



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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

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**To cite this article:** V. Dzenkeviciute\*, J. Badariene, L. Ryliskyte, Z. Petrulioniene, A. Laucevicius (2006) P.020: PLASMA HOMOCYSTEINE IS AN INDEPENDENT RISK FACTOR OF THE INCREASED INTIMA-MEDIA THICKNESS, Artery Research 1:S1, S32–S32, DOI: [https://doi.org/10.1016/S1872-9312\(07\)70043-1](https://doi.org/10.1016/S1872-9312(07)70043-1)

**To link to this article:** [https://doi.org/10.1016/S1872-9312\(07\)70043-1](https://doi.org/10.1016/S1872-9312(07)70043-1)

Published online: 21 December 2019

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

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**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 forearm 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 continuously 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

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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 assessment 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

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**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:** These 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

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**Background:** Patients with mild or moderate chronic kidney disease (CKD) are known 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 Cockcroft-Gault formula.

**Results:** PORH, Aix and GFR were significantly different in healthy controls (-65.08%; 37.56%; 110.14 ml/min) compared to the different patient groups: EH (294.43%; -29.87%; 86.18 ml/min) and EH+PAD (196.81%; 7.75%; 56.15 ml/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.