



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P3.9: METABOLOMIC SIGNATURE OF ARTERIAL STIFFNESS IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE**

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**To cite this article:** M. Zagura, J. Kals, K. Paapstel, K. Kilk, M. Serg, P. Kampus, J. Eha, U. Soomets, M. Zilmer (2014) P3.9: METABOLOMIC SIGNATURE OF ARTERIAL STIFFNESS IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE, Artery Research 8:4, 138–138, DOI: <https://doi.org/10.1016/j.artres.2014.09.120>

**To link to this article:** <https://doi.org/10.1016/j.artres.2014.09.120>

Published online: 7 December 2019

## P3.7

## IMPEDANCE MISMATCHING BETWEEN CENTRAL AND PERIPHERAL ARTERIES FAILS TO EXPLAIN CENTRAL PRESSURE AUGMENTATION: AORTIC RESERVOIR CHARACTERISTICS MAY BE THE PREVAILING FACTOR

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**Background:** It is suggested that central augmented pressure (AP) and augmentation index (Alx) are due to wave reflection from peripheral to central arterial impedance mismatching. Comparatively stiffened peripheral vasculature should equate to increased AP and Alx. However, recent evidence suggests aortic reservoir characteristics may be a more dominant contributor to AP and Alx. This study aimed to determine relationship of central to peripheral impedance mismatch with, and predictors of, AP and Alx.

**Methods:** Carotid-to-femoral (aortic) pulse wave velocity (aPWV) and carotid-to-brachial PWV (bPWV) were measured in 255 patients with treated hypertension (aged 64±8, 47% male). Central AP, Alx and aortic reservoir pressure were derived from radial tonometry. Participants were stratified according to 'high' (bPWV > aPWV, n=64) or 'low impedance mismatch' (bPWV ≤ aPWV, n=191).

**Results:** Conflicting with theoretical expectations, central AP and Alx were significantly higher in participants with low-impedance mismatch compared to those with high-impedance (11±6 vs 7±6 mmHg, p=0.001 and 24±10 vs 21±13 %, p=0.05). Furthermore, impedance mismatch (bPWV-aPWV) was negatively and independently associated with AP (r=0.-0.13, p=0.04) and not associated with Alx (r=0.-0.001, p=0.99). However, aortic reservoir pressure was a positive independent predictor of AP and Alx (r=0.80 and r=0.62, p<0.001 for both).

**Conclusions:** Contrary to prevailing theory, 'high-impedance' mismatch between central and peripheral arteries does not result in higher AP or Alx. Aortic reservoir characteristics, rather than discrete wave reflection from impedance mismatching between peripheral and central arteries, may better explain AP and Alx.

## P3.8

## ACUTE EFFECTS OF CONTRAST MEDIA ON CENTRAL HEMODYNAMICS, ARTERIAL STIFFNESS, INFLAMMATORY AND KIDNEY INJURY BIOMARKERS

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**Introduction:** Contrast-induced nephropathy (CIN) is widely recognized as the third most common type of hospital-acquired acute kidney injury. Despite the impact of CIN on adverse cardiovascular events, little is known about the effects of contrast media on arterial functional properties. The objective of this study was to evaluate effects on central hemodynamics, arterial stiffness as well as changes in biomarkers of inflammation and kidney injury after contrast media administration.

**Methods:** The cohort comprised 36 symptomatic peripheral arterial disease (PAD) patients with GFR ≥ 60ml/min/1.73<sup>2</sup> undergoing a lower extremities digital subtraction angiography (DSA) with intra-arterial isosmolar iodinated contrast media. Central hemodynamics and arterial stiffness parameters were determined by applanation tonometry (on admission, 8h, 24h after DSA). Serum samples and urine samples were also collected. All samples underwent ELISA testing for biomarkers. Statistically significant differences were calculated by one-way ANOVA and paired t-test.

**Results:** Augmentation pressure decreased and pulse pressure amplification increased significantly (p=0.01 ; p=0.02, respectively) compared to baseline, but there were no changes in augmentation index and aortic pulse wave velocity. Increase in the levels of serum neutrophil gelatinase lipocalin, urinary kidney injury molecule-1, beta-2 microglobulin, high-sensitivity CRP, myeloperoxidase and interleukin-6 were observed compared to baseline (p <0.05).

**Conclusions:** This is the first clinical study to evaluate the complex effects of contrast media on arterial stiffness, central hemodynamics and several biomarkers. The results suggest that in PAD patients without impaired renal function contrast media may induce acute inflammation, moderate tubular injury and changes in central hemodynamics.

## P3.9

## METABOLOMIC SIGNATURE OF ARTERIAL STIFFNESS IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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**Background:** Arterial stiffness is an independent determinant of cardiovascular risk. Metabolomics is the comprehensive analysis of low-molecular-weight metabolites, which could provide additional information regarding the pathogenesis of atherosclerosis. The aim of the current study was to compare metabolic signatures and functional-biochemical characteristics of patients with peripheral arterial disease (PAD) and clinically healthy subjects.

**Methods:** We studied 42 men with symptomatic PAD (66±7 years) and 46 healthy men (66±8 years). Aortic pulse wave velocity (aPWV) was assessed by applanation tonometry using the Sphygmocor device. Metabolic profiling was performed with high-performance liquid chromatography and mass-spectrometry. Serum oxLDL level was measured by ELISA.

**Results:** The aPWV as well as serum levels of lactate, free carnitine and 11 amino acids including tyrosine were higher among the patients with PAD. The aPWV correlated significantly with several amino acids: log-phenylalanine, log-tyrosine and log-serine for the patients with PAD. In the control group, aortic PWV was correlated to log-pyruvate. In multiple regression models, aPWV was independently determined by log-tyrosine and log-oxLDL in the patients (R<sup>2</sup>=0.61; p<0.001) and by age, log-pyruvate and log-oxLDL in the controls (R<sup>2</sup>=0.52; p<0.001).

**Conclusion:** Metabolomic signature of patients with advanced atherosclerosis differs compared to clinically healthy controls. The aPWV is independently associated with serum levels of Tyr and oxLDL in the patients with PAD and is related to pyruvate and oxLDL levels in the control group. The measurement of low-molecular metabolites, which are related to changes in vascular phenotypes, may lead to identification of novel vascular risk markers.

## P3.10

## REACTIVITY TO LOW-FLOW IN THE BRACHIAL ARTERY: A POTENTIAL DETERMINANT FOR FLOW-MEDIATED DILATORY RESPONSE

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The reduction in shear stress during cuff-occlusion has been hypothesized to mediate reactivity to low-flow. However, shear stress-dose dependence of reactivity to low-flow in the brachial artery (BA) is unclear. Furthermore, reactivity to low-flow in BA seems to vary from vasoconstriction to vasodilation, which could affect a subsequent flow-mediated dilation (FMD) response. This study examined whether reactivity to low-flow would be dependent on the magnitude of shear rate (SR) reduction in individuals with diverse cardiovascular risk profiles, and whether reactivity to low-flow would influence FMD. Data from 165 individuals were analysed and divided into the increased cardiovascular risk group (CVR: n=115, 85M, 67.0±8.8yrs) and control group (CTRL: n=50, 30M, 63.2±7.2yrs). BA diameter and blood velocity data obtained from Doppler ultrasound were used for calculation of FMD, reactivity to low-flow and estimated SR using edge-detection software. There was no correlation between reactivity to low-flow and the magnitude of SR reduction. There was a significant correlation between FMD and reactivity to low-flow in overall (r=0.261), CTRL (r=0.365) and CVR (r=0.189, all p<0.05) groups. Multivariate regression analysis found that peak SR, reactivity to low-flow and baseline diameter independently contributed to FMD along with sex, diabetes and smoking (R<sup>2</sup>=0.449). This study demonstrated a SR dose-independence of reactivity to low-flow and also a significant association between reactivity to low-flow and FMD. Furthermore, peak SR, reactivity to low-flow and baseline diameter each independently contributed to FMD, suggesting that these haemodynamic factors may in part determine FMD in BA.