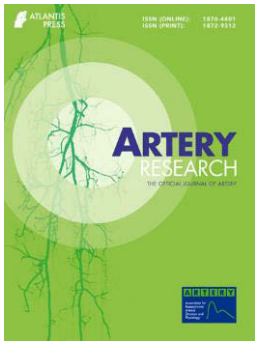

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01.04: NON INVASIVE EVALUATION OF ARTERIAL REMODELING IN PATIENTS WITH FABRY DISEASE AFTER ENZYME REPLACEMENT THERAPY

C.C. Collin, M.B. Briet, H.B. Beaussier, E.B. Bozec, B.L. Laloux, P.B. Boutouyrie, S.L. Laurent

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Young Investigator Presentations

01.01
ARTERIAL STIFFNESS IS INCREASED IN PAEDIATRIC HEART RECIPIENTS

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Introduction: Hypertension is a common complication following paediatric heart transplantation. One potential important factor is arterial stiffness, which has been shown to increase the risk of cardiovascular disease in adults.
Aim: To compare measures of arterial stiffness between paediatric heart transplant recipients (HTR) and healthy children.
Methods: Height, weight and blood pressure were measured in 191 healthy children (5–15 years) and 27 HTR (ages 6–18 years). Peripheral pulses were recorded at the ears, fingers and toes using multi-site photoplethysmography technology. Pulse transit times (PTT) and their differences between sites were calculated as indicators of arterial stiffness. ANCOVA statistical analysis was used to assess differences between the subject groups.
Results: ANCOVA analysis, with adjustments for differences in physical variables, demonstrated that measurements were significantly shorter in the HTR compared to normals for absolute toe PTT (300 ms vs. 312 ms, $p=0.009$) and the differences in toe PTT compared with ear (150 ms vs. 177 ms, $p<0.001$) and finger (101 ms vs. 121 ms, $p<0.001$). In addition, this study also found that HTR had significantly higher diastolic blood pressure (DBP) (69 mmHg vs. 63 mmHg, $p=0.034$) and heart rates (91 bpm vs. 78 bpm, $p=0.001$).
Conclusion: This study shows that heart transplant recipients have significantly shorter PTT than normal subjects. This suggests they have stiffer arteries, which probably contributes to their systolic hypertension. When considered alongside differences in DBP, it would appear that hypertension in HTR is multi-factorial.

01.02
ARTERIAL STRUCTURE AND FUNCTION AND ENVIRONMENTAL EXPOSURE TO CADMIUM

R. Schutte [1], T. Nawrot [1], T. Richart [1], L. Thijs [1], H.A. Roels [2], L.M. Van Bortel [3], H. Struijker-Boudier [4], J.A. Staessen [1]. [1]*University of Leuven, Leuven, Belgium,* [2]*Université catholique de Louvain, Brussels, Belgium,* [3]*Ghent University, Ghent, Belgium,* [4]*Maastricht University, Maastricht, Netherlands*

Background: Controversy exists regarding cadmium's influence on arterial function at the population level.
Methods and results: The associations of cadmium with measures of arterial function were determined in a randomly selected population sample ($n=557$) from two rural areas with low and high environmental exposure to cadmium. 24-h urinary cadmium excretion was significantly higher in the high compared with the low exposure group ($P<0.0001$). Aortic pulse wave velocity ($P=0.008$), brachial pulse pressure ($P=0.026$) and femoral pulse pressure ($P=0.008$) were significantly lower in the high exposure group. Femoral distensibility ($P<0.0001$) and compliance ($P=0.0013$) were significantly higher at high exposure. By determining associations between measures of arterial function and cadmium exposure across quartiles of the 24-h urinary cadmium excretion (adjusted for sex and age), brachial (P for trend $=0.015$) and femoral (P for trend $=0.018$) pulse pressure significantly decreased and femoral distensibility (P for trend $=0.008$) and compliance (P for trend $=0.007$) significantly increased with high cadmium excretion. After full adjustment, the partial regression coefficients confirmed these associations. Pulse wave velocity ($\beta=-0.79$; $P=0.004$) and carotid ($\beta=-4.20$; $P=0.006$), brachial ($\beta=-5.43$; $P=0.0001$) and femoral ($\beta=-4.72$; $P=0.007$) pulse pressures correlated negatively, while femoral compliance ($\beta=0.11$; $P=0.016$) and distensibility ($\beta=1.70$; $P=0.014$) correlated positively with cadmium excretion.
Conclusions: Increased cadmium body burden is associated with lower aortic pulse wave velocity, lower pulse pressure throughout the arterial system, and higher femoral distensibility.

01.03
CAROTID PLAQUE, ARTERIAL STIFFNESS GRADIENT, AND BENDING STRAIN IN HYPERTENSION

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Background: Plaque rupture may involve shearing strain of the arterial wall in the longitudinal direction. We previously determined a longitudinal gradient of arterial strain, named bending strain (BS), along the common carotid artery (CCA), with two distinct patterns (Paini et al. Stroke 2007): Pattern A (outward BS; larger radial strain at the plaque level than adjacent CCA) and Pattern B (inward BS), more often observed in dyslipidemic and type 2 diabetic patients.
Aim: To determine the influence of essential hypertension on patterns of bending strain.
Method: 92 patients with an atherosclerotic plaque on the CCA were included: 66 patients with essential hypertension (HT), either treated or not, and 26 normotensives (NT). A novel non-invasive echotracking system (ArtLab®) was used to measure intima-media thickness, diameter, pulsatile strain, and distensibility at 128 sites on a 4 cm long CCA segment.
Results: NT and HT did not differ except for BP values and an older age (5 years). Pattern A was less frequently observed in HT than in NT. The plaque exhibiting Pattern A were characterized by an inward remodeling whereas plaques exhibiting Pattern B grew according to an outward remodeling (increased external diameter and no change in internal diameter). In multivariate logistic regression analysis, Pattern B was influenced by essential hypertension (OR=6.8[1.35-34.9], $P<0.02$), independently of outward remodeling (OR=4.6[1.6-13.4], $P<0.005$) and lack of RAAS inhibitors (OR=4.7[1.1-20.4], $P<0.05$).
Conclusion: Patients with essential hypertension had a stiffer carotid at the level of the plaque than in adjacent CCA, leading to an inward bending stress.

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01.04

NON INVASIVE EVALUATION OF ARTERIAL REMODELING IN PATIENTS WITH FABRY DISEASE AFTER ENZYME REPLACEMENT THERAPY

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Context: Fabry disease (FD) is a deficiency of lysosomal enzyme α-galactosidase A leading to accumulation of glycosphyngolipids in vascular and renal tissues. Affected patients exhibit neuropathic pain and premature mortality because of renal failure and cardiovascular diseases. We have already described an accelerated hypertrophy of the arterial wall. Although enzyme replacement therapy (ERT) decreases glycosphyngolipids accumulation in tissues, there is no evidence of ERT efficacy on vascular hypertrophy.
Objective: To evaluate efficacy of intravenous ERT at usual dosage on large artery properties.
Design study: Longitudinal follow-up before (23 ± 11 Mo) and after ERT (47 ± 17 Mo). Four to 8 serial measurements of (a) carotid intima-media thickness (IMT) and diameter, obtained with high definition echotracking device, and (b) aortic stiffness, obtained through carotid to femoral pulse wave velocity (PWV).
Patients: 15 patients (12 males and 3 females with clinical manifestations), aged 33 ± 10 years.
Results: Carotid-femoral PWV significantly decreased during follow-up ($P<0.001$). The slope of PWV changes with time did not differ from zero (-0.16 ± 0.90 m/s/yr, NS) before ERT, but was significantly reduced after ERT (-0.50 ± 0.47 m/s/yr, $P<0.01$). IMT increased before ERT and kept increasing after ERT (ANOVA). However, individual slopes did not differ from zero (before ERT $+10 \pm 66$ μm/yr, after ERT: 4 ± 21 μm/yr ($P=0.745$)). Diameter, wall-to-lumen ratio and carotid distensibility did not change after ERT ($P=0.53$, 0.20, 0.44, respectively).
Conclusion: In addition to it's effectiveness on pain and glycosphingolipids storage in tissues, ERT with recombinant algasidase-beta proved to decrease aortic stiffness while carotid wall hypertrophy was still progressing.

01.05

RESPONSE OF BLOOD FLOW AND VASCULAR RESISTANCE IN COMMON CAROTID ARTERY TO HYPERCAPNIA

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Background: Although the brachial artery is appreciated as a representative of the arterial tree for endothelial function tests, it would be favourable to estimate flow mediated dilation (FMD) at clinically relevant locations e.g. the common carotid artery (CCA). Hypercapnia strongly stimulates cerebral blood volume flow, with steady state achieved after 2 mins, inducing FMD in the CCA.
Objective: To develop a complete stimulus-response profile (baseline, peak, steady state) of flow velocity, diameter and heart rate during and after hypercapnia, also to evaluate their interrelationships.
Methods: The CCA was visualised with an ultrasound beam at 60° in Doppler-mode with a P350 ultrasound system. Hypercapnia was induced with a 6.8% CO2 inhalation for a period of 2 mins. Processing of received signals from baseline, during hypercapnia and return to baseline (total 10 mins) clearly revealed in beat-to-beat changes in systolic and end diastolic diameters, blood flow velocity (BFV), blood flow rates, and carotid peripheral resistance.
Results: Continuous long-term measurements indicate a peak at 3 mins, with a steady decay over the remaining follow up time. The BFV (+25%), carotid diameter (+12%), distension and heart rate increase significantly during and post hypercapnia. No significant changes are seen in blood pressure.
Conclusions: Inhalation of CO2 for 2mins increases blood flow and induces carotid artery dilatation. CCA FMD exposes the dynamic interrelationship between blood flow and CCA diameter and is a good tool to test directly endothelial function in atherosclerotic prone arteries.

01.06

BIOMECHANICAL ANALYSIS OF HUMAN COMMON CAROTID ARTERIES BY SEGMENTED APPROACH ON NON-INVASIVE ECHOTRACKING SYSTEMS

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Background: In addition to measurement of diameter, intima-media thickness (IMT) and stiffness, the high resolution of non-invasive echotracking systems (Wall Track System® ArtLab®) permits to have insights in new parameters. First we can study longitudinal segmental inhomogeneities of strain defining gradients of strain and layer-by-layer changes in strain within the arterial wall, defining inhomogeneities in compressibility. The aim of the present report is to present feasibility data and first results for these two parameters.
Methods and results: Multidirectional segmentations of radio-frequency matrix recordings were applied to different diseases. First, longitudinal gradient of strain were measured in 92 patients with plaques, either hypertensive or not. Second, strain gradient within the wall (hence estimated compressibility), was tested in 46 patients with vascular Ehlers-Danlos Syndrome (vEDS) and 72 controls. Different conceptual and operational tools were developed under Matlab® software for these purposes. We observed that remodeling at the level of the plaque deeply influenced the segmental behavior of strain, inward remodeling being associated with exaggerated strain, and outward remodeling with reduced strain. We showed that both vEDS and control subjects exhibited marked excess of compressibility within IMT, and that this highly compressible zone was closer to the lumen and accentuated in vEDS than in controls.
Conclusion: It is possible to make segmental analysis of segmental properties of remodelling and bending stress. In addition, apparently homogeneous arterial walls exhibited mechanical interfaces which exaggerated compressibility and local stresses between different sub-layers within the wall.

05.01

CAN WAVE INTENSITY HELP EXPLAIN THE DIFFERENT VELOCITY FLOW PROFILES IN THE CORONARY ARTERIES?

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Background: In the left coronary arteries, coronary flow is said to occur mainly in diastole, but this is not the case in the right coronary artery (RCA). Since the pressure being applied at the aortic end is identical for both arteries, we hypothesised that differences from the microcirculatory end account for the differences in the flow velocity waveform. We apply a new technique, wave intensity analysis, to explain the differences in these velocity waveforms.
Methods: In 10 subjects sensor-tipped intra-arterial wires were used to measure simultaneous pressure and Doppler velocity in the proximal left main stem (LMS), the left anterior descending (LAD), the left circumflex arteries (LCX) and RCA. Wave intensity analysis was applied to derive proximal- and distal-originating waves.
Results: In all three left coronary artery positions, the systolic-diastolic ratio of peak velocity was significantly lower than the corresponding ratio in the RCA (LMS 0.58 ± 0.13, LAD 0.47 ± 0.12, LCX 0.57 ± 0.15 versus RCA1.09 ± 0.48, $p<0.03$ for each). The cause was a lower diastolic flow velocity in the RCA than the left coronary arteries (RCA 0.37 ± 0.28m/s versus LMS 0.58 ± 0.30m/s, LAD 0.58 ± 0.44m/s $p<0.05$ for each, LCX 0.46 ± 0.33m/s $p=$NS), which is explicable by the lower distal-originating suction wave (RCA $16.6 \pm 5.4\%$ versus LMS $27.6 \pm 7.6\%$, LAD $28.8 \pm 6.3\%$, LCX $26.0 \pm 6.6\%$, $p<0.02$).
Conclusion: The RCA has a flow velocity waveform which is evenly distributed between systole and diastole, in contrast to the diastolic dominant waveform seen in the left coronary arteries. The reason for this difference is the lower diastolic velocity of the RCA which is due to a smaller distally-originating diastolic ''suck'' from its microcirculation.

05.02

HERITABILITY AND INTRAFAMILIAL AGGREGATION OF ARTERIAL CHARACTERISTICS

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