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P2.7: AMELIORATION OF COGNITIVE FUNCTION IN HEMODIALYSIS PATIENTS IN ABSENT OF HYPOTENSIVES EPISODES

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Background: It is suggested that, in resistant hypertension, the presence of particularly pronounced microvascular alterations may contribute to explain the relative lack of response to treatment. Similarly, in diabetic patients, the persistence of an altered microvascular structure, despite the administration of multiple drug combination treatment, might partly explain the difficulty to reach target blood pressure values, especially for systolic blood pressure.

Patients and methods: For this reason, we investigated a population of 94 treated essential hypertensive patients. Secondary forms of hypertension were excluded according to standard clinical evaluations and biochemical or instrumental assessment, and in all patients a 24-hour blood pressure monitoring was performed in order to exclude a white coat effect. In all patients, we evaluated small resistance arteries morphology by a wire micro-miographic approach (Mulvany's technique). A small amount of subcutaneous tissue was obtained by local biopsy or during election surgery and subcutaneous small resistance arteries were dissected and mounted on a myograph; the media to lumen ratio (M/L) was then measured.

Sixteen patients had true resistant hypertension, and were compared with the remaining 78 patients with non-resistant hypertension.

Results: The two groups were different in terms of mean age, pulse pressure/stroke volume, media to lumen ratio and internal diameter of small resistance arteries.

Conclusion: Our data suggest that hypertensive patients with true resistant hypertension have greater microvascular structural alterations compared with non-resistant hypertensive patients. This could explain, at least in part, the resistance to pharmacological treatment and the high cardiovascular risk observed in these patients.

P2.4

THE INFLUENCE OF ANTIHYPERTENSIVE TREATMENT ON ARTERIAL STIFFNESS, SHEAR STRESS AND ACTIVITY OF CHOSEN MATRIX METALLOPROTEINASES

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Objective: Comparison of therapeutic effects of chosen antihypertensive drugs on arterial stiffness, shear stress in carotid arteries and metalloproteinases activity, moreover analysis of relationship of these variables in the course of treatment.

Design and method: 95 never treated patients with HT stage 1 or 2 were randomized to 6 months monotherapy with: quinapril, amlodipine, hydrochlorothiazide, losartan or bisoprolol. Each therapeutic group consisted of 19 patients (N=19). Before and then after 1, 3 and 6 months of treatment carotid-femoral pulse wave velocity (PWV) by using a Complior device, ultrasound of carotid arteries were performed. Blood samples for the measurement of whole blood viscosity were taken during each visit. Shear stress (SS) was calculated on the basis of Irace formula. Serum concentration of metalloproteinase 3 (MMP-3) and plasma concentration of tissue inhibitor of metalloproteinase 1 (TIMP-1) were measured at the initial visit and after 6 months of treatment.

Results: ANOVA for repeated measurements revealed for all groups significant decrease of PWV and MMP-3 concentration and increase of shear stress in carotid artery and TIMP-1 concentration ($p < 0.05$). No between groups differences appeared in above effects ($p > 0.05$).

Conclusion: Irrespectively of chosen drug we observed similar effect for PWV drop. Reduction of arterial stiffness as a result of antihypertensive therapy is strongly connected with shear stress increase that is secondary to blood flow velocity growth and changes in connective tissue metabolism.

P2.5

SEX-DEPENDENT DIFFERENCES IN OBESITY INDICES AND INFLAMMATORY MARKERS IN NON-DIABETIC OBESE PATIENTS

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Background: The aim of the study was to assess sex-dependent differences of obesity indices and inflammatory markers in non-diabetic hypertensive obese patients.

Material and methods: 40 females and 25 males aged 59.8 ± 10.1 and 54.6 ± 11.9 years, respectively, were enrolled into the study. Serum TNF- α , IL-6 and high-sensitivity C-reactive protein (hs-CRP) levels were estimated. Waist circumference (WC), waist-to-hip ratio (WHR), body mass index (BMI), waist-to-height ratio (WHtR), visceral adiposity index (VAI) and body adiposity index (BAI) were measured or calculated.

Results: In males WC and WHR were higher than in females (117.0 ± 10.8 cm vs 108.5 ± 10.4 cm; $p < 0.01$ and 1.01 ± 0.06 vs 0.91 ± 0.06 ; $p < 0.0001$, respectively). In females BAI and hs-CRP were higher than in the males (41.7 ± 6.9 vs 33.5 ± 5.0 ; $p < 0.0001$ and 3.2 ± 2.2 mg/l vs 2.1 ± 1.5 mg/l; $p < 0.05$, respectively).

In females hs-CRP positively correlated with WHtR ($r = 0.321$; $p < 0.05$), BMI and BAI ($r = 0.305$; $p = 0.05$, and $r = 0.309$; $p = 0.05$, respectively). In males hs-CRP positively correlated with WHtR, BAI and VAI ($r = 0.458$; $p < 0.05$; $r = 0.440$; $p < 0.05$ and $r = 0.443$; $p < 0.05$, respectively), IL-6 positively correlated with VAI ($r = 0.472$; $p < 0.05$) and TNF- α negatively correlated with WHR ($r = -0.408$; $p < 0.05$).

Conclusions: Obesity related chronic inflammation is more evident in females than in males. Differences in WC, WHR and BAI are sex dependent.

P2.6

PWV IS AN INDEPENDENT DETERMINANT OF COGNITIVE DYSFUNCTION IN CKD PATIENTS

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Objectives: In the general population aortic stiffening assessed by carotid femoral pulse wave velocity (cf-PWV) is associated with cognitive dysfunction (CO/DY). Data in chronic kidney disease (CKD) are limited. Our study tests the hypothesis that large artery stiffness and microvascular damage in CKD patients are related to brain microcirculation changes reflected by impaired cognitive function.

Methods: Among 244 patients, finally 44 with CKD stage 1; 47 stage 2; 25 stage 3; 35 stage 4, with mean age 58.4 years (64.5% males), were enrolled in a cross-sectional study. Cognitive impairment measured by Mini Mental State Examination (MMSE), Clock – drawing test (Clock-test), and Instrumental Activity of Daily Living (IADL) was considered as primary outcome. We directly measured brachial, aortic, systolic blood pressure, pulse pressure, mean blood pressure and cf-PWV.

Results: Our patients revealed a significant linear deterioration in all the domains of cognitive function according to CKD stages, assessed by MMSE, Clock-test and IADL. The risk of cognitive dysfunction increased significantly from CKD stage 3 to 4 ($p < 0.01$). High levels of cf-PWV ($p = 0.029$) and aortic pulse pressure (aPP) ($p < 0.026$), were independent predictors of cognitive decline according to MMSE.

Conclusions: The present trial supports the interaction between the kidney and the brain injury microcirculation. In clinical practice cf-PWV and aPP measurements may help to predict cognitive decline. Whether, the reduction in aortic stiffness following an aggressive treatment translates into improved cognitive outcomes remains to be determined.

P2.7

AMELIORATION OF COGNITIVE FUNCTION IN HEMODIALYSIS PATIENTS IN ABSENCE OF HYPOTENSIVE EPISODES

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Objective: Patients in hemodialysis frequently have cognitive dysfunction (CO/DY). Hemodialysis session often results in acute intravascular volume loss, fluid shifts, hypotensive episodes, decrease of cerebral perfusion and cerebral ischemia, all of which may cause transient deterioration of cognitive function. On the contrary, improvement in "uremic milieu" after a dialysis session can result in improved cognition. The aim of this study is to evaluate the effect of a single, random hemodialysis session on cognitive function, in absence of hypotensive episodes.

Method: Global cognitive function was assessed, pre- and post-dialysis by using the Mini Mental State Examination.

Results: Forty-eight patients participated in the study. The average age was 60.8 ± 13.4 years. The mean dialysis vintage was 58 ± 66 months. Patients received adequate renal replacement therapy and the mean urea reduction ratio was 72 ± 6.6 . At the onset and at the end of the study, no major hemodynamic changes were detecting (mean systolic/diastolic blood pressure ($147. \pm 20 / 78 \pm 11$ vs $138 \pm 20 / 77 \pm 10$ mmHg) according to our aforementioned criteria. Compared to pre- dialysis, an improvement in the test score was revealed after dialysis, paired t-test ($p=0.03$). Mean values of MMSE pre and post was 26.61 ± 3.24 and 28.86 ± 1.98 respectively (amelioration of 2.25 points).

Conclusions: Our results illustrate the better performance of cognitive function that can be observed after a single dialysis session, in absent of hypotensives episodes. These results may be used as a starting point, in an effort to evaluate the best possible time, pre or post dialysis, to provide medical advice to these patients.

P2.9

A NOVEL SPECKLE TRACKING TECHNIQUE FOR INVESTIGATING REGIONAL MOTION OF THE CAROTID WALL: SPATIO-TEMPORAL VARIATION IN DISTENSION ASSOCIATES WITH PRESENCE OF CALCIFIED PLAQUE

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Background: Arterial calcification may lead to regional variation in distension imposing stresses on the arterial wall that predispose to plaque rupture. The objective of this study was to use a novel speckle tracking method to investigate regional motion of the carotid wall and to determine whether this relates to subclinical disease.

Methods and results: Measurements were obtained on 256 subjects from the Twins UK cohort (mean \pm SD age 62 ± 10.2 years). The left carotid was imaged for an assessment of plaque and calcification. Speckle-tracking was then used to measure regional circumferential strain of the left common carotid in 6 separate 60° segments of the circumference of the arterial wall in a plaque free plane of the common carotid approximately 1 cm proximal to the bifurcation. Regional variation in circumferential strain around the circumference of the arterial wall was characterized by the standard deviation of circumferential strain and that of the time from onset of systole to peak circumferential strain in each segment. Spatio-temporal variation in circumferential strain characterized by variation in the time to peak circumferential strain was associated with age and presence of calcified plaque (regression coefficients 0.73 units/year and 14.2 increase for presence of calcified plaque, each $P < 0.001$) independent of other confounding factors and of other measures of arterial wall damage such as carotid intima-media thickening, carotid distensibility and carotid-femoral pulse wave velocity.

Conclusion: Arterial ageing and calcification are associated with spatio-temporal variation in distension of the carotid artery.

P2.10

EXAGGERATED EXERCISE BLOOD PRESSURE INDEPENDENTLY PREDICTS INCIDENT HYPERTENSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Exaggerated exercise blood pressure (EEBP) independently predicts cardiovascular (CV) events and mortality, but reasons underlying this increased CV risk are unclear. The association between an EEBP and incident hypertension (as a potential underlying risk factor) has been reported, but there has never been a pooled summary of risk estimates (RE). The aim of this study was to conduct a systematic review and meta-analysis of studies assessing the association between EEBP and incident hypertension among normotensive individuals.

Methods: Seven online databases were searched for studies that measured dynamic exercise BP and rates of incident hypertension (defined from clinic BP $\geq 140/90$ mmHg or out of clinic BP above guideline recommended values) among people who were normotensive at baseline. EEBP was defined as systolic BP during exercise (moderate or peak intensity), as well as the change from rest, or in acute recovery after exercise.

Results: 22 studies met inclusion criteria, totalling 31,130 participants aged 42.4 ± 8.9 years followed for 6.0 ± 2.6 years. Pooled meta-analysis at peak and moderate exercise intensity, adjusted for baseline (rest) BP, age, sex and other traditional CV risk factors revealed that an EEBP significantly

increased the risk for incident in-clinic hypertension (peak RE=1.52 [95% CI: 0.99, 2.33], I²=80.4%; moderate RE=1.90 [95% CI: 1.11, 3.28], I²=75.5%).

Conclusions: An EEBP independently predicts incident hypertension, thus indicating that clinicians supervising exercise stress testing should consider additional patient follow-up with respect to BP control and lifestyle intervention to reduce CV risk among patients with EEBP.

P2.11

EXERCISE REVEALS DIFFERENTIAL COUPLING BETWEEN AORTIC HAEMODYNAMICS AND LEFT VENTRICULAR TWIST MECHANICS

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Background: Hypertensive heart disease is characterised by raised left ventricular (LV) mass, a consequence of load-altered ventricular-arterial coupling. Prior to gains in LV mass, early functional changes in ventricular-arterial coupling must occur, however, these are difficult to detect from conventional loading parameters at rest. This study aimed to examine the coupling of systolic LV twist and diastolic LV untwisting rate with alternative central haemodynamic indices [excess pressure (XSP) and reservoir pressure (RP)] at rest and during exercise.

Methods: 44 healthy men (21 ± 2 years) were assessed at rest and during 40% of maximal exercise capacity. Aortic XSP and RP were derived from radial tonometry, with LV systolic twist and diastolic untwisting rate simultaneously quantified using echocardiography.

Results: Associations between LV twist and RP and XSP were observed at rest (0.51 and 0.37, $P < 0.01$ respectively). Whilst total pressure did not differ between those with low and high LV twist (1933 ± 666 vs. 2173 ± 561 Pa.s, respectively, $P=0.24$), the change in LV untwisting rate with exercise was associated with change in XSP in High-twist ($r=-0.60$, $P=0.006$), but not Low-twist ($r=0.10$, $P=0.65$). Conversely, Low-twist showed a significant relationship between the change in LV untwisting rate and change in RP ($r=-0.47$, $P=0.03$), not observed in High-twist ($r=0.27$, $P=0.27$).

Conclusions: Aortic XSP and RP are coupled to LV twist mechanics at rest, but coupling is differentially modified as a result of a standardised exercise challenge. In the absence of structural LV remodelling, these observations may represent an early indication of increased risk for negative LV remodelling in later-life.

P2.12

A NOVEL MARKER EXPRESSES THE EFFECT OF THE NONLINEARITY IN THE ARTERIAL PRESSURE-VOLUME RELATIONSHIP ON THE PULSE PRESSURE: CHARACTERISTICS AND PROGNOSTIC SIGNIFICANCE IN HYPERTENSIVE PATIENTS

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Arterial pressure-volume relationship frequently deviates from the linearity expected from an ideal elastic tube. As a result, pulse pressure (PP) can be split into an 'elastic' component (ePP) and an excess value PP-ePP. We define the ratio (PP-ePP)/ePP as arterial nonlinearity marker (NLM). **OBJECTIVE:** Determining NLM from ambulatory BP (ABP) measurements and investigating its clinical and demographic characteristics and prognostic significance in hypertensive patients. **METHODS:** Following a previously described model-based procedure, NLM was determined from the variability of systolic BP (SBP) and diastolic BP (DBP). The predictive power of NLM was estimated using Cox proportional hazards regression adjusted for age, gender, body mass index, mean heart period, SBP- and heart-rate dipping and hypoglycemic and antihypertensive medication status. NLM variation with age or DBP changes in 10-years or 10-mmHg intervals, respectively, was evaluated using adjusted ANOVA and pairwise comparisons for the grouped variables. **RESULTS:** We analyzed 1,999 ABP records of individual hypertensive patients, (age 56 ± 16 years, 55% women, 60% on antihypertensive medication and 9% with diabetes, average BP $139/79$ mmHg, median DBP 78 mmHg), followed 5 years for all-cause mortality, of whom 103 died. Mean(SD) [range] for PP were $60(14)[27-132]$ mmHg and for NLM $0.20(0.14)[-0.22-1.00]$. PP and NLM were positively correlated ($r=0.53$). NLM increased