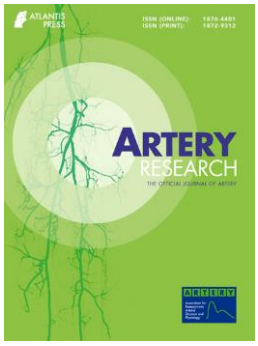

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P9.7: C-REACTIVE PROTEIN, CYSTATIN C AND ARTERIAL STIFFNESS IN RENAL TRANSPLANT RECIPIENTS

M. Harangi, R. Szentimrei, L. Lőcsey, I. Seres, D. Kovács, L. Asztalos, G. Paragh

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Methods: 86 patients (mean age 59±10 years, 41 women) with recently diagnosed (median 1.8 years) type 2 diabetes and 86 controls matched individually for gender and age were included. Radial artery pressure waveforms were obtained non-invasively by applanation tonometry. The central aortic waveform was derived using the SphygmoCor transfer function, which enabled calculation of SEVR. Arterial stiffness was assesses by the carotid-femoral pulse wave velocity (PWV).
Results: SEVR was significantly lower in diabetic women compared with i) diabetic men, (161%±26% vs 178%±32%, $p<0.01$), ii) non-diabetic women (185%±24%) and men (188±28%, $p<0.001$ for both comparisons). The differences remained significant in a multivariate analysis including age, mean blood pressure, heart rate, smoking, total cholesterol and PWV.
Conclusion: SEVR was significantly lower in diabetic women as compared with both diabetic men and non-diabetic subjects. This association was not mediated by arterial stiffness. Low SEVR may independently contribute to the increased cardiovascular morbidity seen in diabetic women.

P9.4
COMPARISON OF DIFFERENT METHODS OF VASCULAR PHENOTYPING IN PATIENTS AT CARDIOVASCULAR RISK

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Objective: Discriminating between patients at high and low cardiovascular risk can be difficult. Screening for the presence of subclinical organ damage may provide additional benefits in predicting cardiovascular events. We aimed to assess the agreement of markers of organ damage with traditional risk scoring methods.
Methods: We performed a comprehensive analysis of vascular health on a cohort of 50 patients recruited from Blood Pressure and Cardiovascular Risk Factor clinics. This included pulse wave analysis, pulse wave velocity (PWV), carotid intima-media thickness (cIMT), brachial flow-mediated dilatation and ankle-brachial pressure index. Patients were subdivided according to the ASSIGN score into low, intermediate and high cardiovascular risk.
Results: PWV (8.63, 8.25 and 11.9 m/s) and cIMT (0.67, 0.73 and 0.91 mm) were the only vascular parameters to display a statistically significant ($p<0.001$) difference according to risk category (low, intermediate and high). Both correlated with age ($r=0.589$, $p<0.001$; and $r=0.646$, $p<0.001$; respectively) and with each other ($r=0.585$, $p<0.001$). When we calculated means and 95% confidence intervals for each risk category we identified 6 low risk, 11 intermediate risk and 6 high risk patients who had test values outwith the ranges expected of their group. For patients with higher or lower values there was no discordance between PWV and cIMT.
Conclusion: PWV and cIMT were the only markers to distinguish between low and high risk patients. We identified patients with higher or lower values than expected according to their risk category, which could reflect higher or lower risk than originally estimated. These findings require prospective studies.

P9.5
VASCULAR STRUCTURE AND FUNCTION AND HEMODYNAMICS ARE NOT ALTERED IN NORMAL-TENSION GLAUCOMA AT REST

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Aims: In normal-tension glaucoma (NTG), optic nerve damage occurs despite a normal intraocular pressure. Studies implicating arterial stiffness in the pathophysiology of NTG have produced conflicting results. Our aim was to investigate whether NTG is associated with alterations in arterial structure or function.
Methods: Cardiovascular measurements included peripheral and central (Sphygmocor) blood pressures, measures of wave reflection (reflection magnitude and augmentation index), segmental and local arterial stiffness measures [carotid-femoral Pulse wave velocity (cf-PWV, Sphygmocor) and carotid artery stiffness (Esaote AU5 Wall track system), respectively], Intima-media thickness (IMT), cardiac output (Esaote AU5) and total peripheral resistance index (TPRI). Symptoms of vascular dysregulation were assessed using a questionnaire.
Results: 30 patients with NTG (mean age 65y, range 46-79) and 33 healthy subjects (mean age 67y, range 42-79) matched for age and sex were recruited. There were no statistically significant differences in cardiovascular measures; for NTG versus controls, respectively: blood pressure 126±15 / 77±8 mmHg vs. 127±16 / 76±7 mmHg, $p=0.81$; cf-PWV 9.8±2.1 m/s vs. 10.1±1.9 m/s, $p=0.60$; TPRI 1833±609 vs. 1779±602 dyne.s/cm5/m^2, $p=0.79$; carotid IMT 0.65±0.14 mm vs. 0.68±0.13 mm; $p=0.39$. Questionnaire reports revealed an increased prevalence of cold extremities in the NTG group (73% vs. 21%, $p<0.001$) suggesting vascular dysregulation is present in most NTG patients.
Conclusion: NTG is not associated with altered arterial stiffness, IMT, TPRI, cardiac output, peripheral or central hemodynamics. Although the majority of NTG patients exhibit symptoms of vascular dysregulation, in the present study this did not translate into alterations in the micro- or macrocirculation at rest.

P9.6
BLOOD PRESSURE VARIABILITY AND TARGET ORGAN DAMAGE IN PATIENTS WITH UNCOMPLICATED HYPERTENSION: AVERAGE 24 HOUR AMBULATORY BLOOD PRESSURE IS MORE RELEVANT TO CHANGES IN LEFT VENTRICULAR MASS INDEX

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Background: Increased blood pressure variability (BPV) is associated with adverse cardiovascular outcomes, particularly incident stroke. However, the impact of increased BPV on target-organ damage related to hypertension is unknown. This study aimed to determine the effect of BPV compared with conventional average BP on left ventricular mass index (LVMI).
Methods: BPV and conventional average BP (24-hour ambulatory BP, 7-day home BP and office BP) were assessed in 286 patients with uncomplicated treated hypertension (aged 64±8 years, 54% male) over 12-months. Short-term BPV (from 24 hour ambulatory BP) was assessed at baseline and 12-months, mid-term BPV (from 7 day home BP) was assessed at 3-month intervals, and long-term BPV (from clinic BP) was assessed from 5 visits over 12-months. Left ventricular mass index (LVMI) was derived from 3-dimensional echocardiography.
Results: Mean changes in LVMI over 12 months were 0.01±2.5 g/m$^{-2.7}$. The strongest independent predictor of the change in LVMI was conventional 24-hour ambulatory systolic BP ($\beta=0.032$; $P=0.02$). However, none of the changes in short-term, mid-term or long-term BPV were associated with changes in LVMI (all $P>0.05$).
Conclusions: The change in conventional average 24-hour ambulatory BP, but not BPV, is relevant to changes in target organ damage determined from LVMI in patients with uncomplicated hypertension. Thus, BPV does not provide additive information on BP control in this patient population.

P9.7
C-REACTIVE PROTEIN, CYSTATIN C AND ARTERIAL STIFFNESS IN RENAL TRANSPLANT RECIPIENTS

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Low grade inflammation renal transplanted (Tx) patients enhances atherogenesis. Cystatin C (CysC) is a sensitive marker of glomerular filtration rate, furthermore inhibits cysteine proteases, therefore anti-atherogenic. Previous studies found elevated C-reactive protein (CRP) and CysC levels in renal transplant recipients. Arterial stiffness parameters such as aortic augmentation index (AIx) and pulse wave velocity (PWV) are established markers of cardiovascular mortality in these patients. However, the association between inflammatory markers, CysC levels and arterial stiffness has not been studied.
131 Tx patients and 63 age- and gender-matched healthy controls (C) were enrolled in the study. Lipid parameters, CRP and CysC serum levels were measured. Arterial stiffness parameters (Aix, PWV, pulse pressure (PP), systolic and diastolic area indexes (SAI and DAI) and mean arterial pressure (MAP) were determined by arteriograph (Tensiomed).
Significantly higher levels of CRP and CysC levels were found in patients compared to controls. Significantly higher MAP, PP, AIx and PWV, while significantly lower DAI and SAI were detected in Tx patients compared to C subjects. Significant positive correlations were found between CRP and PWV, and between CRP and MAP, while there was a significant negative correlation between CRP and DAI in TX patients. We found a non-significant correlation between CysC and PWV. Significant positive correlation was showed between CRP and LDL-C levels.

Chronic low grade inflammation and decreased glomerular characterized by CysC level may contribute to increased arterial stiffness in renal transplant recipients.

P9.8
ARTERIAL STIFFNESS AND PARAOXONASE ACTIVITY IN RENAL TRANSPLANT RECIPIENTS

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Increased lipid peroxidation and dyslipidemia are well known cardiovascular risk factors in renal transplanted (Tx) patients. Human serum paraoxonase (PON1) is the most potent high-density lipoprotein (HDL)-associated antioxidant enzyme. Previously decreased PON1 activity was shown in Tx recipients. Arterial stiffness parameters such as aortic augmentation index (AIx) and pulse wave velocity (PWV) are established markers of cardiovascular mortality in these patients. However, the association between PON activity and arterial stiffness has not been studied.
131 Tx patients and 63 age- and gender-matched healthy controls (C) were enrolled in the study. Lipid parameters and PON1 paraoxonase and arylesterase activities were measured. Arterial stiffness parameters (Aix, PWV, pulse pressure (PP), systolic and diastolic area indexes (SAI and DAI) and mean arterial pressure (MAP) were determined by arteriograph (Tensiomed).
Significantly lower paraoxonase and arylesterase activities were found in Tx patient compared to C subjects. Significantly higher MAP, PP, AIx and PWV, while significantly lower DAI and SAI were detected in Tx patients compared to C subjects. A significant negative correlation was found between arylesterase activity and PWV in Tx patients. Significantly higher total cholesterol (TC) and low-density cholesterol (LDL-C), while significantly lower HDL-C levels were found in Tx patients compared to C. Significant positive correlations were found between TC and PWV, and between LDL-C and PWV, while there were significant negative correlation between TC and DAI and between LDL-C and DAI in Tx patients.
Dyslipidemia and decreased antioxidant capacity characterized by PON1 activity may contribute to increased arterial stiffness in kidney transplant recipients.

P9.9
ALTERED DEPENDENCE OF AORTIC PULSE WAVE VELOCITY ON TRANSMURAL PRESSURE IN HYPERTENSION REVEALING STRUCTURAL CHANGE IN THE AORTIC WALL

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Aortic pulse wave velocity (aPWV), a major prognostic indicator of cardiovascular events, may be augmented in hypertension as a result of the aorta being stretched by a higher distending blood pressure or by a structural change. We used a novel technique to modulate intra-thoracic pressure and thus aortic transmural pressure (TMP) to examine variation of intra-thoracic aPWV with TMP in hypertensive ($n=20$, mean$\pm$SD age 52.1$\pm$15.3 years, BP 159.6$\pm$21.2/92.0$\pm$15.9 mmHg) and normotensive ($n=20$, age 55.5$\pm$11.1 years, BP 124.5$\pm$11.9/72.6$\pm$9.1 mmHg) subjects. aPWV was measured using dual Doppler probes to insonate the right brachiocephalic artery and aorta at the level of the diaphragm. Resting aPWV was greater in hypertensive compared to normotensive subjects (897$\pm$50 cm/s versus 784$\pm$43 cm/s, $P<0.05$). aPWV was equal in hypertensive and normotensive subjects when measured at a TMP of 96 mmHg. However, dependence of aPWV on TMP in normotensive subjects was greater than in hypertensive subjects (9.6$\pm$1.6 versus 3.8$\pm$0.7 cm/s per mmHg increase in TMP respectively, means$\pm$SEM, $P<0.01$). This experimental behaviour was best explained by a theoretical model incorporating strain induced recruitment of stiffer fibres in normotensive subjects and fully recruited stiffer fibres in hypertensive subjects. These results explain previous contradictory findings with respect to isobaric aPWV in hypertensive compared to normotensive subjects. They suggest that hypertension is associated with a profound change in aortic wall mechanical properties possibly due to destruction of elastin leading to less strain induced stiffening and predisposition to aortic dissection.

P9.10
EXCESS PRESSURE IS INDEPENDENTLY RELATED TO LV MASS AND CONCENTRIC GEOMETRY IN ESSENTIAL HYPERTENSION

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Arterial blood pressure (BP) can be decomposed as the sum of reservoir (Pres) and excess (Pexc) pressure. Pres is constant along the arteries and results in the minimum left ventricular (LV) hydraulic work, while Pexc is linked to the excess work of the heart. We evaluated the relationship of Pres and Pexc with cardiac structural features in hypertension
Methods: 446 never-treated hypertensives (mean age 48$\pm$11 years, 62% men, BP 148/92$\pm$16/10 mmHg) were evaluated through echocardiography, radial applanation tonometry (SphygmoCor) and 24-h ambulatory BP monitoring (SpaceLabs).Amplitudes and areas of Pres and Pexc were calculated using proprietary algorithms based on central pressure curves.LV hypertrophy was defined as LV mass >51 g/m2.7. Relative wall thickness (RWT) was expressed as: 2 x posterior wall thickness/LV diameter, and concentric geometry as: RWT>0.43
Results: Pexc and Pres were correlated with LV mass ($r=0.15$ and 0.17, respectively; both $p<0.01$) and RWT ($r=0.16$, $p<0.01$; $r=0.11$, $p=0.02$). After adjustment for age, sex, body mass index and 24-h systolic BP, subjects with LV hypertrophy had higher Pexc (18.4$\pm$10.3 vs 17.0$\pm$5.4 mmHg, $p=0.02$), but not Pres (39.8$\pm$12.6 vs 37.5$\pm$24.2 mmHg, $p=0.09$). In a multivariate model adjusting for multiple cardiovascular risk factors and other confounders, an increased Pexc independently predicted both LV mass ($\beta=0.08$, $p=0.04$, multiple $R=0.58$) and RWT ($\beta=0.10$, $p=0.02$, multiple $R=0.40$), while these relationship were not observed for Pres
Conclusions: LV mass and RWT are linearly and independently associated to Pexc, but not to Pres in untreated hypertension. Structural cardiac abnormalities may be related to an increase in Pexc

P9.11
ANGIOTENSIN-CONVERTING ENZYME ACTIVITY IN NORMOTENSIVE WHITE AND AFRICAN MEN

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Background: The renin-angiotensin system (RAS) is a proteolytic cascade which consists of multiple enzymes and effector peptides. Angiotensin-Converting Enzyme (ACE) is one of the major enzymes in the RAS and catalyzing the decapeptide Angiotensin I to the octapeptide Angiotensin II. There are other non-RAS effects of ACE like mediating and/or modulating inflammation. We aimed to explore the ACE activity in white and black South African men and establish the associations with a marker of inflammation.
Methods: In a bi-ethnic sample ($n=30$) consisting of white and African men, the RAS-Fingerprinting was determined with LC-MS/MS quantification of Angiotensin peptides. Blood pressure and other variables were determined with known methods. Soluble urokinase Plasminogen Activator Receptor (suPAR) levels were determined using the suPARnostic® ELISA kit.
Results: From the RAS-Fingerprinting and ACE activity (product-substrate ratio) it is evident that ACE activity is significantly lower in the normotensive African men compared to white men. The higher ACE activity found in the white men associated positively with reactive oxygen species (ROS) ($r=0.59$; $p=0.02$) and with suPAR ($r=0.63$; $p=0.01$) but not in the African men.
Conclusions: The ACE activity is higher in the white men and it seems that ACE may drive inflammation only in the white participants.

P9.12
THE RELATIONSHIP BETWEEN RETINAL VESSEL CALIBRE AND NOCTURNAL DIPPING STATUS: THE SABPA STUDY

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Introduction: The relationship between a non-dipping blood pressure profile and retinal vessel calibre is not well established. A sustained increase in