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4.5: LOCALISED MICROMECHANICAL REMODELLING OF THE AORTA IN A MODEL OF TYPE 1 DIABETES

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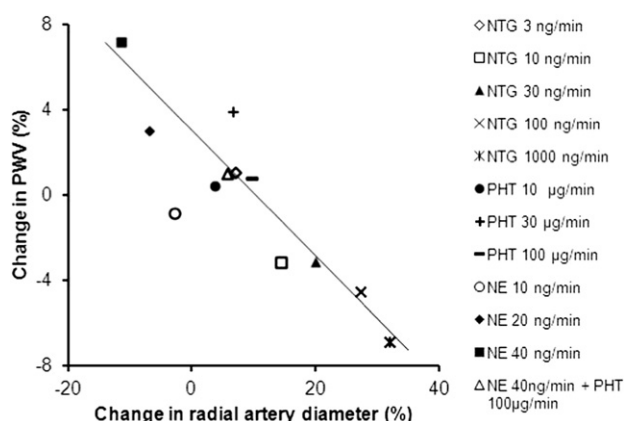
4.4

MODULATION OF ARTERIAL TONE INFLUENCES PULSE WAVE VELOCITY IN PROPORTION TO CHANGE IN ARTERIAL DIAMETER

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Nitric oxide (NO) is known to influence muscular conduit artery pulse wave velocity (PWV). Whether these changes are mediated exclusively by NO or may be a general consequence of a change in arterial tone is unknown. The aim of this study was to examine changes in local PWV over a range of arterial tone modulated by vasoconstrictor/dilator drugs. Healthy normotensive men ($n=7$) aged 19-53 years were studied. The right brachial artery was cannulated using a 27 gauge needle. Nitroglycerin (NTG 0.03, 0.1, 0.3, 1 $\mu\text{g}/\text{min}$), phentolamine (PHT 10, 30, 100 $\mu\text{g}/\text{min}$) and (NE 0.01, 0.02, 0.04 $\mu\text{g}/\text{min}$) alone and with PHT (100 $\mu\text{g}/\text{min}$) were infused intra-arterially on separate occasions. Radial artery diameter (RAD) was measured by high resolution ultrasound; PWV was measured over the brachial to radial path by simultaneous recording from brachial and radial blood pressure cuffs inflated to 60 mmHg. The path distance was taken from the proximal edge of the upper arm cuff to that of the wrist cuff. NE (0.04 $\mu\text{g}/\text{min}$) reduced RAD by $11.4 \pm 4.1\%$ but when co-infused with PHT (100 $\mu\text{g}/\text{min}$) increased RAD by $5.8 \pm 3.5\%$. NTG (1 $\mu\text{g}/\text{min}$) increased RAD by $(32.1 \pm 5.4\%)$. Over this range of arterial tone, changes in PWV were closely related to those in RAD (figure, $R = -0.89$; $P < 0.05$). This suggests that, under physiological conditions, PWV in muscular arteries is determined by smooth muscle tone rather than being influenced by a specific signalling pathway.



4.5

LOCALISED MICROMECHANICAL REMODELLING OF THE AORTA IN A MODEL OF TYPE 1 DIABETES

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Whilst altered arterial stiffness is a hallmark of diabetes, the causative mechanisms and molecular targets remain poorly defined. Using a streptozotocin (STZ)-induced rat model of type 1 diabetes we have: i) mapped the relative micromechanical changes in the elastic lamellae (EL) and inter-lamellar regions (ILR) of the aorta and ii) characterised the effects of diabetes on the structure fibrillin microfibrils (long lived elastic fibre components which sequester TGF- β and hence play a key role in tissue homeostasis).

Diabetes was induced in five adult rats by STZ injection. These rats and five age-matched controls were killed after 8 weeks. Aortic cryosections were imaged by scanning acoustic microscopy to map variations in speed of sound (a measure of tissue stiffness). Fibrillin microfibrils were isolated by bacterial collagenase digestion and imaged by atomic force microscopy.

Exposure to a diabetic milieu affected the mechanical properties of aortic EL and ILR. In diabetic animals mean speed of sound was significantly reduced in EL (control, $1766 \pm 13 \text{ ms}^{-1}$; diabetic, $1722 \pm 11 \text{ ms}^{-1}$, $p < 0.05$) and in the ILR (control, $1902 \pm 8 \text{ ms}^{-1}$; diabetic, $1868 \pm 11 \text{ ms}^{-1}$, $p < 0.001$). Fibrillin microfibril periodicity was also profoundly affected in diabetic animals (control, uni-modal distribution centred at 56nm; diabetic, bi-modal distributions centred at 52 and 78nm).

These observations suggest that profound micro-mechanical changes occur in diabetic blood vessels, in both the EL and collagen-rich ILR, and that pathological changes in the nano-structure of homeostatic components may play a role in driving localised remodelling in these tissues.

4.6

ELEVATION IN CENTRAL BLOOD PRESSURE DURING EXERCISE IS PREDOMINANTLY DRIVEN BY FORWARD-PROPAGATING WAVES: A FIRST IN MAN INVASIVE EXERCISE STUDY

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Introduction: Exercise hypertension independently predicts cardiovascular mortality, but little is known on exercise central haemodynamics. This study aimed to determine contributions of arterial wave travel and aortic reservoir characteristics to central blood pressure (BP) during exercise. We hypothesised exercise central BP would be principally related to forward wave travel and aortic reservoir function.

Methods: Invasive pressure and flow velocity were recorded in the ascending aorta via sensor-tipped intra-arterial wire in 10 participants (age 55 ± 10 years, 70% male) with normal left-ventricular function and free from obstructive coronary artery disease. Measures were recorded at baseline and during supine cycle ergometry. Using wave intensity analysis, dominant wave types throughout the cardiac cycle were identified (forward, backward, compression and decompression), and aortic reservoir and excess pressure were calculated.

Results: Central systolic BP increased significantly with exercise (19 ± 12 mmHg, $P < 0.001$). This was associated with significant increases in early systolic forward compression waves ($15 \times 10^6 \pm 18 \times 10^6 \text{ W} \cdot \text{m}^{-2} \cdot \text{s}^{-2}$, $P = 0.025$) and forward decompression waves in late systole ($9 \times 10^6 \pm 5 \times 10^6 \text{ W} \cdot \text{m}^{-2} \cdot \text{s}^{-2}$, $P < 0.001$). Despite significant augmentation in BP ($+10\%$, $P = 0.023$), backward (reflected) waves did not increase in magnitude ($-1 \times 10^6 \pm 2 \times 10^6 \text{ W} \cdot \text{m}^{-2} \cdot \text{s}^{-2}$, $P = 0.241$). Excess pressure rose significantly with exercise (16 ± 9 mmHg, $P < 0.001$), and reservoir pressure integral fell ($-5 \times 10^5 \pm 5 \times 10^5 \text{ W} \cdot \text{m}^{-2} \cdot \text{s}^{-2}$, $P = 0.010$). The change in reflection coefficient negatively correlated with change in central systolic BP ($r = -0.682$, $P = 0.030$).

Conclusion: Raised exercise central BP is principally driven by increasing aortic forward wave propagation generated by left ventricular ejection, and not wave reflection. These findings have relevance to understanding the pathophysiology of exercise hypertension.

Oral session 5

Free Communication Oral Presentations

In association with the ESH Working Group on Vascular Structure and Function

5.1

PULSE PRESSURE AMPLIFICATION AND RENAL FUNCTION IN HYPERTENSION

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In epidemiological studies including serum creatinine or estimates of glomerular filtration rate (GFR), pulse pressure (PP) emerged as significant predictor of cardiovascular risk and major determinant of age-associated decline in GFR. The finding is mainly observed in subjects with hypertension and/or renal failure but less in atherosclerotic subjects. Blood pressure was measured invasively in the ascending and abdominal aorta (at the level of kidneys) of 101 subjects undergoing coronary angiography. Independently of age, sex, and presence of coronary stenosis, amplification of PP between the ascending and terminal aorta was over 10 mm Hg ($P < 0.001$), whereas mean blood pressure remained unchanged. Irrespective of PP measured in the ascending aorta and at the level of renal arteries, amplification was significantly related to proteinuria. Increased plasma creatinine and aortic pulse wave velocity were independently and positively correlated ($P < 0.001$). The relationship between PP and renal function was mainly present in patients 60 years of age or older. Finally, renal transplant patients and their donors were recruited for evaluation of aortic stiffness and determination of the post-transplant decline trends in GFR. Determinants of filtration rate decline were evaluated at 1 year and at