



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

P.096: ROLE OF ARGINASE PATHWAY IN RESPONSE TO SHEAR STRESS: NEW POTENTIAL THERAPEUTIC TARGETS FOR ATHEROSCLEROSIS?

R.F. da Silva, V. Gambillara, C. Cheng, D. Segers, R. de Crom, R. Krams, N. Stergiopoulos

To cite this article: R.F. da Silva, V. Gambillara, C. Cheng, D. Segers, R. de Crom, R. Krams, N. Stergiopoulos (2007) P.096: ROLE OF ARGINASE PATHWAY IN RESPONSE TO SHEAR STRESS: NEW POTENTIAL THERAPEUTIC TARGETS FOR ATHEROSCLEROSIS?, Artery Research 1:2, 74–75, DOI: <https://doi.org/10.1016/j.artres.2007.07.030>

To link to this article: <https://doi.org/10.1016/j.artres.2007.07.030>

Published online: 21 December 2019

[95% CI: 20.9 to 22.5] versus 23.4 [22.6 to 24.2]; $p=0.004$), larger subendocardial viability index (SVI, 173.8 [171.2 to 176.5] versus 169.6 [166.8 to 172.4]; $p=0.033$) and no significant difference in aorta pulse pressure (APP). **Conclusions:** Regular aerobic-endurance exercise attenuates age-related reductions in central arterial compliance and increases the subendocardial blood flow. This may be two mechanisms by which habitual exercise could lower the risk of cardiovascular disease in this population.

P.093

ROLE OF HEART FAILURE ETIOLOGY ON ARTERIAL WAVE REFLECTION IN HEART TRANSPLANT RECIPIENTS: RELATION WITH CIRCULATING C-REACTIVE PROTEIN

G.L. Pierce¹, R.S. Schofield², W.W. Nichols², J.A. Hill², R.W. Braith².
¹University of Colorado, Boulder, Colorado, USA, ²University of Florida, Gainesville, Florida, USA

Background: Aortic augmentation index (AI_a), a measure of arterial pressure wave reflection related to central and/or peripheral arterial stiffness, is elevated in many heart transplant recipients (HTRs). C-reactive protein (CRP), a marker of systemic inflammation associated with ischemic heart disease, is an independent predictor of cardiac allograft vasculopathy and death in HTRs. We hypothesized that arterial wave reflection would be higher in HTRs with ischemic compared with non-ischemic heart failure etiology and this would be associated with circulating CRP early after transplantation.

Methods: Two months after heart transplantation, 20 HTRs underwent non-invasive measurement of aortic pressure and wave reflection properties adjusted for heart rate (Sphygmocor, AtCor Medical) and plasma metabolic and inflammatory markers.

Results: Aortic AI_a was higher in HTRs with ischemic ($n=12$) compared with non-ischemic ($n=8$) heart failure (mean±SD; 22.5 ± 11.0 vs. $11.6 \pm 10.5\%$, $p<0.01$). Similarly, circulating CRP was higher in HTRs with ischemic compared with non-ischemic heart failure (5.4 ± 4.5 vs. 1.4 ± 1.1 mg/L, log transformed $p<0.05$). Moreover, there was a significant relation between logCRP and AI_a ($r=0.68$, $p<0.05$), roundtrip time of the reflected wave to the peripheral reflecting sites and back ($r=-0.62$, $p<0.01$), and left ventricular wasted energy ($r=0.55$, $p<0.01$). When adjusted for CRP, the difference in AI_a between groups was abolished suggesting that circulating CRP contributed in part to the group differences in wave reflection.

Conclusions: HTRs with ischemic heart failure etiology demonstrated increased arterial wave reflection compared with HTRs with non-ischemic heart failure early after transplantation and this was associated with higher circulating CRP.

P.094

CAROTID ATHEROSCLEROSIS ASSOCIATED TO METABOLIC SYNDROME AND ISCHEMIC HEART DISEASE IN HYPERTENSIVE PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY

I. Tasic¹, D. Lovic², D. Djordjevic¹, M. Lovic¹. ¹Institute of Cardiology Niska Banja, Niska Banja, USA, ²Clinic for Internal disease, InterMedica, Nis, USA

Metabolic syndrome (MS) is one of the numerous risk factors for some patients with cardiovascular diseases. Aims: 1. to prove the presence of MS at patients with hypertension and left ventricular hypertrophy (LVH) analyzing clinical parameters; 2. to estimate the impact of MS on patient prognosis.

Method: There have been analyzed 73 hypertensive patients (43 male), average age 56.3 ± 8.5 with echocardiographically proved LVH (average LVMI 163.5 ± 31.8 g/m²).

Results: 36 patients (55 ± 8 years) fulfilled the criterion of MS. They had significantly higher glucose level, lower HDL cholesterol, higher triglycerides and higher body mass index (29.6 ± 3.8 vs. 27.8 ± 3 , $p<0.03$). This group of patients had more frequent complex VA and significantly lower values of HRV. After nine years of observation, four patients in this group had fatal CV events (3 CVI—3 deaths, 1 sudden death), while in the second group, two patients had two sudden deaths (ns).

The purpose of this study was to investigate the subclinical carotid atherosclerosis prevalence in different groups, with and without metabolic syndrome. ColourDuplex ultrasonography of the carotid arteries was performed on Acuson Sequia C236 with high-frequency linear probe with 8 MHz. The thickness of the intima-media complex in patients with MS was 1.03 ± 0.03 vs. 0.99 ± 0.02 mm in patients without MS. Twelve patients with MS (33%) had carotid plaques, and at 43% of patients had been diagnosed

coronary disease (3 IM, 2 PTCA with inbuilt stent, ten with angina pectoris and positive exercise tests), while 20% of patients with non MS had carotid plaques ($p<0.04$), and 9% had coronary disease (3 with angina pectoris and positive exercise tests) ($p<0.002$).

Conclusions: Results of our study showed that patients with LVH and MS had significantly greater prevalence of the carotid atherosclerosis and CAD, and high correlation between carotid artery disease and presence and severity of CAD.

P.095

THE DISPARATE EFFECTS OF MICROVASCULAR RAREFACTION AND REDUCED COMPLIANCE ON PROXIMAL HAEMODYNAMICS: INVESTIGATION WITH A MATHEMATICAL AND COMPUTATIONAL MODEL OF THE CIRCULATION

G.A. Vaughan², M.K. Johnson⁴, P.B. Mark¹, J.M.C. Connell¹, M.S. Olufsen³, N.A. Hill², C.A.R. Sainsbury¹. ¹BHF Glasgow Cardiovascular Research Centre, Glasgow, United Kingdom, ²Dept Mathematics, University of Glasgow, Glasgow, United Kingdom, ³Dept Mathematics, North Carolina State University, North Carolina, USA, ⁴Scottish Pulmonary Vascular Unit, Western Infirmary, Glasgow, United Kingdom

The fundamental haemodynamic interaction between large and small vessels is important and poorly understood. We aimed to investigate the effect of microvascular rarefaction (MR) and reduced small vessel compliance (SVC) using a mathematical and computational model of the systemic arterial circulation.

Systemic arteries are treated as a bifurcating tree of compliant and tapering vessels. Large and small vessels are treated separately. MR is modelled by altering the area ratio between parent and daughter vessels at bifurcations. Reduced SVC is modelled by altering the value for Young's modulus within structured trees. Aortic flow profiles (from MRI) of 7 healthy subjects (mean age 51.6y) were used as input to the model. Runs were made at baseline (normal parameters), with modelled MR (area ratio 1.08) and reduced SVC (20% reduction). Pressure and flow waveforms were generated at ascending aorta and radial artery.

Results expressed as change from baseline values. Radial artery (i) decreased compliance - SBP[+3.3%], DBP[-2.6%], pulse pressure (PP)[+13.3%] (i) rarefaction SBP[+12.7%], DBP[+21.1%], PP[-1.4%]. Ascending aorta (i) decreased compliance SBP[+3.3%], DBP[-2.6%], PP[+18.5%] (ii) rarefaction SBP[+10%], DBP[+19.3%], PP[-13.4%].

The predominant effect of decreasing SVC was an increase in pulse pressure with a small increase in peak pressure. Increased MR lead to an increase in both systolic and diastolic pressures with reduced central pulse pressure. These results represent modelled changes in small vessel properties only, with no changes made to large artery parameters. These results suggest that such model represents a useful tool in investigating haemodynamic mechanism, with multiple potential physiological and clinical applications.

P.096

ROLE OF ARGINASE PATHWAY IN RESPONSE TO SHEAR STRESS: NEW POTENTIAL THERAPEUTIC TARGETS FOR ATHEROSCLEROSIS?

R.F. da Silva¹, V. Gambillara¹, C. Cheng², D. Segers², R. de Crom², R. Krams³, N. Stergiopoulos¹. ¹Swiss Federal Institute of Technology, Lausanne, Switzerland, ²Erasmus Medical Center, Rotterdam, Netherlands, ³Imperial College London, London, United Kingdom

Introduction: Alterations of wall shear stress can predispose the endothelium to the development of atherosclerotic plaques. Ample evidence indicates that arginase expression and/or activity correlates with several risk factors for cardiovascular disease including atherosclerosis.

Methods: To evaluate the regulation of arginases by different shear stress patterns without neuroendocrine factors, we perfused carotid arterial segments to unidirectional high and low shear stress, and oscillatory shear stress. After 3 days of flow exposure, vascular function, arginase expression and localization were analyzed. We compared these well-controlled measurements to an *in vivo* model of shear stress-induced atherogenesis. In brief, the carotid artery of ApoE^{-/-} mice, fed with high cholesterol diet, was exposed to similar hemodynamic conditions by the placement of a shear stress modifier for 9 weeks.

Results: Our results showed for the first time that exposure of carotid segments to high shear stress conditions (athero-protective) significantly

decrease arginase II protein expression as compared to both low and oscillatory flow conditions. Immunohistochemistry analysis confirmed a pronounced expression of arginase II on SMCs and macrophages on the atherosclerotic plaques formed by oscillatory and low shear stress *in vivo*. **Conclusions:** The present study demonstrates that arginase expression is modulated by shear stress patterns in carotid arteries perfused *ex vivo*. Similar findings are also observed in a model of shear stress-induced atherogenesis *in vivo*. Histopathological analysis of carotid lesions in ApoE^{-/-} mice exposed to shear stress and chronically treated with arginase inhibitors may further elucidate the role of arginases in modulating both plaque size and vulnerability.

P.097

ADRENALECTOMY IS MORE EFFECTIVE THAN SPIRONOLACTONE IN REDUCING ARTERIAL STIFFNESS IN PRIMARY ALDOSTERONISM*

B. Strauch¹, O. Petrak¹, D. Wichterle², T. Zelinka¹, R. Holaj¹, J. Dvorakova¹, L. Safarik³, M. Kasalicky⁴, J. Widimsky jr.¹. ¹3rd Internal Clinic, General Teaching Hospital, 1st Medical School, Prague, Czech Republic, ²Clinic of Cardiology, Institute of Clinical and Experimental Medicine, Prague, Czech Republic, ³Clinic of Urology, General Teaching Hospital, 1st Medical School, Prague, Prague, Czech Republic, ⁴1st Clinic of Surgery, General Teaching Hospital, 1st Medical School, Prague, Czech Republic

Objective: The study was aimed at assessment of the effects of specific treatment of primary aldosteronism (PA) on the arterial stiffness.

Design and Methods: 28 patients with confirmed PA (14 with aldosterone-producing adenoma treated by unilateral laparoscopic adrenalectomy, 14 with idiopathic hyperaldosteronism (treated with spironolactone) were investigated by Sphygmocor applanation tonometer using measurement of pulse wave velocity (PWV) and augmentation index (AI) at the time of the diagnosis and then again 1 year after the specific treatment.

Results: The mean 24h-BP levels decreased from 149 ± 18/92 ± 11 mmHg to 128 ± 15/81 ± 10 mmHg (p<0,01) after adrenalectomy (p<0,01), and from 155 ± 16/94 ± 12 to 140 ± 18/88 ± 8 mmHg (p<0,05; n.s.) on spironolactone. The PWV significantly decreased after surgery from 9,3 ± 3 na 7,6 ± 2,1 m/s (p=0,002), also the AI decreased significantly from 25 ± 9 na 17 ± 8% p=0,006. However, no significant improvement of the arterial stiffness indices was found in the patients treated with spironolactone (PWV before 9,3 ± 1,6, after 8,9 ± 1,3 m/s, n.s.; AI 24 ± 9...25 ± 8%, n.s.). After correction for differences in 24-h BP fall stays the AI fall more significant (p<0,01) in the surgically treated than spironolactone treated patients.

Conclusions: The causal surgical treatment of PA is significantly more effective in improving arterial stiffness than conservative treatment with spironolactone, also after correction for 24-h BP difference. This could indicate a possibility, that the aldosterone receptor blockade by spironolactone doesn't fully prevent arterial wall damage mediated by aldosterone, and that nongenomic aldosterone effects could possibly play a role in pathophysiology of arterial wall damage.

☆ Supported by the Grant NR/8155-5 provided by IGA of the Czech Ministry of Health.

P.098

INCREASED ARTERIAL STIFFNESS AND ARTERIAL WAVE REFLECTIONS ARE ASSOCIATED WITH IMPAIRED FUNCTIONAL STATUS IN PATIENTS WITH NORMAL EJECTION FRACTION

T. Weber¹, J. Auer¹, M. O'Rourke², B. Eber¹. ¹Cardiology Department, Klinikum Wels, Austria, ²St Vincents Clinic and UNSW, Sydney, Australia

Introduction: In asymptomatic men, arterial stiffness and wave reflections have been linked with cardiorespiratory fitness. We previously reported a relationship between arterial properties and objective measures of systolic and diastolic function in patients with preserved ejection fraction (EF). In this study, we investigated the association between symptomatic status and arterial elastic properties in the same patient group.

Methods: In 336 patients undergoing coronary angiography, we assessed pulse wave velocity (PWV) invasively, and arterial wave reflections (Augmentation Index - Aix) non-invasively using radial applanation tonometry and a validated transfer function (SphygmoCor system). Functional status, mainly exertional dyspnea, was judged by one single investigator.

Results: Patients suffering from exertional dyspnea more often were women, and they had higher blood levels of brain natriuretic peptides and higher left ventricular enddiastolic pressures, as

compared to asymptomatic controls. Brachial as well as aortic blood pressures did not differ significantly between the groups. In symptomatic patients, we observed increased PWV (9.4 +/- 2.3 m/sec vs 8.7 +/- 2.6 m/sec in asymptomatic patients, p=0.01), and increased Aix (31.1 +/- 9.7 vs 28.0 +/- 10.8 in asymptomatic patients, p=0.008). In a logistic regression model, female gender, use of nitrates, and higher PWV were independently associated with functional impairment, whereas higher Aix and higher body mass index were of borderline significance.

Conclusion: Exertional dyspnea is associated with increased arterial stiffness and increased/premature arterial wave reflections in patients with normal EF.

P.099

PREDICTIVE VALUE OF AORTIC PULSE WAVE VELOCITY IN ASYMPTOMATIC PATIENTS FOR CAROTID ATHEROSCLEROSIS

B. Benczur¹, R. Bocskei², M. Illyes². ¹Department of Cardiology, County Hospital, Budapest, Hungary, ²TensioMed Arterial Stiffness Centre, Budapest, Hungary

Background: It's widely accepted that carotid ultrasonography can help to identify asymptomatic patients at risk of heart attack and stroke as it's capable of providing direct evidence for the presence and extent of atherosclerosis. Due to limited accessibility of carotid scan the measurement of arterial stiffness is seemed to be suitable functional screening test to select patients who need morphological imaging of arterial tree (eg. carotid scan, multislice-CT or coronarography). However the predictive value of aortic pulse wave velocity for detecting carotid atherosclerosis has been poorly studied.

Method and patients: Authors examined 122 consecutive asymptomatic patients (mean age was 60 ± 9,8 years, 78 female, 44 male) in which arterial stiffness parameters (augmentation index: Aix and aortic pulse wave velocity: PWVao) were measured by an oscillometric device (TensioMed arteriograph). Carotid ultrasonography was performed in all individuals by a blinded investigator (who was unaware of the measured stiffness values). **Results:** Mean blood pressure and heart rate was 137/83 mmHg and 72/min. The average Aix was -2,61% and PWV was 10,43 m/s. Carotid atherosclerosis (presence of local plaque in carotid arteries) was confirmed in 72 patients (C+ group) while the arterial wall was intact in 50 patients (C- group). If the upper limit of normal of PWV was drawn at 9,7 m/s, elevated PWVao was measured in 91 of 122 pts (74,5%). Sensitivity of PWVao was 89% (64 pts had high PWV in C+ group), while specificity was 46% (23 pts had low PWV in C- group). Positive predictive value of PWV was 67% (61 pts of 91 with high PWV value were C+) while negative predictive value was 75% (22 pts of 29 with normal PWV was C-).

Conclusions: Elevated aortic pulse wave velocity was strongly associated with the presence of carotid plaques. Measuring arterial stiffness with arteriograph seems to be suitable as a screening method of preclinical atherosclerosis according to its high negative and positive predictive values. Screening of all asymptomatic men over 45 and women over 55 (or at younger age) would be reasonable approach to identify atherosclerosis in early and probably reversible phase if these correlations were confirmed in further large prospective study.

P.100

INVASIVE VALIDATIONS OF A USER INDEPENDENT OSCILLOMETRIC DEVICE (ARTERIOGRAPH) FOR MEASURING AUGMENTATION INDEX AND AORTIC PULSE WAVE VELOCITY

I. Horvath¹, L. Papp¹, L. Papp², M. Illyes². ¹Heart Institute, Faculty of Medicine, University of Pecs, Pecs, Hungary, ²TensioMed Arterial Stiffness Centre, Budapest, Hungary

Objective: To validate invasively a new apparatus (Arteriograph), which can measure augmentation index (Aix) and aortic pulse wave velocity (PWVao) simultaneously, within 2-3 minutes. According to the available literature data not any non-invasive device for measuring PWVao was validated with invasive method.

Design and Method: Our comparative study was performed on 36 patients who underwent routine coronarography for diagnostic purposes. In 10 cases we measured the brachial Aix with intrabrachial catheter and with Arteriograph, furthermore in 13 cases the intraaortic Aix was compared with brachial Aix on identical pulses. In 25 cases the invasively and non-invasively measured PWVao was compared. In 11 cases we used 2