P.043: APPLICATION OF WOMERSLEY THEORY: ESTIMATION OF PULSE VOLUME FLOW AND WALL SHEAR STRESS IN LARGE ARTERY USING ULTRASOUND

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Poster Presentations

P.039
A MODIFIED AUGMENTATION INDEX (Alx) USING WAVE INTENSITY ANALYSIS
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Augmentation index (Alx) is widely used as a measure of wave reflection in clinical studies. The validity of Alx results rests on the ability to quantify the magnitude of the reflected pressure wave (P) in relation to the pressure pulse (PP). And this is traditionally carried out by determining the inflection point (Ip) on the pressure waveform. In this study we investigate the results of Alx and propose a modified augmentation index (mAlx) that is more sensitive to loading conditions.

In 11 anaesthetised dogs, total sequential occlusions were produced at 3 aortic sites (thoracic, diaphragm, abdominal), and at the left iliac artery. Pressure and flow were measured in the ascending aorta before and during the occlusion at each site, and Ip was ascertained using the 4th derivative of the pressure waveform allowing for the determination of Alx. Magnitude of P was calculated using wave intensity analysis (WIA), and divided by PP giving a modified augmentation index (mAlx = P / PP).

Alx during control were surprisingly not different from those determined during descending pressure occlusion. peak Alx, P, increased significantly during occlusions; resulting in a significant increase in mAlx by 165% during thoracic, 48% during diaphragm and 20% during abdominal occlusions, all compared to control. The Ip is not an accurate method for determining P. This can result in significant errors in the estimation of Alx. The mAlx, derived from pressure–flow relationship in the wave intensity analysis is more sensitive to the determination of P, than Alx which uses only the pressure waveform.

P.040
INCREASED CAROTID INTIMA-MEDIA THICKNESS PREDICTS HIGH CARDIOVASCULAR RISK
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Objectives: The aim of this study was to investigate the relationship between the total cardiovascular risk assessed by SCORE system and vascular markers: carotid intima-media thickness (IMT), arterial stiffness indices, carotid branch pressure flow mediated dilatation (FMD) and the ankle-brachial pressure index (ABI).

Background: Carotid IMT, arterial stiffness indices, FMD and ABI are markers of subclinical atherosclerosis. The SCORE risk system offers direct estimation of ten-year total fatal cardiovascular (CV) risk. The relationship between these markers and SCORE risk has not been investigated.

Methods: We studied 160 subjects without cardiovascular disease (aged 49.91 ± 7.16 years, 69 males). Traditional risk factors, carotid IMT, carotid-radial pulse wave velocity (crPWV), stiffness index (SI), measured by photoplethysmography, brachial artery FMD and the ABI were assessed. Laboratory tests included serum lipid and glucose profile. The total CV risk was evaluated by SCORE system.

Results: By multivariate analysis carotid IMT (p < 0.001) and SI (p = 0.008) were correlated with SCORE risk. Brachial artery FMD, ABI and crPWV didn’t correlate significantly with SCORE risk (p = 0.052, p = 0.110 and p = 0.937 respectively). In stepwise regression models that include carotid IMT, crPWV, SI, FMD and ABI, only carotid IMT > 0.9 mm correlated with high total CV risk (SCORE ≥ 5%). Odds ratio for increased CV risk was 8.56 (CI 95%: 3.109-23.567). The IMT cut-off point at 0.9 mm predicts high CV risk (sensitivity 67.4%, specificity 78.6%).

Conclusions: Carotid artery IMT and arterial stiffness marker SI predict total CV risk. Carotid IMT is a prognostic marker for high CV risk.

P.041
VALIDATION OF SPHYGMOCOR-PROCESSED AUGMENTATION INDEX USING CAROTID ARTERY DISTENSION WAVEFORM
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Arterial tonometry (AT), used for measurement of augmentation index (Alx) at the central level, has been criticized because of artefacts induced by hand motion and deformation of the artery. We hypothesized that carotid distension waveforms, obtained with high definition echotracking device (walltrack system WTS-Atk) could be used to derive augmentation index, a measure of wave reflection, and that those values were comparable with AT, either performed at carotid (CSP-Alx) or on the radial artery (RSP-Alx), using the generalized transfer function (GTF) of Sphygmocor system.

A group of 48 subjects with various diseases was studied. For WTS-Alx, inflexion point was determined from the 0 crossing of the 3rd derivative. For CSP and RSP-Alx, standard reports of Sphygmocor were used. WTS-Alx could be determined with good precision from all tracings in all patients. Agreement between WTS-Alx and CSP-Alx was good (R² = 0.83, RMSE = 5.8), with a 35% systematic underestimation by Sphygmocor: slope = 0.65 [0.56–0.73]. There was a WTS-Alx agreement between WTS-Alx and RSP-Alx was fair (R² = 0.71, RMSE = 6.9), with comparable underestimation. This underestimation was not due to GTF, but to the applation process since bypassing GTF had no influence on it and because AT, estimated with another type of tonometer, was not directly scaled with CSP-Alx (slope 0.93 [0.81-1.05]). CSP-Alx and RSP-Alx were not in good agreement (R² = 0.66, RMSE = 10.7), but correctly scaled (slope = 0.87 [0.81-1.05]).

In conclusion, wave reflections can be assessed from distension waveforms with good accuracy from overestimation with applation techniques rather than from underestimation with distension waveforms.

P.042
MULTIAXIAL MECHANICAL CHARACTERISTICS OF CAROTID PLAQUE: ANALYSIS BY MULTI-ARRAY ECHOTRACKING SYSTEM
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Carotid plaque rupture depends on the various types of mechanical stresses. Our objective was to determine the multiaxial mechanical characteristics of atherosclerotic plaque and adjacent segment of the common carotid artery (CCA).

A novel non-invasive echotracking system was used to measure intima-media thickness, diameter, pulsatile strain, and distensibility at 128 sites on a 4 cm long CCA segment. The included 62 patients with recent cerebrovascular ischemic event and either a plaque on the far wall of CCA (n = 25) or no plaque (n = 37). The mechanical characteristics of the carotid segment devoid of plaque did not differ between the two groups. Among patients with plaque, 16 had a larger radial strain at the level of plaque than at the level of adjacent CCA (pattern A: outward bending strain). The 8 patients who had an opposite pattern (inward bending strain) were more often dyslipidemic (100% vs 56% P < 0.03) and type 2 diabetic (63% vs 12%, P < 0.04) than pattern A patients. Strain gradient significantly decreased in parallel with the presence of dyslipidemia and/or type 2 diabetes. Longitudinal gradients of distensibility and Young’s elastic modulus were consistent with strain gradients.

In conclusion, type 2 diabetes and dyslipidemia were associated with a stiffer carotid at the level of the plaque than in adjacent CCA, leading to an inward bending stress. The analysis of plaque mechanics along the longitudinal axis may afford useful information, since repetitive bending strain of an atherosclerotic plaque may fatigue the wall material and result in plaque rupture.

P.043
APPLICATION OF WOMERSEY THEORY: ESTIMATION OF PULSE VOLUME FLOW AND WALL SHEAR STRESS IN LARGE ARTERY USING ULTRASOUND
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In order to assess pulse volume flow (PVF) and wall skin shear stress (WSS) in large arteries by the means of ultrasound, a Womersey theory based iterative method is proposed. Firstly, the PVF is computed by integrating the estimated velocity profiles obtained from multi-gate ultrasound Doppler; the vessel diameter was assessed through M-mode ultrasound. Secondly, the average WSS was calculated using the Womersey theory applied for tubes with none moving walls. The WSS is consequently computed from the fitted Womersey profiles. The PVF and WSS obtained through this method were compared to the ones obtained by Poiessile theory. The method was applied on measurements performed on the brachial artery, repeated at least three times, of 9 presumed healthy volunteers. The results displayed a large relative difference in average maximal PVF (27.7%, p < 0.01) and WSS (72.36%, p < 0.01), the intra individual variations being 4.9% for the PVF and 11.6% for the WSS. In the case of the mean
PVF and WSS, relative differences of 6.8% (p < 0.05) and 1.15% (p < 1) respectively were evaluated. The estimations based on Poiseuille theory present a significant underestimation of both maximum and mean PVF as well as maximum WSS by comparison to the results obtained through Womersley profiles fitting. No significant difference was observed for the mean WSS.

P.044

ROLE OF INTEGRIN α1β1 IN THE CARDIOVASCULAR EFFECTS OF ANGIOTENSIN II

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Integrin α1 knockout mice (α1−/−) were used to investigate the role of the integrin α1β1 in the cardiac and vascular functions of angiotensin II (AngII)-induced hypertension. Carotid artery (CA) elasticity was measured by incremental elastic modulus (Einc)-wall stress curves using an ultrasonic echo-tracking device and the measurement of medial cross-sectional area (MCSA) to evaluate in vivo CA mechanical properties. Cardiac function was studied by echocardiography in anesthetized animals.

Infusion of Ang II (200ng/kg/min) in α1−/− mice and their control (α1+/+) for 4 weeks led to similar cardiac hypertrophy, vaguely increased elastin (−Δα1+/+ vs +Δα1−/−) and decreased potassium (−Δα1+/+ vs +Δα1−/−). Ang II failed to increase MCSA of CA whereas it did in α1+/+ mice. The Einc-stress curve of Ang II-treated α1−/− was shifted to the right compared to Ang II-treated α1+/+, indicating a decreased arterial stiffness. The α1+/+ had an increased cardiac hypertrophy, evaluated by an increase of the end diastolic thickness of the septum (IVSD: 1.2±1 vs 0.9±0.08 mm) without modification of the posterior wall (UPPWd: 0.10±0.06 vs 0.97±0.07 mm) and without dilation of the ventricular cavity. This septal hypertrophy was not found in the α1−/− mice in response to Ang II. Cardiac fibrosis measured by collagen quantification (total, and type I and III), was lower in the α1−/− mice, compared with the α1+/+.

In conclusion, our results show an impaired cardiovascular response to Ang II-induced hypertension in the integrin α1 knockout mouse. These results suggest the involvement of this integrin in the cardiovascular effects of Ang II.

P.045

STABLE THE REFLECTIVE PROPERTIES OF THE ARTERIAL SYSTEM IN RENAL TRANSPLANTATION (RTX) PATIENTS AT ONE YEAR FOLLOW-UP

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Background: Successful RTx from living-related donors, by removal of the uremic milieu and improvement in cardiovascular risk factors can be associated with improvement in indices of arterial stiffness. The aim of this study was to assess the arterial stiffness after one year of follow-up in live related RTx patients.

Methods: The augmentation index (AIx) was determined from arterial waveforms contour analysis recorded by applanation tonometry using SphygmoCor® device in 31 living related RTx (19 M, age 34.6 ± 13.6 years) and their supernatant for cytokines measurement. PMNC carrying del32 produced oxidative low density lipoprotein (OxLDL) for 24 hours before collecting supernatant for cytokines measurement. PMNC carrying del32 produced

Results: Overall, during follow-up, mean AIx increased from 13.5 ± 13.3% to 15.6 ± 10.5% (p > NS). TTS increased from 107.7 ± 4.9 ms at baseline to 109.3 ± 4.3 ms and the upswing duration 29.7 ± 24.8 ms, mean Crl.Cr. = 62.9 ± 1.2 ml/min. All studies were performed before CsA administration, at baseline and at one-year follow-up. As a surrogate marker of the pulse wave velocity (PVW) we used the time to shoulder (TTS) parameter on the reconstructed central pulse pressure waveform.

Results: Overall, during follow-up, mean Aix increased from 13.5 ± 13.3% to 15.6 ± 10.5% (p > NS). TTS increased from 107.7 ± 4.9 ms at baseline to 109.3 ± 4.3 ms and the upswing duration 29.7 ± 24.8 ms, mean Crl.Cr. = 69.2 ± 1.2 ml/min. All studies were performed before CsA administration, at baseline and at one-year follow-up. As a surrogate marker of the pulse wave velocity (PVW) we used the time to shoulder (TTS) parameter on the reconstructed central pulse pressure waveform.

Conclusions: In our study we demonstrate that there are no significant overall changes in arterial stiffness properties after one-year follow-up in stable renal transplant patients.

P.046

INSIGHTS FROM PULSE WAVE VELOCITY ACROSS CONTRASTING DISEASES

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Objectives: Several disease conditions are associated with an increased risk of vascular events. Direct evaluation of arterial structure and function remains elusive at the clinical level. We now report the results of pulse wave velocity in contrasting diseases.

Patients and Methods: We studied 200 consecutive patients assisted at the out-patient department of a public central hospital: (1) Obesity (OB, n = 60); (2) Type 2 Diabetes Mellitus (DM2, n = 60); Sexual Erectile Dysfunction (SED, n = 80). Patients were compared to controls (C, n = 60). Pulse wave velocity was measured between the carotid-radial arteries (CR) and between the carotid-femoral arteries (CF).

Results: Compared to controls, values at both sites were significantly increased in every disease condition: CR (m/s): (C) 7.03 ± 1.67; (OB) 8.21 ± 2.08; (DM2) 8.44 ± 2.10; (SED) 9.16 ± 3.20; CF (m/s): (C) 5.87 ± 1.92; (OB) 7.80 ± 1.24; (DM2) 11.31 ± 3.27; (SED) 13.08 ± 4.26. CR and CF PWV were directly and significantly related. Higher CR than CF levels were found only in the C group, with no difference in the OB group, and higher CR than CF levels in DM2 and SED groups (p < 0.05). Body volume was a general significant factor for PWV, across diagnostic groups.

Discussion: Non invasive assessment of arterial stiffness by measuring PWV establishes arterial function in several pathologic conditions associated with increased cardiovascular risk, even when this is still a matter of debate, namely OB and SED. Increased arterial stiffness is most marked in larger elastic arteries like the aorta (CF-PWV) and reverses the normal PWV gradient against smaller-muscular arteries (CR-PWV).

P.047

CCR5-DEL32 GENOTYPE MODIFIES PRO-INFLAMMATORY/ANTI-INFLAMMATORY CYTOKINE RATIO: POSSIBLE ROLE IN ATEROGENESIS

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CCR5 is a receptor for several chemokines and is highly expressed on the cells involved in atherogenesis. A 32 bp deletion mutation of CCR5 prevents expression of this molecule on cell surface and is associated with reduced risk of premature coronary artery disease. It was shown that IL-6/IL-10 ratio could be a predictor of further coronary artery events in patients with Non-ST elevation acute coronary syndrome. In the present study we investigated the effect of CCR5-de32 mutation on production of pro-inflammatory and anti-inflammatory cytokines by lymphocytes in basal or stimulated conditions. Subjects were from a cohort of patients admitted to undergo coronary artery bypass graft surgery. Samples from 7 patients who were homozygote for wild type CCR5 allele (CCRS/CRCRS) and 7 patients who were heterozygote for CCR5-de32 allele (CCRS/CRCRS-de32) were used. Peripheral mononuclear cells (PMNC) were separated from whole blood by density gradient centrifugation. The PMNC cultures were either left untreated or incubated with lipopolysaccharide (LPS) or oxidative low density lipoprotein (OxLDL) for 24 hours before collecting their supernatant for cytokines measurement. PMNC carrying del32 produced significantly more IL-6 at baseline and after LPS stimulation. They also produced more IL-10 when stimulated with LPS and OxLDL. However, pro-inflammatory/anti-inflammatory ratio (IL-6/IL-10 and TNF-α/IL-10) tend to be lower under stimulation by LPS and OxLDL in the group with de32 genotype. We concluded that some aspects of the protective effect of CCR5-de32 mutation against premature atherosclerosis can be attributed to modulation of anti-inflammatory and pro-inflammatory cytokine response in inflammatory cells particularly in PMNC.

P.048

AORTIC SYSTOLIC BLOOD PRESSURE: ESTIMATION FROM THE POINT OF SYSTOLIC AUGMENTATION IN THE DIGITAL ARTERY WAVEFORM

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Introduction: Central and peripheral blood pressure and waveforms differ due to effects of wave reflection and amplification. Use of a mathematical transform function to predict central pressure remains controversial. It may be possible to estimate central systolic pressure directly from a peripheral