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### **P4.10: ASSOCIATION OF ARTERIAL STIFFNESS WITH BLOOD PRESSURE VARIABILITY**

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**Results:** After a median of 7.7 [IQR 7.0-8.1] years of follow up, 130 CVD events and 93 deaths were recorded. CWS was 31.7, 31.5 and 34.4 kPa in NGM, IGM and T2D, respectively (Ptrend= 0.06). Greater CWS was associated with incident CVD in T2D only (hazard ratio(95%CI) per SD increase in CWS for NGM: 0.92 (0.70-1.21); IGM: 1.02 (0.66-1.58) and T2D 1.52 (1.09-2.14), after adjustment for age, sex, height and other CVD risk factors.. No associations were observed between CWS and all-cause mortality.

**Conclusion:** T2D is associated with greater CWS compared to NGM and IGM. Greater carotid CWS is associated with incident CVD in T2D but not in NGM or IGM.

#### P4.7

##### PLASMA COPPER AND CERULOPLASMIN IN RELATION TO CAROTID-FEMORAL PULSE WAVE VELOCITY

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Copper participates in the redox mechanisms and is a cofactor of enzymes responsible for appropriate structure of elastic fibres. The aim of the study was to assess the relationship between plasma copper as well as ceruloplasmin concentrations and carotid-femoral pulse wave velocity (cfPWV). The study group, recruited from the population-based family study, included 138 parents (age 61.5±7.9 years, 57M/81F, 80.4% hypertensives) and 165 offspring (mean age 34.8±8.4 years, 79M/86F, 32.7% hypertensives). Information about each participant's clinical data were collected with the use of standardized questionnaires. The cfPWV was measured by Micro-Tip pressure transducer (Model SPT-301, Millar Instruments, Houston, Texas, USA) and the SphygmoCor system (ver. 6.31 AtCor Medical Pty., Ltd., Australia). The plasma copper concentration was determined by ICP-MS (Inductively Coupled Plasma Mass Spectrometry) and plasma ceruloplasmin concentration by ELISA test. Database management and multivariate analyses were performed with SAS software (SAS Institute, Cary, NC, version 9.3).

The average values of plasma levels were: copper (male 620.4±229.7µg/l, female 740.9±339.3µg/l); ceruloplasmin (male 612.6±221.6µg/ml, female 766.7±337.0µg/ml).

With adjustments applied for age, sex, cholesterol level, fasting glucose, body height, use of antihypertensive drugs, smoking and alcohol intake, we observed a positive correlation between the cfPWV and plasma copper concentration (0.00074±0.0003, p=0.011) as well as plasma ceruloplasmin concentration (0.0007±0.0003; p=0.0095).

In our study group, higher plasma copper and ceruloplasmin concentrations were related to higher cfPWV. The excess body copper might contribute to the lower antioxidant status and arterial stiffening.

#### P4.8

##### ASSOCIATIONS OF MID-LIFE CARDIOVASCULAR RISK FACTORS WITH LATER LIFE COGNITIVE FUNCTION

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**Background:** Mid-life cardiovascular risk factors may be detrimental to cognitive function in later life; however results are inconsistent. We investigated the impact of mid-life blood pressure, glucose, cholesterol and obesity on cognitive function.

**Methods:** In a community based sample aged 49.6±6years: waist-to-hip ratio (WHR), fasting blood glucose, HDL cholesterol and blood pressure were measured. 20 years later 1284 of these individuals underwent cognitive function testing to assess global function, executive function, memory and attention. Data are β±SE, \*p<0.05, \*\*p<0.01.

**Results:** After adjusting for age, sex, ethnicity, years of education and smoking no associations were found between cognitive function and mid-life glucose or blood pressure measures. Lower mid-life WHR and higher HDL cholesterol levels were significantly associated with better scores in all cognitive domains. Per unit increase in WHR: Global function -1.45±0.3\*\*; Executive function -1.82±0.3\*\*; Memory -1.27±0.3\*\* and Attention

-1.23±0.03\*\*.. Per mmol/L increase in HDL: Global function 0.19±0.06\*\*; Executive function 0.13±0.06\*\*; Memory 0.14±0.06\*\* and Attention 0.17±0.05\*. These associations remained after further adjustment for current concomitant risk factors: diabetes, hypertension, previous stroke, coronary artery disease and current WHR/ HDL (WHR: Global function -1.05±0.4\*\*; Executive function -2.2±0.4\*\*; Memory -1.1±0.4\*\* and Attention -1.15±0.4\*\*. HDL: Global function 0.20±0.07\*\*; Executive function 0.15±0.07\*\*; Memory 0.19±0.07\*\* and Attention 0.15±0.07\*\*).

**Discussion:** Elevated WHR and lower HDL cholesterol in mid-life are significant risk factors for cognitive decline 20 years later. These mid-life risk factors have effects independent of current risk factors and may be important targets for prevention of cognitive decline in later life.

#### P4.9

##### ENDOTHELIN-1 IS LINKED WITH ARTERIAL STIFFNESS AND INTERLEUKIN-6 IN BLACK SOUTH AFRICAN WOMEN: THE SABPA STUDY

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Up-regulation of ET-1 activates inflammatory cells such as macrophages that release pro-inflammatory mediators such interleukin-6 which promote vascular inflammation and endothelial dysfunction, leading to arterial stiffness.

Included in this study were 194 black and 197 white South-Africans. Cardiovascular variables were recorded using the Finometer and the Compliar. ET-1 and interleukin-6 were determined by recognized biochemical methods.

The participants were divided into black and white men and women due to significant interactions of ethnicity (F(391) = 6.78; p < 0.001) and gender (F(391) = 2.39; p < 0.05) on the association of ET-1 with systolic blood pressure.

No significant difference in ET-1 levels between black and white groups emerged. Black men and women had higher blood pressure and pulse wave velocity in comparison to white men and women (p < 0.05). C-reactive protein and interleukin-6 were higher in the black groups compared to the white group (all p < 0.05). A positive correlation (single) existed between ET-1 and interleukin-6 (r = 0.27; p = 0.007), systolic blood pressure (r = 0.27; p = 0.008), pulse pressure (r = 0.25; p = 0.014) and pulse wave velocity (r = 0.23; p = 0.026) in black women. After partial adjustments for BMI and GGT the correlation remains. With forward stepwise multiple regression ET-1 associated with interleukin-6 (adj.R<sup>2</sup> = 0.13, β=0.278, P=0.005) and measures of arterial stiffness.

ET-1 independently associated with systolic blood pressure, pulse pressure and interleukin-6 in black women. Our results suggest that adverse endothelial function is potentially driven by pro-inflammation.

#### P4.10

##### ASSOCIATION OF ARTERIAL STIFFNESS WITH BLOOD PRESSURE VARIABILITY

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Increase of arterial stiffness is an independent predictor of cardiovascular morbidity and mortality. Short term blood pressure (BP) variability is recognised as a marker and a risk factor for cardiovascular complications. The study aims to determine the relation between arterial stiffness and short -term variability in general population.

**Methods:** We recruited 303 subjects (55.12% Female). Short-term BP variability was calculated as the standard deviation (SD) of 24-hour, daytime, or nighttime BP, and as weighted SD of 24-hour BP defined as the mean of daytime and nighttime BP SD weighted by the duration of each time period. Carotid – femoral pulse wave velocity (PWV) were evaluated by means of pulse wave analysis.

**Results:** In the study group the SD of day- and nighttime Systolic BP (SBP), SD of 24-hour SBP and weighted SD of 24-hour SBP showed a significant association with PWV (P<0.003). Above-mentioned SBP variability indices except SD of night SBP independently predicted PWV along with age, gender, 24-hour SBP and antihypertensive treatment. None of the examined measures of diastolic BP variability had a relation with carotid-femoral PWV.

**Conclusions:** Short-term variability of systolic blood pressure shows an independent relation to aortic stiffness in general population. Our study confirms that those parameters are closely related.

**P4.11**  
**ENDOTHELIAL DYSFUNCTION IN URBANIZED AFRICANS WITH LOW PLASMA RENIN LEVELS: THE SABPA STUDY**

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**Background and objectives:** It is known that high renin levels could damage the vasculature and may cause retinal detachment, stroke, heart failure and kidney failure. The objective of this part of the SABPA study was to determine if renin levels in low and high renin participants could contribute to endothelial dysfunction.

**Methods:** This part of the SABPA study consisted of 113 black urbanized Africans (men and women) from the same socio-economic status (school teachers) from South Africa. The participants were stratified into low (<6.18 pg/ml) and high ( $\geq$ 6.18 pg/ml) renin levels. Blood pressure and other variables were determined with known methods. Active renin levels were determined with a radio-immunometric assay (Renin III Generation, CIS bio-international, Cedex, France). The Von Willebrand Factor (vWF) was analysed with ELISA assay. (DAKO, SA). A calorimetric method were used for urine creatinine and a turbidimetric method for albumin measurement.

**Results:** In single regression analysis, renin levels associated negatively with the Von Willebrand Factor ( $r = -0.3756$ ;  $p = 0.016$ ) only in the low renin African men. With partial regression analysis after adjustment for age and BMI, the association remained. Renin levels also associated negatively ( $r = -0.4846$ ;  $p = 0.002$ ) with systolic blood pressure only in low renin men. No associations could be encountered with markers of inflammation (IL-6; CRP and TNF- $\alpha$ ) as well as stiffness.

**Conclusion:** The results revealed that renin causing endothelial dysfunction in low renin African men and may lead to high blood pressure in later life.

**P4.12**  
**REFERENCE VALUES OF CENTRAL BLOOD PRESSURE IN ADULTS USING A VALIDATED NON-INVASIVE OSCILLOMETRIC METHOD**

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Central systolic pressure (csBP) is strongly correlated with cardiovascular outcomes than brachial pressure. However, until recently there weren't widely accepted reference values of csBP established yet. The aim of this work was to determine this missing values of csBP assessed by oscillometric method. Patients and methods: csBP was assessed in apparently healthy, asymptomatic patient population using an invasively validated oscillometric device (TensioMed Arteriograph). The collected database was divided into age decades in order to determine the age-specific reference values. Statistical analysis was carried out with IBM SPSS 20 statistical software. Results: 9076 normotensive subject aged 18-90 years (3749 male and 5327 female) without any medication were included into the analysis. Mean csBP values were determined (109.26  $\pm$  7.92 mmHg, 109.45  $\pm$  9.09 mmHg, 112.01  $\pm$  9.69 mmHg, 115.88  $\pm$  10.47 mmHg, 119.23  $\pm$  10.56 mmHg, 121.04  $\pm$  10.9 mmHg, 122.65  $\pm$  11.27 mmHg and 122.65  $\pm$  11.96 mmHg from the age of 18 to 90, respectively). Conclusions: This is the first study providing large number of csBP values measured with arteriograph derived from a healthy general population including wide range of age. Our results suggest that csBP values are highly dependent on age, therefore these results might serve as age-specific reference values for oscillometrically measured csBP.

**P4.13**  
**HERITABILITY AND OTHER DETERMINANTS OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN THE FAMILY-BASED POPULATION STUDY**

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**Background:** Understanding to what extent genetic factors influence diastolic Doppler indexes is an important issue in view of the relation of left ventricular (LV) diastolic dysfunction with outcome. We, therefore, investigated in nuclear families recruited from the general population the heritability of LV diastolic traits and the composite diastolic score.

**Methods and results:** A random sample of 316 nuclear families (452 parents and 600 offspring, mean age, 58.5 and 33.3 years) was recruited in Belgium, Poland, Italy and Russia. We measured transmitral early and late diastolic velocities (E and A) by pulsed wave Doppler, and mitral annular velocities (E' and A') by tissue Doppler. Using principle component analysis, we summarized 5 Doppler indexes – namely, E, A, E' and A' velocities, and E/E' – into a single diastolic score. To calculate the heritability of diastolic indexes, we used (1) the regression slope of offspring on mid-parent residual values, (2) variance decomposition in siblings. The parent-offspring concordances of all diastolic indexes were significant and ranged from 0.17 for A ( $P = 0.009$ ) to 0.42 for E' ( $P < 0.0001$ ). In variance decomposition analyses in sibships, the abovementioned traits with adjustment for covariables had moderate heritability in a range of 0.12-0.31 ( $P \leq 0.01$ ). Among the parent-offspring pairs and sibships, the heritability estimates of the composite diastolic score were 0.39 and 0.27, respectively ( $P < 0.0001$ ).

**Conclusions:** Our study demonstrated moderate heritability of various indexes reflecting LV diastolic function in nuclear families. The observation highlights the necessity of further research into the genes that affect LV diastolic function.

**P4.14**  
**PREVALENCE OF DIASTOLIC LEFT VENTRICULAR DYSFUNCTION IN EUROPEAN POPULATIONS BASED ON CROSS-VALIDATED DIAGNOSTIC THRESHOLDS**

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**Objective:** Different diagnostic criteria limit comparisons between populations in the prevalence of diastolic left ventricular (LV) dysfunction. We aimed to compare across populations age-specific echocardiographic criteria for diastolic LV dysfunction as well as their correlates and prevalence.

**Methods:** We measured the E and A peaks of transmitral blood flow by pulsed wave Doppler and the e' and a' peaks of mitral annular velocities by tissue Doppler imaging (TDI) in 2 cohorts randomly recruited in Belgium ( $n = 782$ ; 51.4% women; mean age, 51.1 years) and in Italy, Poland and Russia ( $n = 476$ ; 55.7%; 44.5 years).

**Results:** In stepwise regression, the multivariable-adjusted correlates of the transmitral and TDI diastolic indexes were similar in the 2 cohorts and included sex, age, body mass index, blood pressure and heart rate. Similarly, cutoff limits for the E/A ratio (2.5th percentile) and E/e' ratio (97.5th percentile) in 338 and 185 reference subjects free from cardiovascular risk factors respectively selected from both cohorts were consistent within 0.02 and 0.26 units (median across 5 age groups). The rounded 2.5th percentile of the E/A ratio decreased by  $\sim 0.10$  per age decade in these apparently healthy subjects. The reference subsample provided age-specific cut-off limits for normal E/A and E/e' ratios. In the 2 cohorts combined, diastolic dysfunction groups 1 (impaired relaxation), 2 (possible elevated LV filling pressure) and 3.

**Conclusion:** The age-specific criteria for diastolic LV dysfunction were highly consistent across populations with an age-standardized prevalence of 22.4% vs. 25.1% ( $P = 0.09$ ).