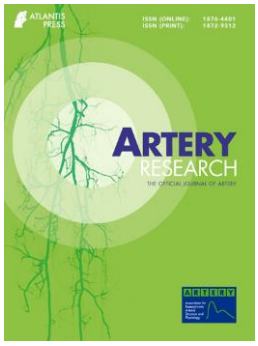

Artery Research

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

P.060: BAROREFLEX SENSITIVITY AND THE QUALITY OF BLOOD PRESSURE REGULATION

K. Cankar, Z. Melik, N. Potocnik

To cite this article: K. Cankar, Z. Melik, N. Potocnik (2007) P.060: BAROREFLEX SENSITIVITY AND THE QUALITY OF BLOOD PRESSURE REGULATION, Artery Research 1:2, 66–67, DOI: https://doi.org/10.1016/j.artres.2007.07.117

To link to this article: https://doi.org/10.1016/j.artres.2007.07.117

Published online: 21 December 2019

thickness (IMT) is a marker of early atherosclerosis that is correlated with traditional risk factors and is predictive of subsequent myocardial infarction and stroke. Furthermore, possible differences in the pathophysiology of common carotid artery IMT and femoral IMT might allow the exploration of differential gene regulation in specific vascular beds.
Methods: The current data included 63 probands (mean age 44.83 ± 7.41) and 77 relatives (mean age 45.35 ± 8.14). from 63 families. B-mode carotid and femoral ultrasonography was used to definite mean IMT of commom carotid (CCA) and common femoral artery (CFA). Variance component methods were used to estimate heritability from the normalized deviates.
Results: Variances explained by all final covariates (includes sex, age, blood pressure, smoking, total cholesterol, HDL cholesterol, triglicerides, diabetus status, body mass index) for mean CCA and mean CFA IMT were 0.393 and 0.394, respectively. Multivariable −adjusted heritability were 0.232 for mean CCA and 0.141 for mean CFA IMT (all P <0.005).
Conclusion: These data suggest that genetic factors independent of traditional cardiovascular risk factors more influence to CCA IMT than to CFA IMT. Although we found that acquired risk factors contribute progressively to IMT. Future studies of genetic linkage and gene candidate association are warranted to identify specific genetic variants predisposing early symptoms of atherosclerosis in specific vascular beds.

P.057
AORTIC DISTENSIBILITY BY NUCLEAR MAGNETIC RESONANCE IN ESENTIAL HYPERTENSION

C. Giannattasio [1], S. Maestroni [1], E. Fantini [1], M. Amigoni [1], M. Rigoldi [1], F. Zerbini [2], A. Capra [1], M. Failla [1], S. Sironi [2], G. Mancia [1]. *[1]Clinica Medica, Milano-Bicocca University and S.Gerardo Hospital, Monza, Italy, [2]UO Radiologia, Milano-Bicocca University and S.Gerardo Hospital, Monza, Italy*

It is demonstrated that Essential Hypertension is accompanied by a reduction of large artery distensibility (Dist), which represents a marker of demonstrated prognostic significance. Dist can be assessed by echotracking derived systo-diastolic changes in aortic diameter versus blood pressure changes. However, a less operator dependent and more precise assessment might be obtained by nuclear magnetic resonance (NMR). This study was done to compare aortic (Ao) Dist obtained by echotracking and NMR in normotensive and hypertensive patients. We studied 14 treated essential hypertensives (age 36 ± 3.5 years, blood pressure 126 ± 3/78 ± 1.7 mmHg means ± SE) and 15 matched normotensives controls (blood pressure 116 ± 3.0/73 ± 2.4 mmHg). Systodiastolic changes in thoracic (T, 1 cm above the celiac tripode) and abdominal (A, 1 cm above bifurcation) Ao were obtained by either method. Dist was calculated via the Reneman formula using tonometric carotid pulse pressure. NMR Dist values were systematically greater than the echotracking one (Hypertensives T 7.2 ± 0.5 vs 3.0 ± 0.5 , A 6.0 ± 0.5 vs 2.9 ± 0.4 1/mmHg 10^{-1} ,Normotensives, T, 8.6 ± 0.5 vs5.2 ± 0.5, A 7.5 ± 0.5 vs3.6 ± 0.3 1/mmHg 10^{-1} p<0.05). The correlation between RMN and echotracking obtaind values was significant. Dist was systematically and significantly lower in H than N (p always <0.05) . No significant differences were observed between NMR T and A aAo arterial diameter. Thus, Ao Dist may be underestimated by echotracking method. Data obtained by the two approaches are similarly capable of detecting Dist reduction in hypertension. This scores in favour of continuing use of the much low expensive echotracking method.

P.058
ENDOTHELIAL DYSFUNCTION AS MEASURED BY FLOW MEDIATED DILATATION (FMD) IN CARDIOVASCULAR RISK ASSESSMENT

S. Holewijn, J. de Graaf, M. den Heijer, A.F.H Stalenhoef. *University Medical Center Nijmegen, Nijmegen, Netherlands*

Introduction: FMD has been proposed as a tool in cardiovascular (CV) risk stratification. However, this has only been studied in relatively small, high risk populations.
Objective: We investigated whether FMD was related to CV risk factors and intima media thickness (IMT) in a low risk population, the Nijmegen Biomedical Study (NBS).
Method: FMD and IMT were measured non-invasively in the brachial and the common carotid artery, respectively, using ultrasound.The NBS is a low risk population based cohort, aged 50—70 years. Interim analysis of FMD and IMT were performed in 337 subjects (mean age 60.3 year, % male 57.5). All traditional clinical and biochemical CV risk factors were determined.
Results: Mean IMT was 0.83 ± 0.11 mm. Mean FMD was 1.45 ± 2.45%. After correction for age and gender, all CV risk factors were significantly correlated to IMT (Pearson's R 0.11-0.33), explaing 42% of the variance in IMT. However, for FMD no significant correlations with any of the CV risk factors were found (Pearson's R 0.007 -0.13), except for TC and apoB . All CV risk factors explained only 9,5% of the variance in FMD whereas 6% of the variation in FMD was explained by IMT.
Conclusion: In our low risk population based cohort, aged 50-70 years old, FMD was not related to most of the CV risk factors whereas IMT contributed significantly to the variation in FMD. Our results question the additive value of FMD compared to IMT in terms of CV risk assessment, in older low risk populations.

P.059
IS INCREASED SYSTOLIC BLOOD PRESSURE THE MAIN REASON FOR CARDIOVASCULAR DISEASES?

Z. Melik, K. Cankar, N. Potocnik. *Institute of Physiology, Ljubljana, Slovenia*

It is very well known that women in reproductive period are naturally better protected against cardiovascular diseases than men of the same age. The reasons for these are not clear.

For better determination of possible differences between gender we measured ECG, systolic (SBP), diastolic (DBP) and pulse pressure (PP), heart rate (HR), variability of HR (HRV) and pressure, cardiac output (CO), stroke volume (SV) and peripheral vascular resistance (SVR) at rest, during mental stress (3 minutes of standard arithmetic challenge) and during recovery in the group of 24 healthy males and 38 aged-matched females (19-22 years old).

HR did not differ between both groups at rest and recovery after stress, but was statistically significant higher (p<0,05) during mental stress in females. There was no difference in SBP, DBP or PP at rest, during stress and during recovery. There were no differences in HRV, variability of SBP or DBP and in SV also. But CO was greater in females, especially during mental stress (p<0.05), and SVR was smaller in females at rest, during mental stress and during recovery (p<0.05) when compared to the group of males.

There were no differences in SBP or DBP between males and females. The main differences observed were in CO and SVR. The question arises: is increased systolic or diastolic pressure the main reason for cardiovascular diseases or the reason lies somewhere in the different CO or SVR between males and females?

P.060
BAROREFLEX SENSITIVITY AND THE QUALITY OF BLOOD PRESSURE REGULATION

K. Cankar, Z. Melik, N. Potocnik. *Institute of Physiology, Ljubljana, Slovenia*

The slope of the simultaneously changing blood pressure with heart rate (baroreflex sensitivity - BRS) is supposed to be a measure of the quality of arterial pressure regulation. In an attempt to discover early mechanisms of cardiovascular alterations we monitored different parameters in healthy, young volunteers: physically trained (N = 24) and aged-matched sedentary controls (N = 35).

We measured ECG, systolic (SBP) and diastolic blood pressure (DBP), cardiac output (CO), stroke volume (SV), peripheral vascular resistance (SVR) and BRS first at rest and then during slow breathing. Slow breathing (6 breaths/min) is one of the manoeuvres that are believed to increase vagal tone.

A spectral analysis of RR intervals was done by the autoregression method. We determined the area under the power spectrum curves over the high frequency (HF) band (0.15-0.4 Hz) and the low frequency (LF) band (0.04-0.15 Hz).

RR intervals, SBP, DBP and BRS were nearly the same in trained and untrained volunteers at rest and during slow breathing. There were also no difference in heart rate variability parameters except the significant difference (p<0,05) between groups in LF/HF during slow breathing. The

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

A. Mahmud, S. Zhou, P. Jerrard-Dunne, J. Spiers, J. Feely. *Department of Pharmacology & Therapeutics, Trinity College & Hypertension Clinic, St. James's Hospital, Dublin, Ireland*

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

S. Zhou, J. Feely, P. Jerrard-Dunne, J. Spiers, A. Mahmud. *Department of Pharmacology & Therapeutics, Trinity College & Hypertension Clinic, St. James's Hospital, Dublin, Ireland*

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

K.M. Maki-Petaja [1], J. Cheriyan [1], F.C. Hall [2], S.M.L. Wallace [1], C.M. McEniery [1], I.B. Wilkinson [1]. *[1]University of Cambridge, Clinical Pharmacology Unit, Cambridge, United Kingdom, [2]University of Cambridge, Department of Clinical Medicine, Cambridge, United Kingdom*

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

A. Mahmud, P. Jerrard-Dunne, J. Feely. *Department of Pharmacology & Therapeutics, Trinity College & Hypertension Clinic, St. James's Hospital, Dublin, Ireland*

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.