVENTIONAL INTERVENTION ON THE HEART IN PATIENTS WITH RESISTANT HYPERTENSION

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**Objective:** The aim of this study was to evaluate of state the heart after distal renal denervation (DRD) in segmental branches of renal artery versus conventional main trunk therapy: 12 month study in patients with resistant hypertension (RH).

**Design and method:** All participants of research have given the informed agreement. This was a double-blind, randomized prospective study (NCT01499810) in 55 patients meeting criteria of true RH. Patients were randomized either to endovascular "conventional" renal denervation (CRD) of the main renal artery (n = 27) or to distal (D) treatment applied in segmental branches after the bifurcation of the main renal artery (n = 28). Echocardiography was making from standards method. It was protocol ASE-convention. Parameters of office BP, IVS - interventricular septum, PSV - posterior wall of the left ventricle, LA - left atrium, LVM - left ventricular mass, and myocardial stress (MS) were performed at baseline and 12 months follow-up. Statistical analysis: descriptive, t-test independent by groups, t-test dependent samples.

**Results:** Forty six patients completed 12 month follow-up: after CRD (n = 24) and after DRD (n = 22). A significantly greater decreased parameters of 24-hour BP (-11.5 ± 16.3 vs -22.0 ± 20.3 mm Hg, p < 0.05) and the left ventricle of heart: IVS - interventricular septum (-0.21 ± 1.3 vs -1.2 ± 1.8 p < 0.05 mm), PSV - posterior wall of the left ventricle (0.20 ± 1.2 vs -0.86 ± 1.7 p < 0.05 mm), LA - left atrium (0.96 ± 2.8 vs -1.36 ± 9.6 p > 0.05 mm), LVM - left ventricular mass (-4.9 ± 37.4 vs -36.3 ± 34.5 p < 0.05 g), and MS (-1784.0 ± 2294 vs -5133.6 ± 1556.2 p < 0.05 dynes/cm<sup>2</sup>) were performed at baseline and 12 months follow-up.

**Conclusions:** Distal RD treatment applied in segmental branches after the bifurcation of the main renal artery compared with "conventional" renal denervation in the main trunk of the renal artery further reduces myocardial stress, as well as a positive impact on the parameters of the left ventricle, but not the left atrium 12 months after renal denervation in patients with resistant hypertension.

# ORAL SESSION

## ORAL SESSION 3D:

## OBESITY AND METABOLIC SYNDROME

### HIGHER MICRORNA-132 IS ASSOCIATED WITH BLOOD PRESSURE AND LIVER STEATOSIS IN OBESE INDIVIDUALS

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**Objective:** Obesity is associated with numerous comorbidities including cardiovascular disease, diabetes and non-alcoholic fatty liver disease (NAFLD). Obesity pathogenesis is complex and incompletely understood and hence therapeutic options to address the global epidemic of obesity are lacking. In addition, NAFLD is strongly linked to cardiovascular disease. Our recent findings in experimental models have shown that microRNA miR-132 is an important regulator of liver homeostasis. Here, we aimed to assess miR-132 expression in liver and fat tissue of obese individuals and its association with blood pressure and hepatic steatosis.

**Design and method:** Obese individuals undergoing bariatric surgery for weight management (n = 14 females/5 males) comprised the cohort of this study. They were 39 ± 2 years old (mean ± SEM) with a body mass index (BMI) of 42 ± 1 kg/m<sup>2</sup>. Extensive clinical and demographic information was collected for each patient. Supine blood pressure, measured with Omron HEM-907 device, was on average 127 ± 4 mmHg (systolic) and 74 ± 2 mmHg (diastolic) and heart rate 67 ± 24 beats/min. According to Adult Treatment Panel III, the participants had 2.2 ± 0.3 metabolic abnormalities. Quantitative PCR was performed to determine tissue expression of miR-132 in liver and matched subcutaneous and visceral fat biopsies in these patients. Liver biopsies were read by a single hepatopathologist using a standardised pathological approach and graded in terms of steatosis, inflammation and fibrosis.

**Results:** Hepatic and visceral fat expression of miR-132 were strongly correlated (r = 0.729, P = 0.005). Hepatic miR-132 expression was also correlated with BMI (r = 0.641, P = 0.018), triglycerides (r = 0.604, P = 0.029), systolic blood pressure (r = 0.577, P = 0.039) and heart rate (r = 0.694, P = 0.009). Visceral fat miR-132 expression was associated with BMI (r = 0.746, P < 0.001) and liver steatosis (r = 0.533, P = 0.33). There was no correlation between subcutaneous and visceral expression of miR-132 (P = 0.210).

**Conclusions:** Our data supports that miR-132 may play a causal role in the cardiovascular and metabolic implications of obesity in humans. Given the increasing public burden of obesity and associated comorbidities, novel therapeutic approaches are needed for prevention and treatment of these diseases. In addition, further targeted search for biomarkers in complex diseases such as obesity, cardiovascular disease and NAFLD are warranted.

### CARDIOVASCULAR PROGNOSTIC FACTORS IN PREDIABETIC PATIENTS WITHIN A HYPERTENSIVE POPULATION

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**Objective:** Prediabetes is a major risk for development of type 2 diabetes, but it is unclear whether it increases the risk for cardiovascular disease (CVD). Our aim was to determine whether prediabetic patients was a higher risk of CVD than non-prediabetic patients in our hypertensive population.

**Design and method:** We conducted a longitudinal, retrospective research with patients attended at a Hypertension Unit. Prediabetes was defined according to American Diabetes Association (ADA) criteria. Our primary outcome was a composite of non-fatal coronary disease, non-fatal stroke, heart failure and cardiovascular (CV) death. We fitted survival analysis using a Cox proportional hazard regression model to estimate the survival and time-to-event rates in prediabetic patients compared to non-prediabetic ones.

**Results:** We selected 1,652 patients, 713 (43%) with prediabetes (table 1). We encoded 13 cases of coronary disease, 26 strokes, 5 cases of heart failure and 27

CV deaths in the prediabetes cohort, and 16 cases of coronary disease, 18 strokes, 14 cases of heart failure and 14 CV deaths in the non-prediabetic group. The risk of developing a CV event was higher in the prediabetic patients (HR = 1.61, 95% CI 1.01- 2.54, p = 0.04), as shown in Figure 1. In a multivariate Cox survival analysis, age and cystatin C were the most relevant prognostic factors within the potential studied predictors (table 2).

**Conclusions:** Prediabetes was associated with a higher risk of CV event in prediabetic patients than non-prediabetic individuals from our hypertensive population. Cystatin C, along with age, was a major prognostic factor for CV risk, and can be useful in the risk assessment in prediabetic, hypertensive patients.

Table 1. Clinical features of our cohorts

	Prediabetes	Non-prediabetes	Total	P value
Patients	713	939	1652	NA
Age (years)	58.9 (12.3)	51.6 (14.8)	54.7 (14.2)	<0.001
Women (%)	51.7	49.5	50.4	1
BMI	31.7 (5.3)	30.1 (5.3)	30.8 (5.4)	0.93
Systolic BP (mmHg)	141.9 (13.9)	139.3 (13.6)	140.4 (13.8)	0.13
Diastolic BP (mmHg)	79.5 (9.1)	80.7 (8.9)	80.2 (9.0)	0.03
LDL-cholesterol (mg/dl)	136.5 (32.1)	132.8 (31.9)	134.4 (32.0)	0.03
HDL-cholesterol (mg/dl)	64.1 (17.6)	64.6 (17.5)	64.4 (17.5)	0.02
HbA1c (%)	6.1 (0.4)	5.6 (0.3)	5.8 (0.6)	0.2
Albumin/creatinine (mg/g)	15.7 (40.0)	10.7 (23.2)	12.5 (29.2)	< 0.001
Creatinine (mg/dl)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.08
Cystatin C (mg/dl)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.01

Data are shown in absolute values, percentage or median (interquartile range), as appropriate. P-value shows the univariate analyses assessing the relationship between the predictors and the CV outcome in the prediabetic cohort.

Table 2. Survival analysis: multivariate Cox regression for CV event

	HR (CI 95%)	P-value
Age		
Non-prediabetic	1 (reference)	
Prediabetic	1.05 (1.02 - 1.08)	0.0001
Cystatin C		
Non-prediabetic	1 (reference)	
Prediabetic	1.45 (1.27 - 2.82)	0.02

Hazard ratio values (HR) were adjusted for systolic BP, LDL- and HDL-cholesterol, and gender. None of these predictors were statistically significant.

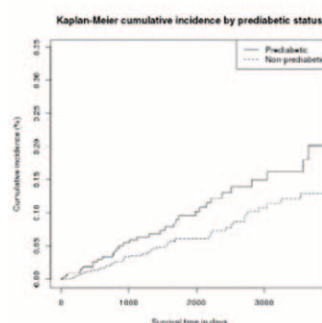


Figure 1. Kaplan-Meier plot showing the cumulative incidence of our prediabetic patients

### AMBULATORY BLOOD PRESSURE PARAMETERS AMONG EXTREMELY OBESE SUBJECTS WITH DIFFERENT STAGES OF FATTY LIVER

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**Objective:** Obesity is one of the main causes of nonalcoholic hepatic steatosis. It is considered that fatty liver in patients with hypertension and without nocturnal dipping of blood pressure is connected with insulin resistance, diastolic heart failure and endothelial dysfunction. The aim of this study was to assess the changes in 24 h ambulatory blood pressure (ABP) mean values and variability to identify predictors of BP values in patients with extreme obesity and different stages of hepatic steatosis

**Design and method:** Subjects were recruited to the study from the patients qualified to bariatric surgery. Body mass index (BMI), waist circumference (WC), hepatic ultrasonography (USG), ABP (Spacelabs 90207) and laboratory investigations were measured. Hepatic steatosis identified by USG was scored using a 0 to 3 scale. Data were analyzed in two groups: I—subjects without or with mild steatosis (USG score:0–1), II—subjects with moderate or severe steatosis (USG score:2–3).

**Results:** Data from 104 patients (mean age  $42.31 \pm 11.15$  years, 41.35% men) were analyzed. Patients in group I ( $n = 47$ ) had lower BMI, WC and liver size values, lower levels of 24 hours and night-time diastolic blood pressure (DBP), day and night-time systolic blood pressure (SBP) and lower SBP short-term blood pressure variability expressed as standard deviation (SD) than group II ( $n = 57$ ). There was no difference in night-time dipping between groups. Levels of glucose, lipids, transaminases, haemoglobin A1C and insulin resistance (HOMA IR) was also lower in group I than II, but hsCRP levels were similar in both groups. Day-time SD SBP positively correlated with BMI ( $r = 0.32$ ) and WC ( $r = 0.34$ ). Similar correlations were observed for day-time SD DBP ( $r = 0.21$ ,  $r = 0.24$ , respectively). Night-time SD SBP positively correlated with WC ( $r = 0.47$ ) and liver size ( $r = 0.54$ ). Positive correlations was observed between 24 h SD SBP and liver size ( $r = 0.26$ ).

**Conclusions:** Besides anthropometric obesity indicators, the liver size may be the clinical predictor of higher blood pressure variability among extremely obese patients.

### VITAMIN D DEFICIENCY AND GLUCOSE METABOLISM IN NON-DIABETIC ESSENTIAL HYPERTENSIVE PATIENTS

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**Objective:** To evaluate the association between 25-hydroxyvitamin D (25OHD) deficiency and glucose metabolism in non-diabetic essential hypertensive (EH) subjects.

**Design and method:** In 180 EH patients (age  $50 \pm 12$  years, 100 males), free of diabetes and cardiovascular events we evaluated clinical variables, fasting and post-oral glucose load (OGTT) levels of glucose and insulin, C-peptide, plasma lipids, serum calcium, PTH, and 25OHD levels, renal function and presence of the metabolic syndrome (MS).

**Results:** Patients with MS had lower 25OHD levels than patients without MS ( $P = 0.015$ ). The 25OHD levels were significantly and directly related to fasting glucose ( $r = 0.172$ ,  $P = 0.021$ ) and HDL-cholesterol ( $r = 0.160$ ,  $P = 0.033$ ) and inversely related to age ( $r = -0.247$ ,  $P = 0.001$ ), systolic blood pressure (SBP) ( $r = -0.147$ ,  $P = 0.020$ ), area under the curve of plasma glucose (G-AUC) ( $r = -0.261$ ,  $P < 0.001$ ) and insulin (I-AUC) ( $r = -0.153$ ,  $P = 0.047$ ), glucose at 120 min of OGTT ( $r = -0.241$ ,  $P = 0.001$ ), triglycerides ( $r = -0.182$ ,  $P = 0.014$ ), and PTH levels ( $r = -0.307$ ,  $P < 0.001$ ).

Subjects with normal 25OHD levels ( $> 30$  nmol/l) had lower SBP, fasting glucose, G-AUC, I-AUC, and PTH levels than patients with 25OHD deficiency ( $< 30$  nmol/l). G-AUC was significantly and directly related to age ( $r = 0.252$ ,  $P = 0.001$ ), body mass index (BMI) ( $r = 0.252$ ,  $P = 0.001$ ), waist-circumference ( $r = 0.383$ ,  $P < 0.001$ ), SBP ( $r = 0.236$ ,  $P = 0.001$ ), alcohol intake ( $r = 0.222$ ,  $P = 0.004$ ), HOMA-index ( $r = 0.001$ ,  $P < 0.001$ ), C-peptide ( $r = 0.254$ ,  $P = 0.001$ ), I-AUC ( $r = 0.266$ ,  $P < 0.001$ ), levels of calcium ( $r = 0.180$ ,  $P = 0.017$ ), PTH ( $r = 0.182$ ,  $P = 0.016$ ), triglycerides ( $r = 0.207$ ,  $P = 0.005$ ), and inversely related to 25OHD ( $r = -0.261$ ,  $P < 0.001$ ) and HDL ( $r = -0.197$ ,  $P = 0.008$ ). Furthermore, G-AUC was higher in men than in women ( $P = 0.013$ ). After correction for age, gender, presence of MS, serum calcium and PTH levels, I-AUC and alcohol intake, G-AUC was independently associated with age ( $B = 0.197$ ,  $P = 0.007$ ), male gender ( $B = 0.162$ ,  $P = 0.026$ ), presence of MS ( $B = 0.337$ ,  $P < 0.001$ ), calcium ( $B = 0.225$ ,  $P = 0.001$ ) and 25OHD ( $B = -0.158$ ,  $P = 0.037$ ) levels.

**Conclusions:** In non-diabetic EH patients low 25OHD levels are related to G-AUC independently of insulin levels. This association could be mediated by the effect of calcium homeostasis on insulin-resistance, given that the modulation of extracellular calcium and calcium flux across cell membranes by 25OHD may affect insulin sensitivity.

### PREVALENCE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH METABOLIC SYNDROME IN THE IBERICAN STUDY

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**Objective:** The general objectives of IBERICAN are to determine the prevalence and incidence of cardiovascular risk factors in Spain, as well as cardiovascular events. The objective of the present work is to analyze the presence of cardiovascular disease in patients with metabolic syndrome (MS)

**Design and method:** IBERICAN is a longitudinal, observational, and multicenter study in which patients from 18 to 85 years of age are included in Primary Care consultations in Spain, until a sample of 7,000 patients is collected, which will be followed for at least 5 years. The basal characteristics of the cut are presented ( $n = 6.007$ ). The Metabolic Syndrome (MS) was defined according to the criteria of the International Diabetes Federation Task Force. Patients were classified in secondary prevention when they presented ischemic heart disease, heart failure, stroke or peripheral arterial disease.

**Results:** The average age of the subjects included was  $57.4 \pm 15.5$  years, and 54.5% were women. 38.2% met MS criteria. Patients with MS were older ( $62.4 \pm 12.9$  years vs.  $54.2 \pm 16.1$  years,  $p < 0.001$ ) and with a lower percentage of women (50.7% vs. 56.8%,  $p < 0.001$ ). The prevalence of cardiovascular disease was higher in patients with MS (21.8% vs 13.1%,  $p < 0.001$ ). Ischemic heart disease (9.8% vs 5.3%,  $p < 0.001$ ), peripheral arterial disease (6.8% vs 3.7%,  $p < 0.001$ ) and heart failure (5.4% vs 1.8%,  $p < 0.001$ ) were more frequent in patients with MS. Stroke (4.7% vs. 3.2%,  $p = 0.267$ ) and retinopathy (0.7% vs. 0.3%,  $p = 0.281$ ) did not reach statistically significant differences

**Conclusions:** cardiovascular disease prevalence is higher in patients with MS, which gives them an extra cardiovascular risk

### BETA3-ADRENOCEPTOR MEDIATED ADIPONECTIN SECRETION IS ESSENTIAL IN MODULATION OF VASCULAR TONE BY PERIVASCULAR ADIPOSE TISSUE

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**Objective:** Healthy perivascular adipose tissue (PVAT) exerts an anti-contractile effect which is vital in regulating blood pressure. Evidence suggests that sympathetic nervous stimulation of PVAT triggers activation of adipocyte beta3-adrenoceptors, and the subsequent release of the vasoactive adipokine adiponectin. In obesity plasma adiponectin is reduced, which may result in a loss of PVAT function and subsequent hypertension. Therefore we examined beta3-adrenoceptor and adiponectin function in the PVAT anti-contractile effect.

**Design and method:** Body weight, blood pressure, and blood glucose were measured in control C57 mice, and adiponectin knockout (Adipo-/-) mice. Following sacrifice, electrical field stimulation (EFS) profiles of isolated C57 and Adipo-/- mesenteric and skeletal muscle resistance arteries ( $< 250$  mm,  $\pm$  PVAT) were characterised using wire myography. Sympathetic denervation of PVAT using 6-hydroxydopamine (6-OHDA) was performed. Beta3-adrenoceptor function was investigated using the agonist CL-316,243 and antagonist SR59203A. The role of the adipokine adiponectin was examined using exogenous adiponectin and a blocking peptide for adiponectin receptor 1 (ABP). The concentration of adiponectin secretion upon EFS was measured using an ELISA kit.

**Results:** Adipo-/- mice exhibit significant elevations in both blood pressure and blood glucose. During EFS of isolated  $\pm$  PVAT arteries, mesenteric and skeletal muscle PVAT from C57 mice elicited an anti-contractile effect, which was absent in the Adipo-/- . Sympathetic denervation of both mesenteric and skeletal muscle PVAT abolished the anti-contractile effect. Inhibition of beta3-adrenoceptors in C57 mesenteric and skeletal muscle PVAT using SR59203A significantly reduced the anti-contractile effect, however activation of beta3-adrenoceptors in Adipo-/- PVAT using CL-316,243 did not restore function. Application of exogenous adiponectin to C57 mesenteric and skeletal muscle -PVAT arteries caused a significant vasodilation. In  $\pm$  PVAT arteries, incubation with ABP significantly reduced the anti-contractile effect. Using an ELISA, adiponectin secretion from PVAT upon EFS was significantly reduced when incubated with SR59203A.

**Conclusions:** These results demonstrate that upon sympathetic stimulation, PVAT from two different vascular beds releases adiponectin via activation of beta3-adrenoceptors, exerting an anti-contractile effect on the blood vessels. In the absence of adiponectin PVAT anti-contractile function is lost, resulting in hypertension and hyperglycaemia, highlighting the importance of adiponectin in vascular function.



# ORAL SESSION

## LATE-BREAKERS: SESSION 1

### DETERMINANTS OF LONG-TERM ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN HYPERTENSIVE PATIENTS – FINDINGS FROM 16-YEAR FOLLOW-UP OF THE ASCOT LEGACY STUDY

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**Objective:** To evaluate the baseline predictors of long-term all-cause- and cardiovascular (CV)-mortality amongst high-risk hypertensive patients, and to develop an integer-based risk score.

**Design and method:** In the Anglo-Scandinavian Cardiovascular Outcomes Trial (ASCOT) legacy study, 8580 UK-based hypertensive patients were followed-up for mortality. All deaths (after the trial closure) were independently adjudicated by a team of 2 physicians.

Cox-proportional hazards models were developed separately for 2 outcomes: all-cause- and CV- mortality using backwards stepwise-selection. All variables were considered for inclusion in the model; but, pre-specified covariates (age, sex, race, socio-economic status [SES], body-mass index [BMI], systolic blood pressure [SBP], total cholesterol, presence of diabetes, smoking history) were included even if statistically insignificant. Continuous variables were categorised if non-linear, or pre-specified based on clinical utility. Goodness-of-fit and C-statistics were calculated.

**Table 1: Baseline determinants of long-term All-cause and CV-related mortality amongst hypertensive patients**

N=7840 (included in model)	All-cause mortality (n=3020)		Cardiovascular mortality (n=1099)	
	Hazard Ratio (95% CI)	P-value	Hazard Ratio (95% CI)	P-value
Age (≥50 years), per 5 years*	1.57 (1.52, 1.62)	<0.001	1.52 (1.45, 1.60)	<0.001
Gender*				
Male, (6432 [81.0%])	1.26 (1.13, 1.40)	<0.001	1.11 (0.94, 1.31)	0.216
Ethnic background*				
White, (7141 [89.9%])	1 (comparator)		1 (comparator)	
Black, (413 [5.2%])	0.81 (0.67, 0.97)	0.082	0.83 (0.62, 1.12)	0.144
Asian, (227 [2.7%])	1.01 (0.78, 1.31)		1.40 (0.96, 2.05)	
Mixed other, (159 [2.0%])	0.82 (0.61, 1.09)		0.84 (0.53, 1.33)	
Socio-economic status (4 levels), per 1 level	0.90 (0.86, 0.94)	<0.001	0.91 (0.84, 0.98)	0.011
BMI (kgm <sup>-2</sup> )*				
20- <25, (1409 [17.8%])	1 (comparator)		1 (comparator)	
<20, (75 [0.9%])	1.79 (1.33, 2.40)	<0.001	1.74 (1.03, 2.96)	0.058
25- <30, (3692 [46.5%])	0.85 (0.78, 0.94)		0.99 (0.84, 1.17)	
30- <35, (2025 [25.5%])	0.97 (0.87, 1.09)		1.14 (0.95, 1.37)	
≥35, (739 [9.3%])	1.02 (0.88, 1.19)		1.20 (0.93, 1.55)	
Current or ex-smoker within 1 year*	1.76 (1.62, 1.92)	<0.001	1.82 (1.58, 2.09)	<0.001
Alcohol units per week#				
1-14, (3762 [47.4%])	1 (comparator)			
15-28, (1334 [16.8%])	0.96 (0.86, 1.07)			
>28, (843 [10.6%])	1.20 (1.06, 1.37)	<0.001		
No-intake, (2001 [25.2%])	1.11 (1.01, 1.21)			
SBP (mmHg), per 10 mm Hg*	1.01 (0.97, 1.04)	0.704	1.03 (0.98, 1.09)	0.278
Pulse Pressure (mmHg)				
<60, (2264 [28.5%])	1 (comparator)		1 (comparator)	
60 - <80, (3745 [47.2%])	1.18 (1.05, 1.32)		1.23 (1.02, 1.48)	
80 - <100, (1565 [19.7%])	1.33 (1.14, 1.55)		1.50 (1.16, 1.94)	
≥100, (366 [4.6%])	1.47 (1.14, 1.90)	0.005	1.54 (1.02, 2.33)	0.022
Heart rate, per 10 beats/minute#	1.06 (1.03, 1.09)	<0.001		
Total cholesterol (per mmol/l)*	0.96 (0.93, 0.99)	0.025	0.99 (0.93, 1.04)	0.656
Diabetes mellitus (Y/N)*	1.07 (0.96, 1.19)	0.225	1.13 (0.95, 1.34)	0.179
Fasting Glucose (≥5.0 mmol L <sup>-1</sup> )	1.07 (1.05, 1.09)	<0.001	1.10 (1.07, 1.14)	<0.001
Creatinine, per 10 μmol L <sup>-1</sup>	1.05 (1.02, 1.07)	<0.001	1.08 (1.05, 1.12)	<0.001
Previous peripheral- / cerebro-vascular event	1.30 (1.19, 1.43)	<0.001	1.44 (1.25, 1.67)	<0.001
Atrial Fibrillation (Y/N)	1.63 (1.31, 2.23)	<0.001	2.07 (1.49, 2.88)	<0.001
Previous aspirin use (Y/N)	1.11 (1.02, 1.21)	0.014	1.27 (1.11, 1.46)	0.001
Major Non - CV Concomitant Disease (Y/N)#	1.10 (1.03, 1.19)	0.008		

\* a-priori covariates forced kept in the model, even if not significant.

#Not found to be significant for CV mortality, and not kept in model (as not a priori)

SBP: systolic blood pressure; CV: cardiovascular; Y/N: Yes/No

**Results:** During median follow-up of 15.7 years, 3282 (38.3%) of 8580 hypertensive patients (mean age at baseline, 64.1 year) died with about a third (n, 1210) from CV-related causes. Figure 1 lists the baseline predictors significantly associated with all-cause- and CV-mortality.

Aside from increasing age and smoking status, increasing baseline levels of fasting plasma glucose and serum creatinine, presence of atrial fibrillation and previous history of peripheral-or cerebrovascular- disease were significant risk factors for 2 outcomes. Notably, increase in pulse pressure (PP) (and not SBP) was an independent risk factor, with 47% and 53% significantly higher risk for all-cause and CV-mortality amongst those with PP ≥ 100 (vs. PP < 60), respectively. BMI and alcohol intake were significantly associated with all-cause-(but not CV-) mortality: BMI < 20 kg/m<sup>2</sup>, and alcohol intake > 28 units/week were associated with 79% and 20% increased risk respectively. Higher SES was associated with a significantly reduced risk for both outcomes.

Both models had an excellent discriminative ability (c-statistics, 0.72 and 0.73, respectively).

**Conclusions:** Our findings suggest that a few baseline determinants in our 2 models are different from those that are routinely used for CV-risk prediction. Particularly, increase in baseline PP (and not SBP) was found to be an independent and better predictor for both all-cause and CV-mortality in this high-risk hypertensive population.

### POPULATION ATTRIBUTABLE RISK FOR CARDIOVASCULAR DISEASE ASSOCIATED WITH HYPERTENSION. RESULTS FROM THE HORTEGA FOLLOW-UP STUDY

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**Objective:** Hypertension (HTN) is the worldwide leading risk factor for cardiovascular morbidity and mortality. As a modifiable risk factor, epidemiological measures derived from cohort studies are important to influence policymakers.

**Objective:** To determine the population attributable risk (PAR) for cardiovascular disease associated with hypertension.

**Design and method:** We included 1244 subjects (mean age 52.3 y, 51% females), who participated in Hortega 13 years Follow-Up Study. HTN was defined as a blood pressure greater than or equal to 140/90 mmHg for systolic and diastolic blood pressure or the use of antihypertensive medication. We used Cox proportional hazard analysis adjusted for traditional CVD risk factors to determine the association of HTN with incident CVD cases. The primary endpoint was incidence of fatal and non-fatal CV events. Due to the presence of confounding factors, the PAR was calculated as  $pd^*(HR-1)/HR$  and 95% confidence interval was calculated using Bonferroni inequality method. Hazard Ratio (HR) estimates and HTN prevalence among cases (pd) were used to calculate sex-specific PARs for heart failure (HF), coronary heart disease (CHD) and stroke.

**Results:** In our population, overall prevalence of hypertension was 34.7% (n = 211) and 34.1% (n = 217) for men and women, respectively. The HR for all CVD and the PAR associated with HTN was 1.89 (95% CI 1.63, 2.18) and 33.1 (95% CI 22.1, 43.8) respectively in men and 1.71 (95% CI 1.4, 2.09) and 33.8 (95% CI 19.4, 47) in women. The HR for CHD plus stroke and PAR associated with HTN was 1.7 (95% CI 1.42, 2.02) and 27.3 (95% CI 14.7, 40.6) in men and 1.91 (95% CI 1.48, 2.46) and 38.3 (95% CI 19.4, 54.6) in women. The HR for HF and PAR associated with HTN was 3.2 (95% CI 2.11, 4.83) and 57.4 (95% CI 31.3, 75) in men and 3.97 (95% CI 2.4, 6.56) and 69.4 (95% CI 41.6, 83.5) in women.

**Conclusions:** In our population, approximately 33% of incident CVD is attributable to hypertension. This study emphasizes the role of hypertension as agent in different cardiovascular diseases, with a burden of up to 70% in women with heart failure.

## DIFFERENCES IN LONG-TERM CHANGES IN CAROTID REMODELING BETWEEN NORMOTENSIVE AND HYPERTENSIVE PERSONS IN A PRIMARY CARE POPULATION

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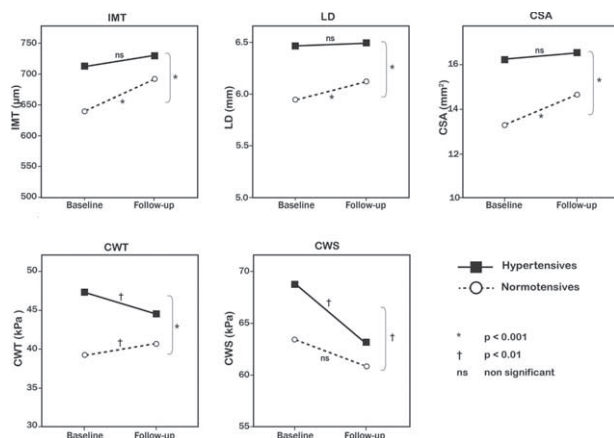
**Objective:** We aimed to prospectively investigate whether there are differences between carotid remodeling between hypertensive and normotensive people over time.

**Design and method:** In a prospective longitudinal cohort study we compared common carotid artery ultrasonography measurements from hypertensive patients with normotensive volunteers from a single general practice. We assessed markers of arterial remodeling intima-media thickness (IMT), lumen diameter (LD), cross-sectional area (CSA), circumferential wall tension (CWT), and circumferential wall stress (CWS), at baseline and after follow-up. We analyzed change in these markers over time as well as differences between both groups, correcting for confounders using GEE-analysis.

**Results:** From a baseline cohort of 174 normotensives and 317 hypertensive participants, a total of 128 normotensives and 94 hypertensives completed follow-up after  $6.1 \pm 1.1$  years. Hypertensives had higher levels of carotid remodeling than normotensives: IMT  $733 \pm 134$  vs.  $649 \pm 130$   $\mu\text{m}$  ( $p < 0.001$ ), LD  $6.5 \pm 0.9$  vs.  $6.0 \pm 0.8$  mm ( $p < 0.001$ ), CSA  $16.7 \pm 4.3$  vs.  $13.7 \pm 3.7$  mm<sup>2</sup> ( $p < 0.001$ ), CWT  $47.2 \pm 8.4$  vs.  $39.8 \pm 7.3$  kPa ( $p < 0.001$ ), and CWS  $67.1 \pm 15.3$  vs.  $63.8 \pm 14.8$  kPa ( $p < 0.01$ ), respectively. Longitudinally, IMT, LD, and CSA did not change in hypertensives, but rose significantly in normotensives (Figure). CWT and CWS fell in hypertensives, whereas in normotensives CWT rose but CWS did not change significantly (Figure).

Normotensives had higher rates of change in IMT (b 9.9  $p < 0.001$ ), LD (b 0.03  $p = 0.044$ ) and CSA (b 0.3  $p < 0.001$ ) but there was no difference in CWS between hypertensives and normotensives. Independent determinants of carotid remodeling were male sex, age, smoking, and pulse pressure. Use of angiotensin receptor blockers was associated with decrease in CWS (b -4.9  $p < 0.05$ ).

**Conclusions:** Established hypertensives have maladaptive carotid remodeling compared to normotensives but arterial dimensions do not change significantly over time. However, in normotensives carotid characteristics change significantly over time. We conclude that although hypertension is associated with maladaptive remodeling the process seems to commence even before overt hypertension is established.



## THE CV PROGNOSIS POWER OF NIGHT SHORT TERM VARIABILITY IN A PORTUGUESE HYPERTENSIVE POPULATION FOLLOWED FOR 12,8 YEARS

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**Objective:** The CV prognosis of short night blood pressure variability is important but still a matter of discussion. It is possible to analyse variability during the

night or in relation to dipping of blood pressure day/night. The authors analysed this subject in an hypertensive population followed during  $12.8 \pm 5.1$  years

**Design and method:** There were  $n = 1200$  ambulatory blood pressure (ABPM) of hypertensive patients (645 women), ageing  $51 \pm 12$  years, BMI  $27 \pm 5$  Kg/m<sup>2</sup>, 53% under antihypertensive medication and without previous CV events. There were 251 CV fatal/non-fatal events (147 strokes, 67 coronary, 37 others CV). We determined the SD of 24 h Systolic blood pressure (SD 24 h SBP), and day and night of SD systolic blood pressure, respectively SD SBPd and SD SBPn. Also the systolic blood pressure dipping the day/night relation calculated has  $100 \times (1 - \text{sleep SBP/awake SBP ratio})$  expressed has a continuous variable. (SBPD)

**Results:** In a multivariate Cox analysis, adjusted to age, gender, OBP, diabetes, BMI, CV therapy, SD SBPn: was predictive of CV events HR 1.29 (IC1.11–1.50), even adjusted to SD SBPd 1.32 (IC 1.05–1.64) and SBPD 1.24 (IC1.05–1.47); for Stroke 1.33 (IC 1.10–1.62) even adusted to SBPD 1.36 (IC 1.10–1.69), Coronary events 1.53 (IC 1.09–2.14), Global mortality 1.30 (IC1.04–1.64).

In a Kaplan Meier curve analysis free of CV events the higher the SD of SBPn the worst survival for CV events (log rank 77.6,  $p < 0.000$ ) Stroke (log rank 94.3,  $p < 0.000$ ) coronary events (log rank 14.4,  $p < 0.05$ ) CV mortality (log rank 67.4,  $p < 0.000$ ), global CV (log rank 78.8,  $p < 0.000$ )

**Conclusions:** n a Portuguese population, the nighttime short term variability of BP was a powerful CV prognosis marker. It is plausible that nighttime BP variability is a more accurate indicator of BP load and of its CV consequences than in relation to dipping of blood pressure day/night.

## IMPORTANCE OF MEAN BLOOD PRESSURE AND BLOOD PRESSURE VARIABILITY FOR THE EFFECT OF VALSARTAN VERSUS AMLODIPINE ON CARDIOVASCULAR EVENTS AND DEATH

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**Objective:** We explored if differences in blood pressure profiles can explain the differences in risks of cardiovascular events and death among patients treated with valsartan or amlodipine in the Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trial.

**Design and method:** The VALUE trial was a randomised, double-masked trial of valsartan versus amlodipine in patients with hypertension. Mean follow-up was 4.2 years. We calculated mean systolic blood pressure as a time-dependent variable and blood pressure variability as the standard deviation (SD) of systolic blood pressure during follow-up in patients with 3 or more visits, and compared blood pressure profiles in the treatment groups. We performed multiple Cox regression analyses to assess the importance of mean blood pressure, blood pressure variability and clinical risk factors for the effects of valsartan versus amlodipine on myocardial infarction, stroke, congestive heart failure, and death.

**Results:** 14,996 patients were eligible for analysis. Mean systolic blood pressure and blood pressure variability was higher in the valsartan group (mean difference 2.2 mm Hg and 1.4 mm Hg,  $p < 0.0001$  and  $p < 0.0001$ , respectively). For myocardial infarction, adjustment for mean blood pressure and blood pressure variability attenuated the risk increase for valsartan towards the null (from HR 1.19 to 1.12), mainly attributable to blood pressure variability. For stroke, adjustment for mean pressure and blood pressure variability both attenuated the risk increase for valsartan (from HR 1.12 to 1.01). For congestive heart failure the risk reduction for valsartan became even more pronounced (from HR 0.89 to 0.77). No clear effect was seen on death (from HR 1.01 to 1.00). The effects were the same if we excluded measurements from the first 6 months.

**Conclusions:** Differences in mean systolic blood pressure and pressure variability during follow-up explained most of the effects of valsartan versus amlodipine on risk of myocardial infarction and stroke. Differences in variability seem to be particularly important for the effect on myocardial infarction. For congestive heart



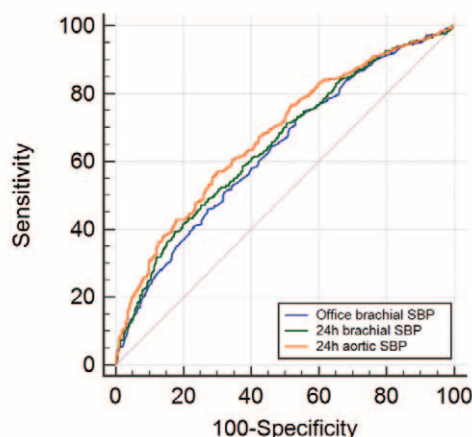
failure, there seems to be a beneficial effect of valsartan versus amlodipine, independent of blood pressure. These data deserve further investigation.

# RELATIONSHIP BETWEEN 24-HOUR AMBULATORY BRACHIAL VERSUS AORTIC SYSTOLIC BLOOD PRESSURE AND LEFT VENTRICULAR MASS. THE INTERNATIONAL 24 HOUR AORTIC BLOOD PRESSURE CONSORTIUM

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**Objective:** There is evidence of a closer relation between 24-hour aortic systolic blood pressure (aSBP) and left ventricular mass (LVM) compared with 24-hour brachial SBP. However, sample sizes are relatively small and there is some inconsistency in findings. We sought to address this by pooling data from 11 centers in Asia and Europe to determine the relationship between LVM and brachial office, as well as brachial and aortic 24-hour ambulatory SBP.

**Design and method:** In all centers, brachial and aortic SBP was measured with the same validated oscillometric device (Mobil-O-Graph, I.E.M. GmbH, Germany), using a transfer function for aortic pressure, and mean/diastolic pressure calibration. LVM was determined by echocardiography.



**Results:** We studied 1299 participants (613 women) with a mean age of 50.8 years. Mean brachial office BP was 139/86 mm Hg, and mean 24-hour bSBP and aSBP was 128 [127.3;128.7] and 131 [130.3;131.7] mm Hg, respectively. Mean LVM indexed to body surface area was 98 g/m<sup>2</sup>, and 34% of participants had left ventricular hypertrophy (LVH). The correlation coefficients between LVM and brachial office SBP, 24-hour bSBP, and 24-hour aSBP were 0.30, 0.35, and 0.42, respectively ( $P < 0.001$  for comparison between brachial office SBP and 24-hour aSBP and  $P = 0.01$  for comparison between 24-hour bSBP and 24-hour aSBP). The areas under the curve for prediction of LVH were 0.634, 0.651, and 0.678 for brachial office SBP, 24-hour bSBP, and 24-hour aSBP, respectively ( $P = 0.004$  for comparison between brachial office SBP and 24 h aSBP, and  $P = 0.001$  for comparison between 24-hour bSBP and 24-hour aSBP) - Figure.

**Conclusions:** In this pooled analysis of international data, we demonstrate that aortic ambulatory 24-hour SBP, measured with an oscillometric cuff, shows a significantly closer association with hypertensive cardiac organ damage (left ventricular mass and hypertrophy) than brachial office/brachial ambulatory systolic blood pressure.

# THE ASSOCIATION BETWEEN BLOOD PRESSURE AND MULTIMORBIDITY IN INCIDENT HYPERTENSION: A COHORT STUDY

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**Objective:** Investigate the trends and association between blood pressure (BP) and a) number of comorbidities, and b) specific comorbidities, in incident hypertension

**Design and method:** We used a random 10% sample of the UK Clinical Practice Research Datalink (CPRD), a population-based general practice dataset covering approximately 7% of the UK population and linked to Hospital Episode Statistics (HES). We identified patients diagnosed with incident hypertension in primary care between 2000 to 2014. We examined 22 comorbidities, classified into six categories: cardiometabolic, respiratory, mental illness, musculoskeletal, cancer, haematological. We used linear regression at annual timepoints up to 10 years after diagnosis of hypertension, to estimate the mean difference in systolic and diastolic BP and 95% confidence intervals (CI). The exposure was number of comorbidities, specific comorbidity and disease category. We adjusted for age, sex, socioeconomic status, ethnicity, antihypertensive medications, year of hypertension diagnosis, cholesterol, body mass index and smoking status.

**Results:** We identified 32,484 patients with incident hypertension. In patients diagnosed with hypertension, systolic blood pressure (SBP) was lower in patients with a higher number of comorbidities, compared to those with only hypertension. At 1 year after hypertension diagnosis, the SBP in patients with one comorbidity was 0.63 (95% CI 0.05 to 1.21) less, and in those with 5 or more comorbidities, was 4.73 (3.39–6.06) less than patients with hypertension alone. This pattern was maintained over time from 1 to 10 years after diagnosis. The greatest difference in SBP was seen in those with cardiometabolic conditions. Diastolic blood pressure (DBP) showed similar patterns and trends to SBP.

**Conclusions:** There is an inverse relationship between number of comorbidities and BP in incident hypertension. Patients with five or more comorbidities have SBP about 5 mmHg less than those without any comorbidities, and this difference is maintained over time. The greatest reductions in BP were seen in those with cardiometabolic conditions. Further research into reasons behind the association between comorbidities and BP is needed to improve hypertension management in primary care.

# AUTOMATED BLOOD PRESSURE MEASUREMENT IN PATIENTS WITH HYPERTENSION AND ATRIAL FIBRILLATION. DATA FROM THE ESH RESEARCH PROJECT "MANAGEMENT OF ARTERIAL HYPERTENSION IN PATIENTS WITH HIGH BLOOD PRESSURE AND ATRIAL FIBRILLATION"

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**Objective:** Atrial fibrillation (AF) is a frequent complication of long lasting hypertension, and carries a high risk of morbidity and mortality as well as of cardiovascular events. AF is also responsible for possible errors in blood pressure (BP) measurement. Limited information is available on the accuracy of blood pressure measurements when automated oscillometric (OSC) devices are used instead of the standard auscultatory approach (AUSC). The aim of this analysis was to compare blood pressure values measured using either a mercury sphygmomanometer or an automated electronic device in patients with AF.

The analysis was limited to 353 patients (mean CHA2DS2-VASc score 3.9), enrolled in the international multicenter ESH Research Project on arterial hyperten-



sion and atrial fibrillation, in whom BP was measured 4 times with the standard AUSC approach (according to Guidelines) and 4 times with an OSC device.

**Results:** mean age was  $72 \pm 11$  (range 20–94), BMI  $28 \pm 5$ , mean CHA2S-2VASC 3.9. Mean BP values were  $130.3 \pm 19.5$  for AUSC-SBP and  $131.5 \pm 20.1$  for OSC-SBP and  $75.8 \pm 11.4$  for AUSC-DBP and  $76.5 \pm 12.3$  for OSC-DBP. Correlation coefficients between automated and manual blood pressure measurements were:  $r = 0.917$  for SBP and  $r = 0.856$  for DBP ( $p < 0.0001$ ). The difference between the oscillometric and manual measurement was on average of 1.2 mmHg for systolic BP (SBP) and of 0.7 mmHg for diastolic BP (DBP). The standard deviations (SD) of the differences were, respectively, 8.07 and 6.39, and progressively increased when 4, 3, 2 or 1 measurements were used. At Bland-Altman analysis the limits of agreement were -17 to 14.7 mmHg for SBP and -13.3 to 11.8 for DBP.

**Conclusions:** In patients with hypertension and AF measurement of BP values with oscillometric devices provides similar BP values, with SD at the upper limit of AAMI criterion for the validation of devices, at least when 4 BP measurements are performed.

### LEFT AND RIGHT ATRIAL FUNCTION AND DIMENSION - MARKERS OF PAROXYSMAL ATRIAL FIBRILLATION IN HYPERTENSIVES

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**Objective:** Introduction: Hypertension increases the risk for atrial fibrillation and is the most common underlying risk factor for the development of atrial fibrillation (1). Discovering predictors for the onset of atrial fibrillation in hypertensives may have prognostic value.

**Objective:** We evaluated left atrium (LA) and right atrium (RA) dimension and function in our attempt to find an echocardiographic marker of paroxysmal atrial fibrillation in hypertensive patients without other significant heart disease.

LA Strain/Type of patient group LA PALS	Group 1 (N=20) 21.69 ± 10.23	Group 2 (N=41) 25.94 ± 6.89	Group 3 (N=19) 17.13 ± 6.56	p F(2,77)=8.579, p<0.001*
LA PACS	-11.71 ± 3.59	-1.86 ± 2.15	-2.39 ± 2.61	F(2,76)=95.536, p<0.001*
RA Strain/Type of patient group RA PALS	Group 1 (N=19) 19.163 ± 8.499	Group 2 (N=39) 15.603 ± 6.643	Group 3 (N=17) 12.441 ± 6.548	p F(2,72)=4.011, p=0.022*

**Design and method:** Methods: We prospectively enrolled three groups of patients: 21 healthy patients (Group 1); 42 hypertensive patients without paroxysmal atrial fibrillation (Group 2) and 22 hypertensive patients with paroxysmal atrial fibrillation (Group 3). Secondary causes of HTN and other coexistent severe pathology were excluded.

LA and RA diameters and volumes were measured by echocardiography, using modified Simpson biplane method. Peak longitudinal strain of LA and RA walls were analyzed using 2D speckle-tracking echocardiography. We also measured the LV mass using the M-mode method, but also area-length method.

**Results:** LA and RA diameters, as well as all the volumes were significantly greater in hypertensive groups compared to controls ( $p < 0.001$ ).

There was found a significant difference between peak LA and RA longitudinal strain parameters in the three groups, with the lowest values in Group 3 ( $p < 0.001$ ). There was also found a significant difference of LV mass between the three groups ( $p < 0.001$ ); the highest values of the LV mass are found in the patients with hypertension and atrial fibrillation ( $p < 0.001$ ,  $R = 0.453$ ). A strong negative correlation between LV linear mass/BSA and LA PALS (peak atrial longitudinal strain) was determined ( $p = 0.003$ ,  $R = -0.645$ ) which means that patients with LV linear mass/BSA at high values have also low values of LA PALS in group with atrial fibrillation compared with the other 2 groups.

**Conclusions:** In our study hypertension was associated with structural and functional remodeling of both LA and RA. So, speckle tracking methods and volumes applied for both atria can be successfully used in identifying hypertensive patients with LA and RA dysfunction at high risk to develop atrial fibrillation.

### IMPACT OF BLOOD PRESSURE CONTROL ON STROKE IN PATIENTS WITH ATRIAL FIBRILLATION. RESULTS FROM NATIONWIDE CROSS-SECTIONAL REGISTRY OF PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION

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**Objective:** Atrial fibrillation (AF) and arterial hypertension (AH) are highly prevalent conditions that often coexist together. Even they are both responsible for high morbidity and mortality, adequate AH control is only marginally followed. Adequate antihypertensive treatment is a paramount to protect patients from devastating consequences of structural heart disease (LV hypertrophy, LV dilatation and impaired LV function) that increases risk of thromboembolic complications. At the same time uncontrolled high blood pressure (BP) increases the risk of stroke and bleeding events (ie intracranial bleeding) and furthermore may lead to recurrent AF.

**Design and method:** All 1975 consecutive patients with non-valvular (NV) AF that visited 150 out-patient clinics were enrolled to nationwide prospective cross-sectional registry.

**Results:** AH was the most frequent comorbidity in the registry that was observed in 1756 (88.9%) pts. Coronary artery disease was disproportionately frequent, documented in 833 (42.2%) pts; 329 (16.7%) pts suffered from previous stroke/transient ischemic attack, heart failure was presented in 587 (29.7%) pts. Target BP levels according to ESC guidelines were achieved in 91% pts. (mean SBP  $133.6 \pm 15.1$  mmHg; DBP  $79.5 \pm 9.5$  mmHg). Those with inadequate BP control had mean SBP  $157.9 \pm 21.8$  and DBP  $89.5 \pm 12.6$  mmHg. AH control in this selected population with NVAF was much better than in other nationwide registries of patients with other cardiovascular conditions that were done previously. The results of BP measurements in the SLOV-FIB registry dispute the truth of essential impact of BP control for development of stroke/TIA in observed pts. Better BP control could be explained by better adherence of pts with AF to antihypertensive treatment. Nevertheless, the fact that pts were managed dominantly by specialists in internal medicine and cardiology may also play role in better BP control.

**Conclusions:** More attention should be paid to rigorous blood pressure control in AF pts. It is an integral part of their management both in primary as well in secondary prevention of AF and its complications.

### THE ASSOCIATION OF INTRACRANIAL ARTERIAL STENOSIS WITH HOME BLOOD PRESSURE LEVEL AND VARIABILITY

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**Objective:** Intracranial arterial stenosis (ICAS) is a major cause of ischemic stroke. However, the associations of ICAS with home blood pressure (BP) and variability remains unclear.

**Design and method:** Outpatients not on antihypertensive medications were recruited from 2009 to 2013. ICAS was defined if the peak systolic flow velocities measured with transcranial Doppler sonography were respectively of at least 140 cm/s, 120 cm/s, or 100 cm/s at middle, anterior, or posterior and vertical cerebular arteries. Home BP was self-measured by Omron HEM-7051 device for seven days. BP variability was assessed as variability independent of the mean, standard deviation, maximum–minimum difference, and average real variability.

**Results:** The prevalence of ICAS in the 801 participants (average age 51 years, 50% males) was 7.9% (63 cases). Patients with ICAS compared to those without had significantly higher clinic ( $135.8$  vs  $131.9$  mmHg,  $P = 0.01$ ) and home systolic BPs ( $134.8$  vs  $128.6$  mmHg,  $P < 0.001$ ). In multivariate-adjusted regression model, home systolic BPs, irrespective of at morning or evening, were associated with ICAS independently of other risk factors including any BP variability indices (OR, 1.47 to 1.82;  $P < 0.005$ ). However, after similar adjustment including home systolic BP, ICAS was only associated with seven-day morning systolic BP variability (OR, 1.35 to 1.47;  $P < 0.02$ ), neither with evening BP variability ( $P > 0.47$ ), nor any day-to-day BP variability indices ( $P > 0.07$ ).

**Conclusions:** Asymptomatic ICAS was moderately prevalent in Chinese untreated patients. Both home morning and evening systolic BPs were important determinants of ICAS, and BP variability in the morning was also associated with ICAS.

# ASSOCIATION OF HOME BLOOD PRESSURE WITH PRECLINICAL ORGAN DAMAGE IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS: COMPARISON WITH AMBULATORY BLOOD PRESSURE

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**Objective:** This study compared home (HBP) versus ambulatory (ABP) blood pressure (BP) monitoring in terms of agreement in the diagnosis of hypertension and their association with preclinical organ damage in young individuals.

**Design and method:** Apparently healthy subjects aged 6–26 years referred for elevated BP or healthy volunteers were subjected to: (i) 24 h ABP monitoring (20-min intervals) and 7-day HBP monitoring (duplicate morning and evening measurements) using validated upper-arm cuff oscillometric devices, (ii) left ventricular mass index (LVMI) determination (echocardiography); (iii) common carotid intima-media thickness (IMT) measurement (ultrasonography), (iv) pulse wave velocity (PWV) measurement.

**Results:** A total of 218 young subjects (mean age  $14.4 \pm 4.3$  years; 152 males) were analyzed (201 had LVMI measurement, 127 IMT and 113 PWV). 24 h ABP was  $121.5 \pm 11.7/68.6 \pm 7.3$  (systolic/diastolic, mmHg) and HBP  $122.1 \pm 12.6/70.8 \pm 8.1$ . 28% of the subjects had hypertension based on HBP and 31% based on 24 h ABP (agreement 84%, kappa 0.61,  $p < 0.01$ ). LVMI was correlated with systolic BP (coefficient  $r = 0.37/0.35/0.37$  for 24 h/day/night ABP, and 0.33 for HBP; all  $p < 0.01$ ). IMT was correlated with systolic BP ( $r = 0.36/0.36/0.34$  for 24 h/day/night ABP, and 0.37 for HBP; all  $p < 0.01$ ). PWV was closely associated with systolic BP ( $r = 0.49/0.48/0.46$  for 24 h/day/night ABP, and 0.47 for HBP; all  $p < 0.01$ ). In multivariate stepwise regression analysis (age, gender, body mass index [BMI], systolic HBP, 24 h/day/night systolic ABP as independent variables), LVMI was determined ( $R^2 = 0.28$ ) by BMI and night-time systolic ABP, IMT ( $R^2 = 0.17$ ) by systolic HBP and male gender, and PWV ( $R^2 = 0.36$ ) by systolic 24 h ABP and age.

**Conclusions:** In young individuals there is reasonable agreement between HBP and ABP measurements in diagnosing hypertension and similar associations with indices of preclinical target-organ damage.