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### **P.070: ARTERIAL STIFFNESS ALTERATIONS DURING HEMODIALYSIS**

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## P.066

## PERIPHERAL VASCULAR DISEASE IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS

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**Objective:** Aortic pulse wave velocity (aPWV) is a powerful and independent predictor of all cause cardiovascular mortality. Patients with peripheral vascular disease (PVD) are at a higher risk of cardiovascular events. We hypothesized that patients with PVD would have a higher aPWV than age-matched healthy controls, and that aPWV would be inversely related to ankle brachial pressure index (ABPI).

**Methods:** We studied 212 patients with PVD (mean age 71 ± 9 years, 68% male) with a mean ABPI of 0.64 ± 0.16 and 455 age-matched controls (mean age 70 ± 7 years, 64% male). Aortic augmentation index (AIx) augmentation pressure (AP) and central blood pressure were determined by pulse wave analysis using the SphygmoCor<sup>®</sup> system. PWV was derived using sequential carotid to femoral waveform recordings for aPWV and carotid and radial waveforms for brachial PWV.

**Results:** aPWV was significantly higher in patients with PVD compared with age-matched controls. (11.7 ± 3.5 vs. 9.9 ± 2.6m/s,  $P < 0.0001$ ). Both peripheral and central, systolic and pulse pressures were significantly higher in the PVD group compared to age-matched controls. AP was higher in the PVD group (19 ± 10 vs. 14 ± 7mmHg) but AIx was not. The difference in aPWV persisted after correction for mean arterial pressure (10.57 ± r 2.31 vs. 9.02 ± r 3.46,  $P < 0.0001$ ). In regression model, age, mean pressure, diabetes and previous myocardial infarction predicted aPWV ( $r = 0.6$ ,  $p < 0.001$ ). aPWV was inversely associated with ABPI ( $R^2 = -0.19$ ,  $P < 0.0001$ ).

**Conclusions:** The increased aortic stiffness provides a possible explanation for the increased cardiovascular events seen in PVD patients but exact mechanisms underlying this need to be addressed.

## P.067

## EFFECTS OF INHIBITION OF AUTONOMIC NERVOUS SYSTEM ON AORTIC STIFFNESS FOLLOWING SYSTEMIC INFUSION OF GLYCERYL TRINITRATE IN HEALTHY VOLUNTEERS

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**Objective:** Nitric oxide (NO) contributes to smooth muscle tone relaxation, however, in humans the role of smooth muscle tone and NO in regulating aortic stiffness is controversial. We hypothesized that the nitric oxide donor GTN would reduce aortic PWV in vivo, but this effect would be partly attenuated by reflex activation of the sympathetic nervous system. The aim of this study was to investigate whether the autonomic nervous system (ANS) masked any effect of NO on aortic stiffness.

**Methods:** 10 healthy subjects; mean age, 28 ± 6 years were studied on two visits, in a double-blinded, placebo controlled 2-way crossover design. On both visits, subjects were randomly selected to have either a bolus administration of pentolinium (ganglion blocker) or placebo followed by an infusion of GTN or placebo. The opposite arm of the study was then carried out following a 60 minute break.

Heart rate variability, blood pressure, cardiac haemodynamics, brachial and aortic pulse wave velocity (PWV) were measured at regular intervals throughout the study.

**Results:** The main findings from this study were that incremental doses of GTN led to a significant 9% fall in brachial PWV ( $P < 0.0001$ ), with no effect on aortic PWV. Despite blockade of the ANS, aPWV remained unaffected by incremental doses of GTN.

**Conclusions:** The major findings were that despite blockade of the both the parasympathetic and sympathetic nervous system, subsequent systemic infusion of GTN had null effect on aortic pulse wave velocity suggesting that there are other mechanisms involved in the regulation of aortic stiffness.

## P.068

## A NON-INVASIVE APPROACH TO QUANTIFY VENTRICULAR-ARTERIAL INTERACTION: COMPARING VASCULAR TYPE EHLERS-DANLOS SYNDROME PATIENTS AND NORMAL INDIVIDUALS

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**Introduction:** We hypothesized that the pressure rate ratio (PRR), defined as the arterial upstroke  $dP/dt$  normalized by isovolumic ventricular  $dP/dt$ , is less sensitive to inter-subject variance and therefore better in identifying individuals with abnormal ventricular-arterial function than single hemodynamic parameters.

**Methods:** We studied the characteristics of PRR in 21 normals (age-range 19-32 yrs) and 7 age-matched vascular type (IV) Ehlers-Danlos syndrome (EDS) patients. ECG, brachial pressure and right common carotid artery (CCA) diameter waveforms (M-mode ultrasound) were obtained in supine position. LV systolic time intervals, i.e. isovolumic-contraction (ICP) and ejection periods (EP), were extracted from diameter waveforms using a previously described algorithm. We calculated diastolic blood pressure-to-ICP ratio (DBP/ICP), ICP/EP, CCA-distension ( $\Delta D$ ), diastolic diameter (Dd), maximum diameter velocity ( $dD/dt, \max$ ), and distensibility (DC) and compliance (CC) coefficients. PRR was defined as  $100\% \cdot (K \cdot dD/dt, \max) / (DBP/ICP)$ , with  $K = (\text{mean blood pressure} - DBP) / (\text{mean diameter} - Dd)$ . Results are given as mean ± SD.

**Results:** EDS subjects had higher heart rate (+9bpm,  $p = 0.045$ ), but lower  $\Delta D$  ( $0.62 \pm 0.11$  vs  $0.74 \pm 0.15$ mm,  $p = 0.027$ ) and DC ( $33 \pm 8$  vs  $41 \pm 9$ /MPa,  $p = 0.055$ ). All other variables, including PRR ( $26 \pm 7$  vs  $27 \pm 6\%$ ), were not significantly different between groups, reflecting similar ventricular-arterial interaction. With both groups pooled, two individuals presented with elevated PRR (40%). In a normal subject (age 20 yrs) this was associated with abnormally low sympathetic activity. The other subject (EDS, age 24 yrs) exhibited increased sympathetic activity and decreased DC (20/MPa), shorter EP (-10%) and depressed LV function.

**Conclusions:** Our findings suggest that PRR enables identification of individuals with abnormal ventricular-arterial function in a heterogeneous population.

## P.069

## OSTEOPOROSIS IS ASSOCIATED WITH INCREASED AORTIC PULSE WAVE VELOCITY

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**Objective:** Arterial stiffening and osteoporosis both occur predominantly in late life. Osteoporosis has been associated with increased peripheral pulse pressure and arterial stiffness, but its effect on aortic pulse wave velocity (aPWV) is unclear. The aim of this study was to examine the relationship between arterial calcification and aPWV in healthy subjects and a cohort of patients with osteoporosis.

**Methods:** aPWV and bone mineral density (BMD) were measured non-invasively in 42 patients with osteoporosis and 120 healthy volunteers. Subjects with cardiovascular disease, renal disease or hypertension were excluded. aPWV was assessed using the SphygmoCor system, and vertebral / hip BMD from thoraco-lumbar CT images, using Mindways software.

**Results:** The mean ± SD aPWV was significantly higher in patients with osteoporosis than controls ( $9.6 \pm 2.9$  vs  $8.2 \pm 1.7$  m/s;  $P = 0.01$ ). Brachial PWV and augmentation index did not differ. Although mean arterial pressure did not differ between the groups, peripheral and central pulse pressures were significantly higher in the osteoporotics (by  $6 \pm 2$  and  $5 \pm 2$  mmHg respectively;  $P > 0.01$  for both). In pooled data for osteoporosis patients and controls, aortic PWV correlated inversely with T-score ( $r = -0.27$ ,  $P = 0.001$ ).

**Conclusion:** Patients with osteoporosis have increased aortic stiffness compared with healthy volunteers, independent of their mean arterial pressure. We speculate that arterial calcification may be involved in the development of arterial stiffness and osteoporosis.

## P.070

## ARTERIAL STIFFNESS ALTERATIONS DURING HEMODIALYSIS

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Arterial stiffness is an independent predictor of cardiovascular morbidity and mortality in hemodialysis (HD) patients. Determinants of arterial stiffness and its change during HD are not well characterized, and it is not known if parameters of calcium-phosphate metabolism predict arterial wall properties.

We measured carotid-femoral pulse wave velocity (PWV) and carotid augmentation index (AI) before and after HD in 96 chronic HD patients using the PulsePen device. Detailed medical history was taken and blood drawn for routine biochemistry before and after HD. Determinants of PWV and AI and their corresponding changes during HD were assessed by stepwise forward multivariate linear regression models.

Mean pre- and postdialysis PWV was  $11.0 \pm 2.9$  and  $11.6 \pm 2.9$  m/s ( $P=0.004$ ) respectively. Mean pre- and postdialysis AI was  $23.5 \pm 12.2$  and  $22.1 \pm 12.4\%$  ( $P=NS$ ). Significant and independent predictors of predialysis PWV ( $R$  for the whole model = 0.79) were higher age, systolic blood pressure and CRP level, lower serum sodium level, and the presence of peripheral artery disease. Predictors of predialysis AI ( $R=0.42$ ) were higher systolic blood pressure and higher time averaged creatinine value. The increase in PWV during dialysis was independently associated ( $R=0.53$ ) with lower predialysis PWV, higher baseline heart rate, higher urea level and systolic blood pressure change during dialysis. Change in AI during dialysis was significantly and negatively associated ( $R=0.55$ ) with predialysis AI and the heart rate change during dialysis.

Our results confirm previously described predictors of PWV and AI. Parameters of calcium-phosphate metabolism do not seem to influence arterial stiffness before or after dialysis. The relation of serum sodium level to predialysis PWV may imply volume overload that is to be explored.

#### P.071

##### METABOLIC SYNDROME DEFINITIONS AND VASCULAR PHENOTYPE

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**Background:** The increasing prevalence of obesity has recently become a major public health concern. Controversy has arisen regarding how best to characterise this risk with several definitions of a "metabolic syndrome" (MS) proposed to identify those at greatest risk. Controversy has arisen regarding the ability of these definitions to predict cardiovascular risk. We assessed the relationship between MS criteria and arterial phenotype in a large population based cohort.

**Methods:** 3437 British civil servants aged 51-74 who were free from clinical cardiovascular disease and diabetes mellitus were studied (Whitehall II study). RFs were measured and carotid intima-media thickness (cIMT) assessed. Participants were categorised into 3 groups according to IDF and ATP<sub>III</sub> criteria; Groups 1 (no MS;  $n=2712$ ); 2 (MS by IDF criteria only;  $n=349$ ); 3 (MS by ATP<sub>III</sub> only or both ATP<sub>III</sub> and IDF criteria;  $n=376$ ).

**Results:** cIMT was increased in groups 2 and 3 compared to controls (both  $p<0.001$ ). These differences remained after adjusting for other RFs. Groups 2 and 3 had similar cIMT. In addition, non obese participants with one or more MS risk factors (defined by IDF criteria) had significantly greater cIMT compared to controls ( $p<0.001$ ), an association that remained after further adjustment for RFs.

**Conclusion:** MS, defined by both ATP<sub>III</sub> and the recent IDF criteria, identifies a population with increased cIMT. However, we also show that restricting the diagnosis of MS to those with abdominal obesity, as recommended by the IDF, may miss an important population with MS risk factors who have an adverse vascular phenotype.

#### P.072

##### PARENTAL SMOKING AND VASCULAR DAMAGE IN YOUNG ADULT OFFSPRING: IS EARLY LIFE EXPOSURE CRITICAL? THE ATHEROSCLEROSIS RISK IN YOUNG ADULTS STUDY

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**Background:** little is known of the consequences of tobacco smoking in pregnancy for cardiovascular risk in offspring.

**Objectives:** To estimate the association between foetal tobacco smoke exposure and vascular damage in young adulthood.

**Participants:** A birth cohort of 732 young adults born between 1970-1973.

**Measures:** Registered pregnancy and birth data, anthropometry and cardiovascular risk profiles in young adulthood, including ultrasound measurement of common carotid artery intima-media thickness (CIMT). Pregnancy and current smoking habits data of parents were obtained by standardized questionnaires.

**Results:** Twenty nine percent of the mothers reported to have smoked during their pregnancy. Adult offspring of mothers who smoked had  $13.4 \mu\text{m}$  thicker CIMT (95% CI: 5.5, 21.3;  $p=0.001$ ) than offspring of mothers who did not smoke in pregnancy. Adjustment for known CIMT risk factors (participant's age, gender, BMI, pulse pressure, and LDL-cholesterol) did not abolish this estimate ( $9.4 \mu\text{m}$ , 95% CI: 1.9, 16.3;  $p=0.01$ ). Similarly, adjustment for current smoking of parents did not change the association ( $10.6 \mu\text{m}$ , 95% CI: 0.4, 20.8;  $p=0.04$ ) nor did adjustment for participants' current smoking (yes/no) and pack-years ( $11.5 \mu\text{m}$ , 95% CI: 3.5, 19.4;  $p=0.004$ ). Offspring of parents who both smoked in pregnancy had thicker CIMT than offspring with one or no smoking parent ( $p$  linear trend  $<0.0001$ ), and offspring of particularly mothers who smoked an above median number of cigarettes in pregnancy had thicker CIMT than those smoking less than median or no cigarettes ( $p$  linear trend  $<0.0001$ ).

**Conclusion:** Permanent vascular damage due to tobacco smoke exposure is initiated in gestation.

#### P.073

##### LONGITUDINAL DEVELOPMENT OF WAIST AND HIP CIRCUMFERENCES: INDEPENDENT AND OPPOSITE ASSOCIATIONS WITH PRE-CLINICAL ATHEROSCLEROSIS. THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY

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**Introduction:** Anthropometric measures of body fat distribution have shown that waist (WC) and hip (HC) circumferences have opposite and independent associations with atherosclerotic risk factors and disease. However, this evidence is confined to cross-sectional studies only. How the development over time of these anthropometric measures impact on pre-clinical atherosclerosis is not known.

**Methods:** Longitudinal data on WC and HC were derived from the Amsterdam Growth and Health Longitudinal Study ( $n=372$ , 197 women; 3 follow-up measures at the ages of 27, 32 and 36 yrs). Carotid intima-media thickness (IMT), a marker of pre-clinical atherosclerosis, was assessed by non-invasive ultrasonography when subjects were 36-yrs-old. We used generalized estimating equations to compare the patterns of development of WC and HC (adjusted for each other and for potential confounders – i.e. physical fitness, alcohol and smoking habits) over the 9-yr follow-up period between those subjects with 'high' (highest sex-specific quartile) vs. 'normal' (lower 3 quartiles) of carotid IMT at the age of 36 yrs.

**Results:** In men, WC increased and HC decreased significantly between the ages of 27 and 36 ( $p<0.001$ ), but no differences in these longitudinal patterns of development were found between those with 'high' vs. normal carotid IMT at age 36. In women, however, the increase in WC was 3.47 cm (0.98 to 5.96) greater in those with 'high' vs. 'normal' IMT; in addition, the HC decreased considerably more in those with 'high' vs. 'normal' IMT [-3.60 cm (-6.54 to -0.65)].

**Conclusion:** The development of broader waist (possibly reflecting accumulation of abdominal fat throughout the years) and narrower hip circumferences (reflecting loss of peripheral fat and/or muscular mass) during young adulthood are independent determinants of pre-clinical atherosclerosis, particularly in women.

#### P.074

##### EFFECT OF SMOKING ON ARTERIAL STIFFNESS IN PATIENTS WITH WHITE COAT HYPERTENSION

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**Background:** Patients with essential hypertension have higher arterial stiffness indices, while smoking is related to a stiff vascular tree. However,