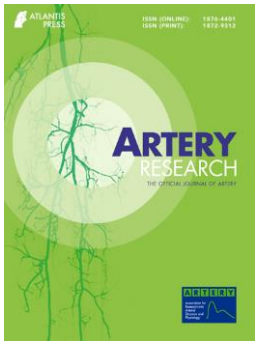

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P9.3: LOWER SUBENDOCARDIAL VIABILITY RATIO IN DIABETIC WOMEN–CONTRIBUTING TO THE ABROGATED CARDIOPROTECTIVE EFFECT OF FEMALE GENDER IN DIABETES?

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P8.12
ARTERIAL DISTENSION-PRESSURE LOOP ANALYSIS IN HYPERTENSIVE RATS: ADVANTAGES, PITFALLS AND POSSIBILITIES

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Arterial wall viscosity (AWV) of central arteries, as well as distensibility, is important to properly buffer systolic ejection pressure. AWV is measured either by the area within the hysteresis of distension-pressure (DD-P) loop, defined as the viscous energy (AWV=Ve) or the ratio of Ve/Ve+energy stored during systole (=AWV%). We record DD-P loop via echotracking; averaged over 30 cardiac cycles, AWV and AWV% are calculated via MatLab software. Here we perform a post analysis of the DD-P loop in 12 groups of rats (n=5-8): normo- or hypertensive, with and without arterial remodeling, at different operating blood pressures (BP), using different compounds. AWV decreases and DD-P loop is flattened with increased BP; moreover it is differently altered if pulse pressure (PP) is altered and remains low at any operating BP in models with vascular wall remodeling. However in all conditions the ratio AWV% is poorly modified. Our results suggest that the AWV as the Ve (hysteresis loop area) is the most relevant in defining the viscous properties of the artery; they indicate that mean operating BP, PP and structural distensibility independently participate in modifying the shape of the loop which is largely dependent on the delay between peak systolic pressure and peak systolic diameter, apparent in the higher BP of the loop. This suggests that isobaric distensibility cannot be compared in the lower and upper part of the loop but only at a similar mean BP. Further studies will aim to confirm these suggestions and determine how to improve loop hysteresis evaluation

P8.13
A 1-D MODEL OF THE SYSTEMIC ARTERIAL TREE IN MICE

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Cardiovascular diseases are often studied at a pre-clinical stage using dedicated mouse models. However, (non-)invasive measurements in the murine cardiovascular system are difficult to obtain, limited to a restricted number of aortic locations, and need to be justified from an ethical perspective. In this work we present a 1-D model of the systemic circulation in mice. Murine arterial tree dimensions have been acquired and averaged from the segmentation of Micro-Computed Tomography (μ-CT) scans of 3 wild-type C57Bl/6 mice (12-15 weeks old). The resulting geometry consists of 85 arterial segments, including all major aortic branches as well as the tail and the cerebral tree. The remaining input to the model has been obtained from a wide range of literature data. An empirical relationship has been fitted to estimate the local arterial wall distensibility in all segments. Peripheral vessels are terminated with three-element windkessel models to account for the resistance and compliance of the distal vasculature. The integrated form of the momentum and continuity equations is solved numerically to yield pressures and flows throughout the arterial network. The model predicts pressure and velocity waveforms in good qualitative and semi-quantitative agreement with invasive pressure measurements as well as high-frequency ultrasound Pulsed-Wave Doppler aortic velocity and M-mode aortic distensibility measurements. In conclusion, a well-tuned and appropriately validated 1-D model for the murine cardiovascular system has been developed, which is ready to serve as a versatile study tool in the field of pre-clinical cardiovascular research.

P9.1
INFLUENCE OF INSULIN SENSITIVITY AND RELATED METABOLIC FEATURES ON CAROTID AND AORTIC STIFFNESS IN NORMAL SUBJECTS

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Insulin resistance (IR) underlies a cluster of metabolic abnormalities contributing to atherosclerosis. Relations between IR and large artery involvement in subjects without atherosclerotic disease are still debated.

Aim: to investigate in normal subjects the relations between IR and its associated metabolic abnormalities with tissue biomarkers of preclinical vascular involvement.
Methods: Eighty-two healthy volunteers (45 men; age 46±9) underwent a glucose tolerance test and a euglycemic hyperinsulinemic clamp to estimate IS (M/I, i.e. M value normalized by FFM and mean plasma insulin). Metabolic parameters measured included fasting and 2-hour glucose and insulin, detailed lipid profile, leptin, adiponectin and hs-CRP. Vascular examination included carotid-femoral pulse wave velocity (PWV) and radiofrequency-based ultrasound (QIMT® and QAS®, Esaote), for IMT and local stiffness estimate (beta index, BI). Acoustic properties of carotid wall were evaluated by videodensitometry and described as mean grey levels (MGL).
Results: in multiple regression models adjusted for sex and smoking, IMT was independently related directly to age and carotid diameter, and inversely to adiponectin (R2=0.34), IMTmax to age, systolic BP and adiponectin (R2=0.35), and carotid MGL to age and adiponectin (directly and inversely, respectively; R2=0.30). BI was related to age and M/I (directly and inversely, respectively; R2=0.44) and carotid-femoral PWV to age and glucose (directly; R2=0.39).
Conclusions: metabolic factors related to IR influence structure and function of carotid artery behind the main role of age. Adiponectin has an independent effect on carotid structure, while IS and plasma glucose mainly influence carotid and aortic stiffness.

P9.2
VASCULAR ADAPTATIONS TO BODY SIZE AND COMPOSITION IN ADOLESCENTS

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Background: increase in body mass index is accompanied by metabolic alterations but also by increased stroke volume (SV). Therefore, associated changes in vascular structure and function can not reflect only preclinical atherosclerosis but physiologic adaptation to body composition-related hemodynamic changes.
To evaluate the relationships between body composition and arterial structure and function without the influence of atherosclerotic risk factors, we assessed carotid intima-media thickness (IMT), luminal diameter (LD), wave speed (WS) and local pulse pressure (cPP)by radio-frequency based ultrasound (QIMT® and QAS®, Esaote), in 80 healthy children-adolescents with wide range of age (8-16 years) and BMI (15-40 kg/m2). Body composition was assessed by bioimpedance, visceral fat (VF) by ultrasound, and SV by Doppler. Plasma lipids, glucose and insulin were determined.
Results: body weight (BW) and fat free mass (FFM) were related to IMT (r=0.61 and 0.50), LD (r=0.54 and 0.53), WS (r=0.43 and 0.56) and cPP (r=0.36 and 0.49); fat mass (FM) was related to IMT and LD (r=0.40 and 0.29), and VF to IMT (r=0.41). SV was more strongly related to FFM than to FM (r=0.70 and 0.24). In multivariate models, IMT was determined by BW and triglycerides (R2=0.44), LD by BW and male sex (R2=0.37), WS by FFM and systolic BP (R2=0.39), cPP by FFM (R2=0.24). When SV was included into the models, it replaced FFM in model of cPP. Conclusion: adiposity-related changes in carotid function are depending on FFM-related increase in SV. Changes in carotid geometry also reflect an increase in body fat and plasma lipids.

P9.3
LOWER SUBENDOCARDIAL VIABILITY RATIO IN DIABETIC WOMEN—CONTRIBUTING TO THE ABROGATED CARDIOPROTECTIVE EFFECT OF FEMALE GENDER IN DIABETES?

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The cardioprotective effect of female gender is abrogated in the presence of type 2 diabetes, and female diabetic patients thus face comparable cardiovascular risk as men with type 2 diabetes. The SubEndocardial Viability Ratio (SEVR) is an index of myocardial oxygen supply and demand that can be assessed non-invasively by applanation tonometry. We hypothesized that diabetic women would have lower SEVR than diabetic men and non-diabetic subjects independently of conventional risk markers and arterial stiffness.

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.