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### **P1.07: CAROTID FUNCTION AND BARORECEPTOR SENSITIVITY IN MODERATE CHRONIC KIDNEY DISEASE: THE EPP3 STUDY**

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waveforms. We used it here to investigate whether systolic ventricular function is different in patients requiring chronic beta-blockade (BB) compared to controls.

**Methods and Results:** In 81 patients on BB and 87 age- ( $61 \pm 7$  yrs) and sex-matched untreated controls, we obtained untreated STI and blood pressures. BB patients discontinued medication 1 day prior to measurements. Intra-session coefficients of variation for  $T_{ej}$  and  $T_{ic}$  were 0.8% and 6.8%; and inter-session 2.7% and 8.4% (i.e.  $100\% \cdot SD_{intra/inter}/mean$ ).

$T_{ej}$  and pulse pressure (PP), thus the  $PP \cdot T_{ej}$  product reflecting ventricular stroke work, were significantly greater in (untreated) BB patients (all  $p < 0.002$ ).  $T_{ic}$  was not different between the groups. The  $T_{ic}/T_{ej}$  ratio was smaller for the BB group ( $p = 0.04$ ), indicating increased systolic ventricular function, likely matching the greater stroke work required.

	$T_{ic}$ ms	$T_{ej}$ ms	R-R int. ms	$T_{ic}/T_{ej}$ %	DBP mmHg	SBP mmHg	PP mmHg	$PP \cdot T_{ej}$ mmHg · s
BB	$34 \pm 7$	$286 \pm 27$	$908 \pm 148$	$12 \pm 3$	$75 \pm 10$	$137 \pm 19$	$61 \pm 13$	$18 \pm 5$
Ctrls	$35 \pm 7$	$274 \pm 22$	$885 \pm 145$	$13 \pm 3$	$77 \pm 10$	$133 \pm 17$	$56 \pm 11$	$15 \pm 3$
*p-val.	0.36	0.0017	0.32	0.04	0.41	0.15	0.006	0.0005

\*Paired t-test.  $T_{ic}/T_{ej}$ : approximate Tei index;  $PP \cdot T_{ej}$ : stroke work (pressure-time product).

**Conclusions:** Patients requiring chronic beta-blockade have longer ventricular ejection periods combined with greater pulse pressures, indicating greater ventricular stroke work and thus enhanced systolic function. Our findings readily demonstrate the accessibility and reproducibility of non-invasive STI measurement in a clinical population.

#### P1.05

##### EFFECT OF AGING ON THE ANNUAL CHANGES OF CENTRAL HEMODYNAMIC INDICES IN MIDDLE-AGED MEN: A PROSPECTIVE EVALUATION

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**Objective:** To examine the effects of aging on the annual changes of the pressure wave reflection (PWR) and central blood pressures (CBPs), prospectively. Background: Such prospective study has not been conducted.

**Methods:** In 1291 middle-aged men, the first and second peaks of the radial systolic pressure waveform (SBP1 and SBP2), the radial augmentation index (rAI), reflected wave transit time (RWTT) and the brachial-ankle pulse wave velocity (baPWV), were measured twice in a 3-years' interval.

**Results:** Subjects were divided into three groups {aged <40 years old (aged 30); <40 aged <50 years old (aged 40); and aged >50 years old (aged 50)}. The change of rAI was higher and that of RWTT was lower in aged 30 group than in aged 50 group ( $p < 0.01$ ), but that of SBP2 was similar among the groups. The change of RWTT, but not that of baPWV, had a significant inverse relationship with that of rAI in all groups ( $p < 0.01$ ). Stepwise multivariate analysis demonstrated that the accounting rate of change of SBP1, but not that of rAI, for the variance in that of SBP2 was increased in a phased manner along with age.

**Conclusion:** In middle-aged men, aging may differently affect PWR and CBPs. Aging may prolong the time of PWR and blunt that arterial stiffness increases PWR. These phenomena may contribute to the aging-related attenuation of annual increase of PWR. However, aging may not affect the annual elevations of CBPs, because the incident pressure wave may compensate the aging-related attenuation of their elevations by PWR.

#### P1.06

##### BLOOD PRESSURE VARIABILITY IN RELATION TO AUTONOMIC NERVOUS SYSTEM DYSREGULATION: THE X-CELLENT STUDY

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To investigate the association of autonomic nervous system dysregulation with blood pressure variability. Of 2370 participants in the X-CELLENT study, 577 patients ( $59.0 \pm 10.2$  years) were randomly selected to participate in an ambulatory blood pressure monitoring ancillary study. We proposed a novel autonomic nervous system regulation index termed dSBP/dHR, which was defined as the steepness of the slope of the relationship between 24h systolic blood pressure and heart rate for each participant. Within-subject standard deviation of systolic blood pressure, weighted for the time interval between consecutive validated readings from 24h ambulatory blood pressure monitoring, was used to evaluate blood pressure variability. When dSBP/dHR

was divided into tertiles, from tertile 1 to tertile 3, we observed a progressive increase in daytime systolic blood pressure, a progressive decrease in nighttime systolic blood pressure, and consequently a progressive increase in day-night systolic blood pressure gradient ( $P < 0.001$ ). On the contrary, standard deviation of both daytime and nighttime systolic blood pressure were consistently and significantly increased from tertile 1 to tertile 3 ( $P < 0.01$ ). Both before and after adjustment for age, gender and 24h mean blood pressure, all of these increasing or decreasing trends reached statistical significance ( $P < 0.01$ ). Furthermore, in our sensitivity analysis, when men and women were considered separately, the present finding remained unaltered. In summary, autonomic nervous system dysfunction was associated with the enlarged day-night systolic blood pressure gradient and more variable systolic blood pressure in 24 hours in patients with essential hypertension.

#### P1.07

##### CAROTID FUNCTION AND BARORECEPTOR SENSITIVITY IN MODERATE CHRONIC KIDNEY DISEASE: THE EPP3 STUDY

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**Introduction:** Short-term variation of blood pressure (BP) is largely controlled by autonomic function though the baroreflex. Carotid distension rate was recently introduced instead of BP to evaluate the carotid function and neural component of the baroreflex in small populations. Autonomic dysfunction and arterial stiffness occurs in patients with severe chronic kidney disease (CKD) but little is known in moderate CKD.

**Aims:** To study the baroreflex and to analyse the link with the carotid function in moderate CKD.

**Methods:** From the EPP3 cohort, 123 patients with moderate CKD (Stage 3A) and 615 controls with  $GFR \geq 60 \text{ ml/min/1.73m}^2$ , matched for age, gender and body surface area were enrolled (age  $64 \pm 6$  years). Carotid measurements were performed by a high-resolution echotracking device. Spontaneous BRS was calculated with the fast Fourier transform of carotid distension rate and R-R interval in the low-frequency (LF) range (0.04-0.15 Hz).

**Results:** Internal diastolic diameter, intima-media thickness, circumferential wall stress, carotid pulse pressure, R-R interval and BRS were comparable between the two groups. Carotid strain and distensibility were significantly reduced, elastic incremental modulus and carotid stiffness were significantly increased in CKD.

Neural baroreflex appeared very sensitive to vascular component since carotid strain was the strongest determinants of BRS in both groups (Fig-1). The explained BRS variability was higher in patients with CKD ( $R^2 = 0.31$ ) than in controls ( $R^2 = 0.14$ ).

**Conclusions:** In moderate CKD we detected carotid dysfunction and no changes in neural baroreflex. The role of carotid strain, as a determinant of neural baroreflex, is confirmed in moderate CKD and in controls.

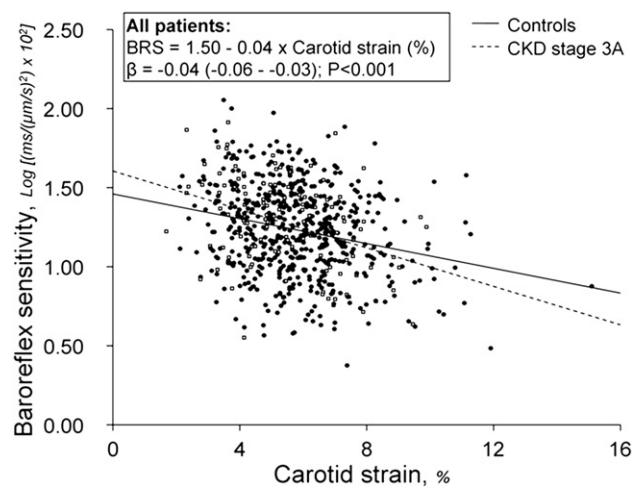


Fig -1

## P1.08

## THE ROLE OF PULSE PRESSURE FOR COGNITIVE DECLINE IN HYPERTENSION

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**Objective:** Pulse pressure (PP), as a marker of large artery stiffness, is a risk factor for target organ damage in hypertension (HT). We hypothesized that elevated PP, as a marker of enhanced arterial stiffness, may be correlated with specific early target organ damage (TOD) of the brain - mild cognitive impairment (MCI).

**Design and methods:** 148 treated HT patients (Pts) - males 51 (34.5%), females 97 (65.5%) with mean age 64.16±11.18 years and mean hypertension history 13.1±11.05 years were included. Full medical history, esp. HT history, physical examination and laboratory screening were gathered. Only Pts in sinus rhythm were included. We screened the Pts for MCI with a battery of neuropsychological tests (NPTs): Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). Ambulatory Blood Pressure Monitoring was conducted: mean day PP was 56.85±12.02 mmHg and mean night PP - 55.15±16.13 mmHg. **Results:** Regression analysis found correlation between day and night PP and NPTs' results. With Mann-Whitney Test ( $\alpha < 0.05$ ) we found that there is a significant difference (sig. 0.023 for MMSE) in the mean values of the NPTs' results between the groups with PP>50 and PP≤50 mmHg. Again with Mann-Whitney Test we assessed the significance of the difference between mean values of day-PP (sig. 0.01) and night-PP (sig. 0.02) between Pts with MCI and those without (resp. >55 and <55 mmHg).

**Conclusion:** Elevated PP in treated HT is a risk factor for MCI. We should screen Pts with HT for specific TOD - MCI.

## P1.09

## RELATION OF CENTRAL AND BRACHIAL BLOOD PRESSURE TO ECG LEFT VENTRICULAR HYPERTROPHY. THE CZECH POST-MONICA STUDY

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**Objective:** Central blood pressure (BP) has been shown to be a better predictor of target organ damage and cardiovascular events than brachial BP. Whether central BP is a better predictor of left ventricular hypertrophy (LVH) determined by electrocardiography is not known.

**Methods:** Radial applanation tonometry and ECG were performed in 728 subjects from the Czech post-MONICA study (a randomly selected 1% population sample). LVH was determined using the Sokolow-Lyon index and Cornell product; central pressure was derived from radial pulse.

**Results:** Of 657 subjects included in the analysis, 17 (9.4%) below 45 years and 43 (9%) over 45 years had LVH. In multiple linear regression analysis, the Sokolow-Lyon index in younger individuals was only associated with male sex and low BMI, with no association with BP found. In older individuals, LVH was associated with higher central and brachial BP. In separate binary logistic regression analyses adjusted for covariates, the odds ratios for central systolic pressure was higher than those for brachial systolic and pulse pressure in LVH prediction.

**Conclusion:** Noninvasively determined central pressure in subjects over 45 years is more strongly related to ECG LVH than brachial pressure. This further supports a closer association of central pressure with target organ damage. Neither central nor brachial blood pressure is associated with Sokolow-Lyon voltage criteria in younger individuals.

## P1.10

## PREVALENCE OF RESISTANT HYPERTENSION IN A GENERAL POPULATION IN NORTHERN ITALY: ASSOCIATED CARDIOVASCULAR RISK FACTORS AND TARGET ORGAN DAMAGE

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**Background:** Resistant hypertension (RH) is defined by most guidelines as blood pressure that remains above goal despite use of at least 3 antihypertensive agents of different classes, including a diuretic, prescribed at optimal doses. Few data are available on the clinical characteristics and

on the prevalence of different forms of organ damage in these patients. Aim of the study was to evaluate the prevalence of RH and the presence of associated cardiovascular (CV) risk factors and target organ damage (TOD) in a group of hypertensive patients selected from a general population sample in Northern Italy (Vobarno Study). **Methods:** 478 subjects (mean age 58±3 yrs, 44% males, 66% hypertensives) underwent laboratory examinations and both clinic and 24 hours BP measurement (Spacelabs 90207). Left ventricular (LV) and carotid artery structure were assessed by ultrasound and carotid-femoral PWV was measured using Complior SP (Artech, Pantin, France). **Results:** among treated hypertensive patients 9.5% were defined as resistant. Patients with RH were older (mean age 69±4 vs 60±9 yrs,  $p < 0.01$ ), had higher glucose values (115±47 vs 103±24 mg/dl,  $p < 0.05$ ) and were more often of female gender (female 73% vs male 27%,  $p < 0.05$ ); no difference in BMI and lipid levels was observed. Estimated glomerular filtration rate (MDRD) was lower in RH (72±17 mL/min/1.73 m<sup>2</sup> vs 82±16,  $p < 0.01$ ). Patients with RH had greater LV mass index (47.7±10.5 vs 40.7±10.0 gr/m<sup>2.7</sup>,  $p < 0.001$ ), LV relative wall thickness (0.42±0.08 vs 0.38±0.05  $p < 0.001$ ), intima media thickness (Meanmax 1.47±0.42 vs 1.18±0.30 mm,  $p = 0.01$ ) and PWV (13.3±2.8 vs 11.8±2.8 m/sec,  $p < 0.05$ ). **Conclusions:** in a group of hypertensive patients selected from a general population in Northern Italy the prevalence of RH was relatively high. Patients with RH were older, had higher glucose values and a higher prevalence of cardiac, vascular and renal organ damage.

## P1.11

## INCREASED AGE, BODY MASS INDEX AND LOW HDL-C LEVELS RELATE TO AN ECHOLUCENT STRUCTURE OF THE CAROTID INTIMA-MEDIA THICKNESS: THE METEOR STUDY

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**Introduction:** Echolucent plaques have high lipid contents and are related to a higher cardiovascular risk. Studies relating echolucency to cardiovascular risk in early stages of atherosclerosis are limited. We studied the relation between cardiovascular risk factors and the echolucency of the carotid intima-media thickness (CIMT) in low-risk individuals.

**Methods:** Data were used from the METEOR (Measuring Effects on Intima-Media Thickness: an Evaluation of Rosuvastatin) study. In this post-hoc analysis, duplicate baseline ultrasound images from the far wall of the left and right common carotid arteries were used for evaluation of the echolucency of the CIMT, measured by grey-scale median (GSM), scale: 0-256. Low GSM values reflect echolucent, lipid-rich structures, whereas high values reflect echogenic structures. The relations between GSM and cardiovascular risk factors were evaluated with linear regression models.

**Results:** Baseline GSM was 83.96 (standard deviation: 29.40). Lower GSM of the CIMT was associated with older age, high body mass index (BMI), and low levels of high-density lipoprotein cholesterol (HDL-C) (beta, 95% confidence interval [CI]: -4.49 [-6.50;-2.49], -4.51 [-6.43;-2.60], and 2.45, [0.47;4.42], respectively). Thickness of the common CIMT was inversely related to GSM of the CIMT (beta -3.94 [-1.98;-5.89]).

**Conclusion:** Older age, high BMI, and low levels of HDL-C are related to echolucency of the CIMT, reflecting high lipid levels in the arterial wall. Hence, echolucency of the CIMT may be used as marker for cardiovascular risk profile that covers more than thickness alone.

## P1.12

## B-PROOF: IS ARTERIAL STIFFENING ASSOCIATED WITH HOMOCYSTEINE?

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**Introduction:** Recently in elderly, homocysteine alone has been shown to be a better predictor of cardiovascular mortality than models based on classical risk factors. The pathophysiological pathway is however still unclear. Current view is that increased thrombogenicity, increased oxidative stress and over-activation of redox-sensitive inflammatory pathways, leads to impaired endothelial function.