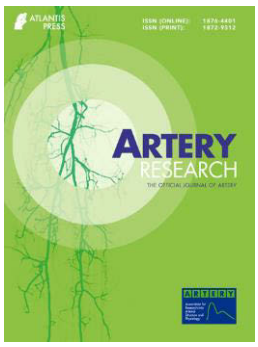

Artery Research

ISSN (Online): 1876-4401 **ISSN (Print): 1872-9312**
Journal Home Page: https://www.atlantis-press.com/journals/artres

P.017: THE ROLE OF THE CORONARY MICROCIRCULATION IN DETERMINING BLOOD FLOW

J.E. Davies*, N. Hadjiloizou, J. Aguado-Sierra, A.D. Hughes, K.H. Parker, J. Mayet

To cite this article: J.E. Davies*, N. Hadjiloizou, J. Aguado-Sierra, A.D. Hughes, K.H. Parker, J. Mayet (2006) P.017: THE ROLE OF THE CORONARY MICROCIRCULATION IN DETERMINING BLOOD FLOW, Artery Research 1:S1, S31–S32, DOI: https://doi.org/10.1016/S1872-9312(07)70040-6

To link to this article: https://doi.org/10.1016/S1872-9312(07)70040-6

Published online: 21 December 2019

P.013
LONGITUDINAL STUDY OF VASCULAR MARKERS OF PREMATURE ATHEROSCLEROSIS AND METABOLIC CORRELATES IN HIV-INFECTED CHILDREN

T. Bradley*, A. Bitnun, C. Slorach, C. Arneson, M. Cheung, E. Sochett, B. McCrindle, S. Read, S. King. *The Hospital for Sick Children, Toronto, Canada*

Purpose: To determine the presence of vascular markers of premature atherosclerosis and metabolic correlates in a prospectively followed cohort of antiretroviral treated HIV-infected children.
Methods: Vascular assessment included: carotid intima-media thickness and brachial artery reactivity using vascular ultrasound; peripheral pulse wave velocity (PWV) using photoplethysmography; central PWV, arterial stiffness and impedance indices using an Echo-Doppler method; and only at follow-up, augmentation index and PWV by applanation tonometry. Disease markers, oral glucose tolerance, fasting lipid profiles and abdominal fat (single slice CT scan) were also determined.
Results: Twenty children were assessed at baseline (median age 12.6 [range 8.5–18.5] years; 50% female) and follow-up 21–25 months later. All were on combination antiretroviral therapy at baseline, but 5 were off therapy at follow-up with fewer receiving protease inhibitors. Resting systolic blood pressure and pulse pressure increased significantly over the study period (both $p < 0.0001$), as did elastic modulus, stiffness index and input impedance ($p = 0.0018$, $p = 0.0004$, $p = 0.0082$, respectively). PWV measures by the different methods were not shown to correlate significantly. Dyslipidemia and abnormal glucose metabolism were present in 14 and 2 at baseline, and in 7 and 0 at follow-up, respectively. Visceral, subcutaneous and total abdominal fat content increased over time, but not significantly so.
Conclusions: An increase in measures of large arterial wall stiffness was observed over time. The reduction in dyslipidemia at follow-up may be related to fewer children receiving protease inhibitors. The potential risk of premature atherosclerosis in HIV-infected children on anti-retroviral therapy warrants long-term monitoring of metabolic profiles and vascular function.

P.014
VASCULAR MARKERS OF PREMATURE ATHEROSCLEROSIS IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND DISEASE, THERAPY, METABOLIC AND INFLAMMATORY CORRELATES

T. Bradley*, L. Nukumizu, C. Boros, C. Slorach, P. Tyrrell, M. Cheung, B. McCrindle, E. Silverman. *The Hospital for Sick Children, Toronto, Canada*

Purpose: Controversy exists as to whether the dyslipidemia and premature atherosclerosis which occurs in Systemic Lupus Erythematosus (SLE) is more due to disease activity or the therapy. We sought to determine the presence and correlates of vascular markers of premature atherosclerosis in paediatric SLE.
Methods: Vascular assessment included: carotid intima-media thickness and brachial artery reactivity using vascular ultrasound; peripheral pulse wave velocity (PWV) using photoplethysmography; central PWV, arterial stiffness and impedance indices using an Echo-Doppler method. These vascular indices were converted to z-scores from normal population data, and tested for normality with single sample t-tests. Augmentation index and PWV, using applanation tonometry, were only assessed in the latter half of the cohort. Disease activity scores, disease duration, cumulative prednisone dose, other medication use and fasting lipid, glycemic and inflammatory profiles were also determined and Pearson correlations performed.
Results: Seventy paediatric SLE were assessed (median age 15.7 [7.3–18.7] years and diseased duration 1.4 [0.1–11.0] years, 80% females). The mean z-score adjusted data was significantly increased from normal for central PWV (+1.1, $p < 0.0001$), input (+0.3, $p < 0.04$) and characteristic impedance (+0.8, $p < 0.0001$). Correlations were found between aortic elastic modulus and higher fasting glucose (R 0.34, $p < 0.007$), and between stiffness index and homocysteine levels (R 0.38; $p < 0.008$).
Conclusions: In treated paediatric SLE of relatively short duration, dyslipidemia, abnormal glycemic and inflammatory profiles were relatively common. Some stiffness measures were increased and others correlated with known atherosclerotic risk factors. These patients warrant long-term monitoring of vascular function and traditional and non-traditional risk factors.

P.015
ARE NITRIC OXIDE SYNTHASE AND CYCLOOXYGENASE PRODUCTS INVOLVED IN ACETYLCHOLINE VASODILATING EFFECTS "IN VIVO"?

L.B.M. Resstel, F.M.A. Corrêa*. *Department of Pharmacology, School of Medicine of Ribeirão Preto-USP, Ribeirão Preto, Brazil*

It is current understanding in the literature that acetylcholine (ACh) vasodilating effect is endothelium-dependent. Also, different endothelial substances such as NO, EDHF and prostanoids can mediate ACh-induced vasorelaxation in different vessels. Although ACh-induced relaxation of isolated rat aorta rings is mainly related with NO release it is also dependent on prostanoids because pretreatment with indomethacin shifted the ACh curve to the right, reducing maximal effect (Vizioli et al., J Smooth Muscle Res, 41: 271–281, 2005). Consequently, one should expect that nitric oxide synthase (NOS) and cyclooxygenase (COX) inhibition should affect ACh-induced vasodilation "in vivo". To test this hypothesis we studied the effect of i.v. pretreatment with L-NAME (20 mg/kg), indomethacin (5 mg/kg) or its combination on the response to i.v. infusion of ACh in urethane-anesthetized rats. ACh infusion caused progressive blood pressure (BP) fall up to –40 mmHg, which was completely abolished by homatropine methylbromide (1 mg/kg). Although L-NAME significantly increased baseline BP (~50 mmHg) indicating NOS blockade, the response to ACh was not significantly affected. Indomethacin shifted the ACh curve to the left, suggesting that COX blockade potentiates the response to ACh "in vivo", as opposed to what was observed in isolated aortic rings. After the combined NOS and COX inhibition, the hypotensive response to ACh infusion was not significantly different from that observed prior to pretreatment. The present results disagree with those reported in isolated vessels and raise doubts on the mechanism actually involved in the hypotensive response to ACh "in vivo".

P.016
INCREASED ARTERIAL STIFFNESS IN YOUNG PATIENTS WITH RHEUMATOID ARTHRITIS

A. Cypiene[1]*, A. Laucevicius[2], A. Venalis[1], L. Ryliskyte[2], J. Dadoniene[1], Z. Petrulioniene[2], M. Kovaite[2]. [1]*Institute of Experimental and Clinical Medicine at Vilnius University, Vilnius, Lithuania,* [2]*Clinics of Heart Diseases, Vilnius University; Centre of Cardiology and Angiology, Vilnius, Lithuania*

Background: Chronic inflammation may impair arterial function and lead to an increase of their stiffness and risk of developing early atherosclerosis.
Aim of the study was to assess whether rheumatoid arthritis (RA) and high level of C-reactive protein can influence systemic arterial stiffness and aortic pulse wave velocity (PWV) in patients with RA.
Methods: We studied 53 RA patients (age 40.1±9.8 years) with moderate and high disease activity (DAS28 3.21–7.05) and 55 controls (age 39.7±8.1 years). Blood test included serum lipid profile, glucose and high-sensitivity CRP (hsCRP) measurement. The carotid-radial PWV and augmentation index (AIx) were assessed noninvasively by applanation tonometry (Sphygmocor v.7.01, AtCor Medical).
Results: In RA patients the adjusted for heart rate AIx (21.3±13.3% vs. 12.7±13.2%; $p < 0.001$) and hsCRP (31.32±40.29 mg/l vs. 1.58±3.36 mg/l; $p < 0.001$) were significantly higher as compared to the controls. Multivariate regression analysis revealed that RA is significant predictor of increased PWV adjusted for mean blood pressure ($p < 0.001$). In RA patients and control group correlations were not found between hsCRP and AIx ($r = -0.044$; $p = 0.752$ vs. $r = 0.215$; $p = 0.121$) as well as between hsCRP and PWV ($r = -0.076$; $p = 0.589$ vs. $r = -0.014$; $p = 0.921$).
Conclusion: RA is associated with the increase of aortic and systemic arterial stiffness. Elevation of serum hsCRP is not related to the increase of arterial stiffness neither in RA patients nor in controls.

P.017
THE ROLE OF THE CORONARY MICROCIRCULATION IN DETERMINING BLOOD FLOW

J.E. Davies*, N. Hadjiloizou, J. Aguado-Sierra, A.D. Hughes, K.H. Parker, J. Mayet. *International Centre for Circulatory Health, St Mary's Hospital & Imperial College, London, United Kingdom*

Background: The coronary flow velocity profile is strikingly different from that of the proximal aorta, even though they are only a few centimetres apart and have almost identical pressure waveforms. We use wave intensity analysis to help explain this phenomenon, and to explore the importance of the coronary microcirculation in the regulation of coronary blood flow.
Method and Results: In 18 subjects (mean age 54 years, 12 female) we measured simultaneous pressure and Doppler velocity using intra-arterial wires in the proximal left main stem, left anterior descending, circumflex artery and proximal aorta. Wave intensity analysis was used to separate the

pressure waveform into its proximal- and distal-originating components. In the aorta the flow velocity waveform follows the aortic pressure waveform reasonably closely, although the peak velocity occurs before the peak pressure. Using wave intensity analysis we found that more than 70% (47.3 versus 19.7 mmHg, $p < 0.001$) of the increase in the aortic pressure waveform was from proximally-originating pressure. In contrast, in the coronary arteries, only 48% of the increase in pressure came from a proximal origin and the remainder from a distal (microcirculatory) origin (31.3 $\pm$11.5 versus 33.7 $\pm$8.4 mm Hg, $p = 0.47$). Distal-originating pressure rises prior to proximal-originating pressure (41$\pm$28 ms versus 104 $\pm$25 ms, $p < 0.001$). This excess distal-originating pressure attenuates the rise of coronary flow velocity (0.2$\pm$0.23 m/s), which is only reversed during cardiac relaxation when distal-originating pressure falls rapidly, and coronary flow velocity peaks (0.58$\pm$0.49 m/s).
Conclusion: Aortic flow velocity is largely driven by the proximally-originating aortic pressure. In contrast, coronary blood flow velocity is heavily regulated by the coronary microcirculation. During cardiac contraction distal coronary pressure exceeds proximal-originating pressure – restricting blood flow. Only after cardiac relaxation begins does distal pressure fall, allowing coronary flow velocity to rise rapidly.

P.018
OPTIMIZATION OF ULTRASOUND BRACHIAL ENDOTHELIAL FUNCTION MEASUREMENTS

E. de Groot[1]*, J.J.P. Kastelein[1], A. Donald[2], J. Deanfield[2]. *[1]AMC Vascular Imaging, Vascular Medicine, Amsterdam, Netherlands, [2]Vascular Physiolgy Unit, Institute of Child Health and Great Ormond Street Hospital, London, United Kingdom*

Objective: Ultrasound measurements of brachial arterial lumen dilatation following induced blood flow increase – brachial flow mediated dilatation (FMD) – describes endothelial function. FMD is known to have great differences in methods and variability. We therefore standardized the protocol and optimized instrumentation. Reproducibility was evaluated.
Methods: Room environmental conditions, positioning and preparation of subjects and instrumentation were defined. Subjects refrained from food, caffeine and exercise from the night before measurements. A stable, yet flexible, ultrasound probe holder and arm positioning/fixation device were used. Three sonographers investigated right brachial arteries of 35 healthy non-smoking young adults aged 23.8 (SD10.8) years on two separate occasions (Acuson Aspen, L7, 5–12MHz transducer). Blood flow was induced upon release of 5 minute fore arm cuff inflation (250 mmHg). Every third heart beat ECG-triggered DICOM still frames were captured on R-wave from start, 1 minute prior to forearm cuff inflation (250 mmHg), to 4 minutes after cuff release. Brachial lumen was measured continously with automated edge detection (Sonka, Brachial Analyzer, MIA, IA, USA). FMD was defined as % maximum lumen change after cuff release compared to start lumen diameter.
Results: For initial and replicates, the start lumen diameters were 3.88(SD0.64) and 3.89(0.65) mm; FMD's 5.85(3.43) and 5.61(3.08)%. Mean paired difference between scans was 0.25(1.12)%: CV = 19.6%.
Conclusions: Standardization, stable setup of equipment and automated image analysis allow for consistent reproducible FMD measurements. Trial specific DICOM application protocols makes FMD fit for QAQC, applicable in multicentre studies on CVD risk and treatment regimens.

P.019
PREREQUISITES FOR CAROTID ULTRASOUND IMAGING STUDIES IN THE IDENTIFICATION AND PREVENTION OF ATHEROSCLEROSIS

E. de Groot*, J.J.P. Kastelein. *AMC Vascular Imaging, Vascular Medicine, Amsterdam, Netherlands*

B-mode ultrasound carotid intima-media thickness (IMT) measurements have increasingly proven their value as an in-vivo, non-invasive vascular research tool.
IMT can document arterial wall changes as a continuous variable, from a normal arterial wall to complete occlusion, throughout life, in groups at cardiovascular disease risk and in the unaffected.
Supported by the results of epidemiological studies and drug trials, the method can investigate the need for vascular disease prevention and evaluate cardiovascular disease risk reduction by therapeutic regimens in populations at risk.
IMT also complies with the statistical definition of a validated biomarker. Consequently, IMT is considered a truly validated surrogate endpoint for atherosclerosis progression and future and present atherosclerotic disease risk.
Presently, ultrasound arterial wall imaging studies go through a series of rapid methodological, technical and procedural developments.
The approach to imaging studies is therefore standardization so observational epidemiological and trial data become complementary. Moreover, image acquisition and administration using DICOM based trial specific application protocols, allow for regulatory compliant imaging procedures and quality assessement and quality control.
We address how and why this fascinating and elegant tool has widespread scientific and clinical applications in atherosclerosis research as well as its implications on cardiovascular disease prevention.

P.020
PLASMA HOMOCYSTEINE IS AN INDEPENDENT RISK FACTOR OF THE INCREASED INTIMA-MEDIA THICKNESS

V. Dzenkeviciute[2]*, J. Badariene[2], L. Ryliskyte[2], Z. Petrulioniene[1], A. Laucevicius[1]. *[1]Clinic of Heart Diseases, Vilnius University, Vilnius, Lithuania, [2]Center of Cardiology and Angiology, Vilnius University Hospital Santariskiu Klinikos, Vilnius, Lithuania*

Background: Clinical studies showed the association of mild to moderate hyperhomocystinemia not only with coronary artery disease (CAD), but also with stroke and peripheral artery disease.
The aim of study was to assess the relationship between intima media thickness (IMT) measured by B-mode ultrasound and conventional risks factors in families with premature CAD.
Methods: The study population consisted of 40 families with premature CAD. Totally n = 87 subjects were studied. Each family in the cohort has at least one affected sibling with premature CAD. Plasma level of homocysteine, Il-6 and serum lipid profile was measured. All conventional risk factors were analyzed. Carotid and femoral IMT was assessed by high-resolution B-mode carotid ultrasound (GE, 13 MHz). The carotid and femoral IMT was scanned at the near wall 15–20 mm proximal to the tip of the flow divider into the common carotid or femoral artery.
Results: A total of 66.6% subjects had increased IMT (>0.09 cm). Plasma levels of homocysteine (10.29$\pm$2.64 vs 8.58$\pm$2.61, $p = 0.006$), Il-6 (3.79$\pm$6.63 vs 2.30$\pm$0.74, $p = 0.05$), arterial hypertension (56% vs 43%; $p = 0.004$) and waist circumference (98.33$\pm$11.09 vs 91.40$\pm$8.45, $p = 0.044$) were significantly higher in increased IMT group compared with normal IMT group. Logistic regression analysis of data detected that only homocysteine strongly (Exp(B) 1.3, CI 1.0–1.62) and independently predicts increased IMT ($p = 0.015$).
Conclusion: Theses data show that in families with premature CAD, elevated plasma homocysteine is an independent risk factor of the increased IMT.

P.021
RENAL INSUFFICIENCY IS ASSOCIATED WITH AUGMENTATION INDEX AND ENDOTHELIAL DYSFUNCTION

J. Egresits*, J. Nemcsik, T. el Hadj Othmane, E. Finta, K. Farkas, A. Tisler, I. Kiss. *Department of Angiology, Dept. of Nephrology, St Emeritus Teaching Hospital, Budapest, Hungary*

Background: Patients with mild or moderate chronic kidney disease (CKD) are know to have a significant increase in cardiovascular morbidity in which alterations in large arterial as well as endothelial function may play a role. In the present study, we investigated the relationship between glomerular filtration rate (GFR), augmentation index and endothelial function.
Methods: Cross sectional study with healthy controls (CONT, n = 16), patients with essential hypertension (EH, n = 14), and those with essential hypertension and peripheral artery disease (EH+PAD, n = 26). The effect of postocclusive reactive hyperemia (PORH; 220 mmHg, 3 min, %) was measured on skin microcirculation with laser Doppler flowmetry (Periflux 5001). Augmentation index (Aix, %) was evaluated with the newly developed TensioClinic Arteriograph instrument which registers the pulse wave curves with the oscillometric method and automatically calculates AIx. GFR was estimated by the Cocroft-Gault formula.
Results: PORH, AIx and GFR were significantly different in healthy controls (–65.08%; 37.56%; 110.14ml/min) compared to the different patient groups: EH (294.43%; –29.87%; 86.18 ml/min) and EH+PAD (196.81%; 7.75%; 56.15ml/min). Subjects were divided into three groups based on their GFR: 1. GFR > 90; 2. 90 > GFR > 60; 3. 60 > GFR > 30. In the different groups of GFR a deterioration of PORH (1.: 328.54%; 2.: 278.67%; 3.: 200.85%) and AIx (–58.38%; –2.73%; 8.80%) was observed (all $p < 0.05$). Significant ($p < 0.01$) correlation was found between GFR and PORH ($r = 0.50$), and between GFR and AIx ($r = -0.81$).
Conclusions: AIx and PORH is associated with early renal function loss, suggesting that arterial stiffening and endothelial dysfunction may be involved in the vascular complications of CKD.