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### **P.075: PREDICTORS OF LARGE ARTERIAL STIFFENING AND WAVE REFLECTIONS IN DIABETES: THE EFFECTS OF AUTONOMIC NEUROPATHY AND ERECTILE DYSFUNCTION**

S. Bunce, A. Stride, C. Matthews, J.C. Smith\*

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**Methods:** Forearm flow-mediated dilatation (FMD) was used as a measure of endothelial nitric oxide (NO)-dependent vasodilation, and brachial artery dilation in response to sublingual glyceryl trinitrate (GTN 25 µg) was used to assess endothelial-independent dilation. Carotid intima media thickness (IMT) and pulse wave velocity (PWV), an index of arterial stiffness, was assessed using the Sphygmocor® system. All data were expressed as mean±SEM.  $P < 0.05$  (two tailed) was taken as indicating statistical significance.

**Results:** We studied 20 patients with HF (IHD-14 & DCM-6) and 24 controls of similar age and sex. Patients were studied on usual medication. FMD was impaired in patients with HF compared to controls ( $4.4 \pm 0.6\%$  vs.  $6.6 \pm 0.6\%$ ,  $p = 0.025$ ), whereas GTN-induced dilatation was similar to controls ( $10.9 \pm 0.9\%$  vs.  $11.1 \pm 1.4\%$ ). IMT was higher in HF patients ( $1.19 \pm 0.09$  mm vs.  $0.83 \pm 0.04$  mm,  $p = 0.0008$ ), and PWV was greater in patients with HF ( $10.7 \pm 1.1$  m/s vs.  $8.5 \pm 0.4$  m/s,  $p = 0.048$ ). In subgroup analysis of the HF subjects, IMT was elevated specifically in the patients with IHD ( $1.16 \pm 0.03$  mm vs.  $0.80 \pm 0.04$  mm in controls,  $p < 0.01$ ) but not in those with DCM ( $0.96 \pm 0.11$  mm vs.  $0.81 \pm 0.05$  mm in controls,  $p > 0.05$ ); furthermore, the patients with IHD had higher PWV ( $11.5 \pm 1.3$  m/s vs.  $8.9 \pm 0.3$  m/s in controls,  $p < 0.01$ ), whereas those with DCM did not ( $8.1 \pm 0.6$  m/s vs.  $8.9 \pm 0.3$  m/s in controls,  $p > 0.05$ ). FMD impairment was similar in IHD and DCM subjects.

**Conclusions:** Patients with HF have endothelial dysfunction as well as elevated arterial stiffness and increased IMT, and that the latter two changes are seen specifically in patients whose HF is secondary to IHD.

#### P.075

##### PREDICTORS OF LARGE ARTERIAL STIFFENING AND WAVE REFLECTIONS IN DIABETES: THE EFFECTS OF AUTONOMIC NEUROPATHY AND ERECTILE DYSFUNCTION

S. Bunce, A. Stride, C. Matthews, J.C. Smith\*. *Department of Diabetes & Endocrinology, Torbay Hospital, Torquay, Devon, United Kingdom*

**Background and Aim:** Premature arterial stiffening (AS) may contribute to macrovascular complications in diabetes. Cardiovascular autonomic neuropathy (CAN) and erectile dysfunction (ED) are also associated with adverse cardiovascular outcomes. The aim of this observational study was to investigate the relationships between CAN, ED and AS in men with diabetes.

**Methods:** Thirty male subjects with diabetes (type 1 and 2) (age range 39-74 yrs) but without overt cardiovascular disease were studied. AS and wave reflections were assessed by measuring pulse wave velocity (PWV) (carotid-femoral [cf] and carotid-radial [cr]) and augmentation index (AIX) (Sphygmocor). Cardiovascular autonomic function was assessed by measures of blood pressure and heart rate variability during continuous ECG recording following standard postural and breathing manoeuvres. Erectile function was evaluated using the validated International Index of Erectile Function IIEF-5 questionnaire.

**Results:** (Mean±SD); Comparing subjects with CAN (n=16) versus subjects without CAN (n=14), cfPWV was higher ( $10.8 \pm 2.8$  m/s vs  $8.9 \pm 1.5$  m/s,  $p < 0.05$ ) despite no differences in age, brachial blood pressure, erectile function, crPWV or AIX. Comparing subjects with severe ED (n=17) versus normal erectile function (n=13) there were no differences in arterial function despite higher systolic and diastolic blood pressure in subjects with severe ED. Multiple regression analysis ( $R^2 = 0.83$ ,  $p < 0.01$ ) identified CAN (autonomic score) ( $\beta = 0.66$ ,  $p = 0.01$ ) and ED (IIEF score) ( $\beta = -0.62$ ,  $p = 0.014$ ) as independent predictors of cfPWV but not of crPWV or AIX.

**Conclusion:** Both CAN and ED are independently associated with increased aortic stiffness in diabetes. CAN appears the stronger predictor and may exert a pathophysiological role in the process of aortic stiffening.

#### P.076

##### VENTRICULAR-ARTERIAL COUPLING IN A RAT MODEL OF REDUCED ARTERIAL COMPLIANCE

N. Stergiopoulos<sup>1</sup>\*, D. Jegger<sup>1</sup>, R. Da Silva<sup>1</sup>, I. Lartaud<sup>2</sup>, J. Atkinson<sup>1</sup>, L. von Segesser<sup>1</sup>. <sup>1</sup>EPFL, Lausanne, Switzerland, <sup>2</sup>University of Nancy, Nancy, France, <sup>3</sup>CHUV, Lausanne, Switzerland

Rodent models of isolated systolic hypertension (ISH) are rare. One exception is the vitamin D and nicotine (VDN) model, in which arterial calcification raises arterial stiffness and vascular impedance. Complete analysis of the effect of VDN on ventricular-arterial interaction is lacking. Wistar rats were treated with VDN (VDN group, n=9) and a control untreated group (CTRL, n=10) was included. At sacrifice, invasive indexes of cardiac function were obtained using a conductance catheter. Aortic pressure and flow were measured to derive impedance and ventricular-arterial interaction. VDN caused significant increases in systolic ( $138 \pm 6$  mmHg vs.  $116 \pm 13$  mmHg) and pulse pressure ( $42 \pm 10$  mmHg vs.  $26 \pm 4$  mmHg). Arterial compliance decreased ( $0.12 \pm 0.08$  ml/mmHg vs.  $0.21 \pm 0.04$  ml/mmHg CTRL) and pulse

wave velocity increased significantly ( $8.8 \pm 2.5$  m/s vs.  $5.1 \pm 2.0$  m/s CTRL). Elastic modulus rose in the VDN group. Preload recruitable stroke work and end-systolic elastance were both elevated in the VDN group thus decreasing the ratio of arterial elastance over end-systolic elastance ( $0.94 \pm 0.30$  vs.  $1.57 \pm 0.60$  CTRL). Wave reflection was augmented in the VDN group, expressed by the increase in the wave reflection coefficient ( $0.63 \pm 0.06$  vs.  $0.52 \pm 0.05$  CTRL), as well as the amplitude of the reflected pressure wave ( $13.3 \pm 3.1$  mmHg vs.  $8.4 \pm 1.0$  mmHg CTRL). VDN lead to development of ISH and provoked alterations in cardiac function, arterial impedance, arterial function, and ventricular-arterial interaction, which in many aspects are similar to effects of an aged and stiffened arterial tree. The VDN model may be a useful model to study the patho-physiological effects of increased arterial stiffness.

#### P.077

##### ARTERIAL WALL REMODELING USING A CONSTITUENT-BASED MODEL

N. Stergiopoulos\*, M. Zulliger, S. Roy, E. Fonck, R. Rezakhanliha, A. Tsamis. EPFL, Lausanne, Switzerland

Earlier studies in experimental hypertension have shown that acute hypertension leads to wall remodelling, which, in general, aims in restoring mean wall stress to control levels. This postulate has not been yet thoroughly studied, mainly because precise knowledge of stresses acting on each wall constituent and in all parts of the wall is still a difficult task. This requires a constituent-based modelling and analysis of the arterial wall. The three-dimensional biomechanical behavior of the vascular wall is best described by means of strain energy functions, which allow for the analysis of stresses over a wide range of deformations. The Zulliger et al. model developed by our group uses a strain energy function, which accounts for the constituents and structural properties of the wall (i.e., collagen, elastin and vascular smooth muscle as well as a statistical description for collagen engagement). The Zulliger et al. model was subsequently challenged by the work of Roy et al., which showed that significant residual stresses are released when the arterial wall is decellularized, suggesting an in-series arrangement of the VSM with elastin. The in-series elastin would be in tension, whereas the in-parallel elastin would be in compression. Upon VSM disruption, the in-series elastin cannot bear tension anymore and thus the compressed elastin expands relieving the additional residual strains. Treatment with Cytochalasin D partially destroys stress fibres and disengages the VSM cytoskeleton, leading to further release of residual stresses and to a more compliant wall, all being consistent with the model of Roy et al.

#### P.078

##### REFERENCE VALUES IN WHITE EUROPEANS FOR THE ARTERIAL PULSE WAVE RECORDED BY MEANS OF THE SPHYGMOCOR DEVICE

W. Wojciechowska<sup>1</sup>\*, J.A. Staessen<sup>2</sup>, T. Nawrot<sup>2</sup>, M. Cwynar<sup>3</sup>, J. Kucerova<sup>4</sup>, K. Stolarz<sup>1</sup>, J. Gasowski<sup>3</sup>, M. Tichá<sup>4</sup>, L. Thijs<sup>2</sup>, T. Grodzicki<sup>3</sup>, K. Kawecka-Jaszcz<sup>1</sup>, J. Filipovsky<sup>4</sup>. <sup>1</sup>First Cardiac Department, Jagiellonian University Medical College, Krakow, Poland, <sup>2</sup>Study Coordinating Centre, Hypertension and Cardiovascular Rehabilitation Unit, Department of Molecular and Cardiovascular Research, University of Leuven, Leuven, Belgium, <sup>3</sup>Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Krakow, Poland, <sup>4</sup>Department of Internal Medicine II, Charles University Medical School, Pilsen, Czech Republic

**Aim:** Measurement of blood pressure together with applanation tonometry at the radial artery allows the reproducible assessment of various indexes of arterial stiffness, including the peripheral (PPp) and central (PPc) pulse pressures and the peripheral (Alp) and central (Alp) augmentation indexes. We defined preliminary diagnostic thresholds, using the distributional characteristics of these haemodynamic measurements in a reference population.

**Methods:** We randomly recruited 870 subjects from 3 European populations. PPp was the average difference between systolic and diastolic BP measured five times. For measurement of PPc, Alp and Alc, we used the SphygmoCor device. We selected subjects without hypertension, diabetes, dyslipidemia or previous and concomitant cardiovascular disease.

**Results:** Study population included 228 men and 306 women (mean age 34.9 years). All haemodynamic measurements were curvilinearly related to age and Alp and Alc were lower in men than in women. In men at age 40, the upper 95% prediction bands of the relations of the haemodynamic measurements with age approximated to 60 mmHg for PPp, 40 mmHg for PPc, 90% for Alp, and 30% for Alc. For PPc, Alp and Alc, these thresholds must be adjusted for age, leading to more lower and higher thresholds at younger and older age, respectively. In addition, in women of any age, the Alp and Alc thresholds must be increased by 10% and 7%, respectively.

**Conclusion:** Pending validation in prospective outcome studies, distributional characteristics of arterial stiffness indexes in a reference population can be used to generate operational thresholds for use in clinical practice.