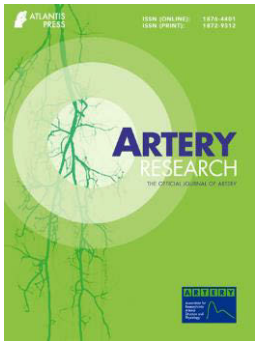

Artery Research

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

P.066: PERIPHERAL VASCULAR DISEASE IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS

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To cite this article: S.M.L. Wallace, B. McDonnell, M. Munnery, K.M. Maki-Petaja, J. Cheriyan, C.M. McEniery, S. Hill, J. Cockcroft, K. Varty, I. Wilkinson (2007) P.066: PERIPHERAL VASCULAR DISEASE IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS, Artery Research 1:2, 68–68, DOI: https://doi.org/10.1016/j.artres.2007.07.123

To link to this article: https://doi.org/10.1016/j.artres.2007.07.123

Published online: 21 December 2019

increase in this ratio was greater in physically trained than in untrained. CO ($p<0,05$) and SV ($p<0,01$) were significantly greater in trained individuals. SVR was constantly but insignificantly smaller in trained individuals.

The conclusion of our measurement is that physical training presumably changes CO, SV and SVR, but not BRS. Does that mean that BRS is not a valuable measure of the quality of blood pressure regulation?

P.061

A HAPLOTYPE AT THE MMP-9 LOCUS IS ASSOCIATED WITH HIGHER BLOOD PRESSURE AND GREATER ARTERIAL STIFFNESS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Arterial stiffness is the result of a complex interplay between gene and environment. The metalloproteniases (MMPs) play an important role in vascular remodelling and plasma MMP-9 levels predict cardiovascular disease.We studied the effect of two MMP-9 polymorphisms ; -1562C>T and -836G>A on blood pressure (BP) and arterial stiffness in essential hypertension.

We measured BP, pulse wave velocity (PWV) and augmentation index (AIx) in 217 untreated hypertensive patients (mean age 46 ± 1 years (108 male). MMP-9 polymorphisms were screened using RFLP. Haplotypes were determined using HAP analysis. Results analysed with JMP Version 5.0 and expressed as Mean $\pm$ SEM, $p<0.05$ considered significant.

Aortic PWV and BP were significantly higher in −1563T (TT homozygotes and CT heterozygotes) and 836 A allele carriers (AA homozygotes and GA heterozygotes). The predicted haplotypes were independently associated with aortic PWV and BP with a significant gene dose effect. In stepwise regression analysis, the −1562T and 836A alleles were independent determinants of PWV, in addition to age and BP. These polymorphisms were also independent determinants of both systolic and diastolic BP, either individually or when included together in the model.

Variation in the MMP-9 gene may modulate BP and aortic stiffness probably through accelerated turnover of vascular extracellular matrix. The significant gene-dose effect suggests that even one copy of the rare allele (A & T) may increase the risk of arterial stiffness and higher BP.A future challenge would be to use genotyping to identify high-risk individuals and to tailor anti-hypertensive treatment for achieving optimum BP control and reduced arterial stiffness.

P.062

ADIPONECTIN GENE POLYMORPHISM -276G>T CONTRIBUTES TO ARTERIAL STIFFNESS IN ESSENTIAL HYPERTENSION

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Adiponectin levels, the anti-inflammatory adipocytokine is reduced in hypertension and related to arterial stiffness[1]. The adiponectin -276G>T polymorphism is associated with type 2 diabetes and insulin resistance. However, whether this polymorphism contributes to arterial stiffness is not known.

We measured pulse wave velocity (PWV) and index (AIx) in untreated hypertensive patients ($n = 221$, 109 Female). G>276T polymorphism was determined by RFLP. Fasting plasma insulin and adiponectin concentrations were determined using ELISA. Fasting lipids and glucose were measured by standard methods and insulin resistance estimated using HOMA index. Results expressed as Mean $\pm$ SEM, $p<0.05$ considered significant.

The genotypes frequencies were G/G 53%, G/T 37%, and T/T 10%. Adiponectin levels were significantly reduced and associated with insulin resistance in patients with GG genotype. Patients with GG genotype had significantly higher systolic blood pressure (BP) ($p = 0.01$) and pulse pressure ($p = 0.008$) with no difference in diastolic BP. The aortic PWV was significantly higher ($p = 0.004$) in patients with GG genotype compared with T allele carriers. In a stepwise regression model, the -276G>T polymorphism was an independent determinant of PWV, in addition to age and BP and explained 46% of the variability in PWV. However, there was no difference in AIx between the two genotypes. The -276G>T genotype is associated with aortic stiffness and high BP as well as insulin resistance syndrome and may guide anti-hypertensive therapy in the future.

[1] Mahmud A, Feely J. Adiponectin and arterial stiffness. Am J Hypertens. 2005 Dec;18:1543—8.

P.063

INDUCIBLE NITRIC OXIDE SYNTHASE ACTIVITY IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS AND ENDOTHELIAL DYSFUNCTION

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Background: *In vitro* studies suggest that inducible nitric oxide synthase (iNOS) activity mediates endothelial dysfunction, but the role of iNOS in the process of arterial stiffening (AS) and endothelial function (EF) *in vivo* is unknown. Rheumatoid arthritis (RA) is a chronic inflammatory condition and as such can provide an interesting model to study this. The aim was to establish the contribution of iNOS to AS and EF.
Methods: Forearm blood flow (FBF) was measured during intra-arterial infusions of acetylcholine (ACh), sodium nitroprusside (SNP), N-monomethyl-L-arginine (L-NMMA) and aminoguanidine (AG), a selective iNOS inhibitor, in 12 RA patients and 13 control subjects. Aortic pulse wave velocity (aPWV) was also assessed.
Results: FBF response to ACh was reduced in RA patients compared to controls (384 ± 72 v. 179 ± 29%, respectively; $P = 0.01$), whereas SNP response was preserved ($P = 0.5$). AG reduced FBF in RA patients, but not in controls (-15 ± 2% v. 13 ± 4%, $P<0.001$), while the response to L-NMMA was not different between the groups ($P = 0.4$). RA patients had higher aPWV than controls ($P = 0.01$). In multiple regression models logCRP, LDL and AG response were found to be independent predictors of EF ($R^2 = 0.617$, $P<0.001$), and EF, AG response, and age independently predicted aPWV ($R^2 = 0.616$, $P<0.001$).
Conclusion: RA patients have increased aPWV and iNOS activity, and blunted EF in comparison to controls. iNOS activity independently predicts aPWV and EF. Additionally, aPWV is independently associated with EF. However, the causal relationship between these conditions remains unclear; possibly they exist in parallel, driven by common risk factors, such as inflammation.

P.064

AMBULATORY ARTERIAL STIFFNESS INDEX, PULSE WAVE VELOCITY AND AUGMENTATION INDEX—INTERCHANGEABLE OR MUTUALLY EXCLUSIVE MEASURES

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The ambulatory arterial stiffness index (AASI) has been proposed as a novel measure of arterial stiffness and has been prospectively shown to predict stroke and cardiovascular death, but not cardiac death. This index has prompted considerable controversy as to whether it is a true measure of arterial stiffness.

The aim was to examine three different measures of arterial stiffness, i.e., pulse wave velocity (PWV, Complior), wave reflection (augmentation index, AIx) and AASI in a large hypertensive population, comparing their determinants and inter-correlations, both unadjusted and adjusted for confounders and using Bland Altman analysis to determine 95% confidence intervals for the ability of the AASI to predict PWV, the proposed gold standard of arterial stiffness.

The AASI correlated univariately with both PWV and AIx in subjects overall ($r= 0.28$ for PWV and 0.24 for AIx; $p<0.001$ for both) and in those with untreated or treated hypertension. Adjustment for age in the current study negated entirely the positive correlation between AASI, PWV and AIx. Additional adjustment for confounders did not significantly alter these non-significant relationships. Furthermore, the 95% prediction limits for AASI to predict PWV were $\pm$ 4.18 meters/second and for AASI to predict AIx were +/-25.4%, suggesting that the methods would not be interchangeable in a clinical setting. Direct comparative studies would be required to establish the relative predictive strength of each measure and whether combining measures can provide additional risk prediction. Until such data become available, we propose that the measures should not be considered interchangeable.

P.066
PERIPHERAL VASCULAR DISEASE IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS

S.M.L. Wallace [1], B. McDonnell [3], M. Munnery [3], K.M. Maki-Petaja [1], J. Cheriyan [1], C.M. McEniery [1], S. Hill [4], J. Cockcroft [3], K. Varty [2], I. Wilkinson [1]. [1]*University of Cambridge, Cambridge, United Kingdom,* [2]*Vascular Unit, Addenbrooke's Hospital, Cambridge, United Kingdom,* [3]*Wales Heart Research Institute, Cardiff, United Kingdom,* [4]*Vascular Unit, Heath Hospital, Cardiff, United Kingdom*

Objective: Aortic pulse wave velocity (aPWV) is a powerful and independent predictor of all cause cardiovascular mortality. Patients with peripheral vascular disease (PVD) are at a higher risk of cardiovascular events. We hypothesized that patients with PVD would have a higher aPWV than age-matched healthy controls, and that aPWV would be inversely related to ankle brachial pressure index (APBI).
Methods: We studied 212 patients with PVD (mean age 71 ± 9 years, 68% male) with a mean ABPI of 0.64 ± 0.16 and 455 age-matched controls (mean age 70 ± 7 years, 64% male). Aortic augmentation index (AIx) augmentation pressure (AP) and central blood pressure were determined by pulse wave analysis using the SphygmoCor® system. PWV was derived using sequential carotid to femoral waveform recordings for aPWV and carotid and radial waveforms for brachial PWV.
Results: aPWV was significantly higher in patients with PVD compared with age-matched controls. (11.7 ± 3.5 vs. 9.9 ± 2.6m/s, $P<0.0001$). Both peripheral and central, systolic and pulse pressures were significantly higher in the PVD group compared to age-matched controls. AP was higher in the PVD group (19 ± 10 vs. 14 ± 7mmHg) but AIx was not. The difference in aPWV persisted after correction for mean arterial pressure (10.57 ± r 2.31vs. 9.02 ± r 3.46, $P<0.0001$). In regression model, age, mean pressure, diabetes and previous myocardial infarction predicted aPWV($r=0.6$, $p<0.001$). aPWV was inversely associated with ABPI ($R^2=$ -0.19, $P<0.0001$).
Conclusions: The increased aortic stiffness provides a possible explanation for the increased cardiovascular events seen in PVD patients but exact mechanisms underlying this need to be addressed.

P.067
EFFECTS OF INHIBITION OF AUTONOMIC NERVOUS SYSTEM ON AORTIC STIFFNESS FOLLOWING SYSTEMIC INFUSION OF GLYCERYL TRINITRATE IN HEALTHY VOLUNTEERS

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Objective: Nitric oxide (NO) contributes to smooth muscle tone relaxation, however, in humans the role of smooth muscle tone and NO in regulating aortic stiffness is controversial. We hypothesised that the nitric oxide donor GTN would reduce aortic PWV in vivo, but this effect would be partly attenuated by reflex activation of the sympathetic nervous system. The aim of this study was to investigate whether the autonomic nervous system (ANS) masked any effect of NO on aortic stiffness.
Methods: 10 healthy subjects; mean age, 28 ± 6 years were studied on two visits, in a double-blinded, placebo controlled 2-way crossover design. On both visits, subjects were randomly selected to have either a bolus administration of pentolinium (ganglion blocker) or placebo followed by an infusion of GTN or placebo. The opposite arm was of the study was then carried out following a 60 minute break.

Heart rate variability, blood pressure, cardiac haemodynamics, brachial and aortic pulse wave velocity (PWV) were measured at regular intervals throughout the study.
Results: The main findings from this study were that incremental doses of GTN led to a significant 9% fall in brachial PWV ($P<0.0001$), with no effect on aortic PWV. Despite blockade of the ANS, aPWV remained unaffected by incremental doses of GTN.
Conclusions: The major findings were that despite blockade of the both the parasympathetic and sympathetic nervous system, subsequent systemic infusion of GTN had null effect on aortic pulse wave velocity suggesting that there are other mechanisms involved in the regulation of aortic stiffness.

P.068
A NON-INVASIVE APPROACH TO QUANTIFY VENTRICULAR-ARTERIAL INTERACTION: COMPARING VASCULAR TYPE EHLERS-DANLOS SYNDROME PATIENTS AND NORMAL INDIVIDUALS

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Introduction: We hypothesized that the pressure rate ratio (PRR), defined as the arterial upstroke dP/dt normalized by isovolumic ventricular dP/dt, is less sensitive to inter-subject variance and therefore better in identifying individuals with abnormal ventricular-arterial function than single hemodynamic parameters.
Methods: We studied the characteristics of PRR in 21 normals (age-range 19-32 yrs) and 7 age-matched vascular type (IV) Ehlers-Danlos syndrome (EDS) patients. ECG, brachial pressure and right common carotid artery (CCA) diameter waveforms (M-mode ultrasound) were obtained in supine position. LV systolic time intervals, i.e. isovolumic-contraction (ICP) and ejection periods (EP), were extracted from diameter waveforms using a previously described algorithm. We calculated diastolic blood pressure-to-ICP ratio (DBP/ICP), ICP/EP, CCA-distension (ΔD), diastolic diameter (Dd), maximum diameter velocity (dD/dt,max), and distensibility (DC) and compliance (CC) coefficients. PRR was defined as 100%(K·dD/dt,max)/(DBP/ICP), with K=(mean blood pressure − DBP)/(mean diameter − Dd). Results are given as mean±SD.
Results: EDS subjects had higher heart rate (+9bpm, $p=0.045$), but lower ΔD (0.62 ± 0.11 vs 0.74 ± 0.15mm, $p=0.027$) and DC (33 ± 8 vs 41 ± 9/MPa, $p=0.055$). All other variables, including PRR (26 ± 7 vs 27 ± 6%), were not significantly different between groups, reflecting similar ventricular-arterial interaction. With both groups pooled, two individuals presented with elevated PRR (40%). In a normal subject (age 20 yrs) this was associated with abnormally low sympathetic activity. The other subject (EDS, age 24 yrs) exhibited increased sympathetic activity and decreased DC (20/MPa), shorter EP (−10%) and depressed LV function.
Conclusions: Our findings suggest that PRR enables identification of individuals with abnormal ventricular-arterial function in a heterogeneous population.

P.069
OSTEOPOROSIS IS ASSOCIATED WITH INCREASED AORTIC PULSE WAVE VELOCITY

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Objective: Arterial stiffening and osteoporosis both occur predominantly in late life. Osteoporosis has been associated with increased peripheral pulse pressure and arterial stiffness, but its effect on aortic pulse wave velocity (aPWV) is unclear. The aim of this study was to examine the relationship between arterial calcification and aPWV in healthy subjects and a cohort of patients with osteoporosis.
Methods: aPWV and bone mineral density (BMD) were measured non-invasively in 42 patients with osteoporosis and 120 healthy volunteers. Subjects with cardiovascular disease, renal disease or hypertension were excluded. aPWV was assessed using the SphygmoCor system, and vertebral / hip BMD from thoraco-lumbar CT images, using Mindways software.
Results: The mean±SD aPWV was significantly higher in patients with osteoporosis than controls (9.6 ± 2.9 vs 8.2 ± 1.7 m/s; $P = 0.01$). Brachial PWV and augmentation index did not differ. Although mean arterial pressure did not differ between the groups, peripheral and central pulse pressures were significantly higher in the osteoporotics (by 6 ± 2 and 5 ± 2 mmHg respectively; $P > 0.01$ for both). In pooled data for osteoporosis patients and controls, aortic PWV correlated inversely correlated with T-score ($r = -0.27$, $P = 0.001$).
Conclusion: Patients with osteoporosis have increased aortic stiffness compared with healthy volunteers, independent of their mean arterial pressure. We speculate that arterial calcification may be involved in the development of arterial stiffness and osteoporosis.

P.070
ARTERIAL STIFFNESS ALTERATIONS DURING HEMODIALYSIS

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