P.077: ARTERIAL WALL REMODELING USING A CONSTITUENT-BASED MODEL

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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 dilatation in response to sublingual glyceryl trinitrate (GTN 25 μg) was used to assess endothelial-independent dilatation. 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: 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±0.6% vs. 6.6±0.6%, p = 0.025), whereas GTN-induced dilatation was similar to controls (10.9±0.9% vs. 11.1±0.6%). IMT was higher in HF patient (1.19±0.09 mm vs. 0.83±0.04 mm, p = 0.008), and PWV was greater in patients with HF (10.7±1.1 m/s vs. 8.5±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±0.03 mm vs. 0.80±0.04 mm in controls, p = 0.01) but not in those with DCM (0.96±0.11 mm vs. 0.81±0.05 mm in controls, p = 0.05); furthermore, the patients with HF had higher PWV (11.5±1.3 m/s vs. 8.9±0.3 m/s in controls, p = 0.01), whereas those with DCM did not (8.1±0.6 m/s vs. 8.9±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 REFECTIONS IN DIABETES: THE EFFECTS OF AUTONOMIC NEUROPATHY AND ERECTILE DYSFUNCTION
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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 whether CAN (carotid-femoral [cf] and carotid-radial [cr]) and augmentation index (Alx) (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±2.8 m/s vs. 8.9±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 = 31) there were no differences in arterial function despite higher systolic and diastolic blood pressure in subjects with severe ED. Multiple regression analysis (R²=0.83, p = 0.01) identified CAN (autonomic score) (β=0.66, p = 0.01) and ED (IIEF score) (β=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 arterial 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
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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. Mice 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±6 mmHg vs. 116±13 mmHg) and pulse pressure (42±10 mmHg vs. 26±4 mmHg). Arterial stiffness decreased (0.12±0.08 mm Hg/ml vs. 0.21±0.04 mm Hg/ml and control) and pulse wave velocity increased significantly (8.8±2.5 m/s vs. 5.1±2.0 mm/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±0.30 vs. 1.57±0.60 CTRL). Wave reflection was augmented in the VDN group, expressed by the increase in the wave reflection coefficient (0.63±0.06 vs. 0.52±0.05 CTRL), as well as the amplitude of the reflected pressure wave (13.3±3.1 mmHg vs. 8.4±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
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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 tends to be released, while bearing a non-constant shearing load. This results in residual radii that differs in various lengths. 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
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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 (AIC) 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. Pp was the average difference between systolic and diastolic BP measured five times. For measurement of Pp, 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 approached to 60 mmHg for Pp, 40 mmHg for PPc, 90% for Alp, and 30% for Alc. For Pp, Alp and Alc, these thresholds must be adjusted for age, leading to lower and higher thresholds at younger and older age, respectively. In addition, in women of any age, the Alp and Alc thresholds were 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.