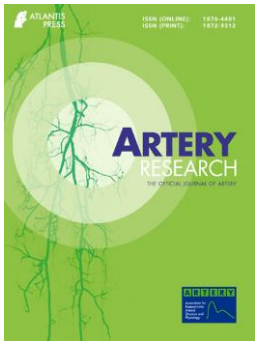

Artery Research

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

P4.16: INSULIN RESISTANCE IS ASSOCIATED WITH INCREASED LARGE ARTERY STIFFNESS IN NORMOTENSIVE HEALTHY ADULTS

J.E. Ochoa, M.M. Correa, A.M. Valencia, J.G. McEwen, J.A. Gallo, G. Bilo, P. Salvi, D. Aristizabal, G. Parati

To cite this article: J.E. Ochoa, M.M. Correa, A.M. Valencia, J.G. McEwen, J.A. Gallo, G. Bilo, P. Salvi, D. Aristizabal, G. Parati (2012) P4.16: INSULIN RESISTANCE IS ASSOCIATED WITH INCREASED LARGE ARTERY STIFFNESS IN NORMOTENSIVE HEALTHY ADULTS, Artery Research6:4, 187–188, DOI: https://doi.org/10.1016/j.artres.2012.09.164

To link to this article: https://doi.org/10.1016/j.artres.2012.09.164

Published online: 21 December 2019

where the strongest correlate was central systolic BP ($r=0.587$; $p<0.001$). aPWV was not related to AIx in either group ($p>0.05$ both).
Conclusions: Haemodynamic determinants of AIx in T2DM patients are significantly different to healthy people where BP is a dominant factor. In patients with T2DM, however, a high output, low resistance haemodynamic environment is associated with AIx.

P4.14
EXERCISE AORTIC RESERVOIR FUNCTION IN PATIENTS WITH TYPE 2 DIABETES IS ASSOCIATED WITH BRAIN ATROPHY

R. E. Climie [1], V. Srikanth [2], R. Beare [2], L. J. Keith [1], J. E. Davies [3], J. E. Sharman [1]
[1]*Menzies Research Institute Tasmania, Hobart, Australia*
[2]*Stroke and Ageing Research Group, Melbourne, Australia*
[3]*International Centre for Circulatory Health, London, United Kingdom*

Objectives. Vascular mechanisms underlying brain atrophy and white matter lesions (WML) in patients with type 2 diabetes (T2DM) are unknown. Increased exercising blood pressure (BP) is associated with end-organ damage and could explain these brain abnormalities. This study examined associations between exercise central haemodynamics and brain structure.
Methods: Forty healthy participants (53±9 years; 50% male) and 40 T2DM (62±9 years; 50% male) were examined at rest and during light exercise. Resting and exercise central haemodynamics, including systolic BP (SBP), pulse pressure (PP) augmented pressure (AP), augmentation index (AIx), aortic stiffness and aortic reservoir function (including excess pressure integral [xsP]) were recorded by tonometry. Segmented grey (GM) and white matter (WM) and WML volumes were derived from magnetic resonance imaging.
Results: T2DM participants had lower WM ($p=0.004$) and GM ($p=0.07$) volumes, and significant elevation of all central hemodynamic variables during exercise ($p<0.01$ all). At rest, greater central (not brachial) haemodynamics (SBP, AP, AIx and PP) were independently associated with greater WML volume ($\beta=0.54$, $p=0.031$, $\beta=0.55$, $p=0.01$; $\beta=0.46$, $p=0.046$ and; $\beta=0.48$, $p=0.01$, respectively) in controls (not T2DM). During exercise, increased xsP was independently associated with reduced WM ($\beta=-0.54$, $p=0.006$) and GM ($\beta=-0.63$, $p=0.013$) volumes only in T2DM independent of age, sex, heart rate, and 24-hour ambulatory SBP.
Conclusions: In T2DM, aortic reservoir function and transmission of excess pressure during exercise is associated with brain atrophy. These findings suggest that vascular mechanisms underlying structural brain changes may differ between healthy individuals and those with T2DM.

P4.15
RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, CARDIAC BAROREFLEX SENSITIVITY AND BLOOD PRESSURE VARIABILITY IN NORMOTENSIVE HEALTHY ADULTS

J. E. Ochoa [1,3], M. M. Correa [2], A. M. Valencia [2], J. G. McEwen [2], J. A. Gallo [2], G. Bilo [3], P. Salvi [3], D. Aristizabal [2], G. Parati [1,3]
[1]*Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, Italy*
[2]*Corporación para Investigaciones Biologicas, Clinical and Research Center, SICOR, Medellin, Colombia*
[3]*Department of Cardiology, S. Luca Hospital, Istituto Auxologico Italiano, Milan, Italy*

An increased arterial stiffness (AS) has been proposed as a likely mechanism for a reduced cardiac baroreflex sensitivity (BRS) and the associated increases in 24h blood pressure (BP) variability (BPV). Aim of the present study was to explore this issue in a group of 90 normotensive, non-obese, healthy adults (mean age 48±10 yrs, 50% F).
Methods: BRS was assessed by computer analysis of 10 min beat-to-beat BP and ECG recordings obtained in resting supine. The linear regression slope of spontaneous concomitant increases or decreases in systolic BP and RR interval were calculated, averaged and expressed as total slope of BRS (ms/mmHg). Simultaneous recordings of pulse waveform were obtained by means of a validated oscillometric device for ABPM (Mobil-O-Graph NG, IEM, Stolberg, Germany) with inbuilt transfer-function like method, and pulse wave velocity (PWV, m/s) calculated. BPV was assessed for systolic and diastolic BP as 24h standard deviation (SD), weighted 24h SD (wSD), daytime and night-time SD from 24h ABPM.
Results: In multiple linear regression analysis AS (assessed through PWV), had the strongest effect on BRS variation (beta:-0.50, $p<0.0001$), followed by HR and male sex. No significant effect was observed for age or MAP on BRS (See table). A similar independent analysis, showed a significant inverse relationship between BRS and daytime systolic BP SD (beta:-0,23; $p=0.036$)
Conclusion: Our findings suggest that in normotensive, otherwise healthy adults, decreased BRS and, indirectly, the associated increased day-time systolic BPV might be largely explained by an increased AS, independently of age and BP levels.

Predictors of cardiac BRS (Multiple linear regression analysis)

Variable (mean±SD)	Regression Coefficient	95% CI	Beta Coefficient	P value	R^2
PWV (6.12±1.53 m/s)	-3.619	-5.0, -2.2	-0,503	<0,0001	0,25
HR (64.2±9.4 bpm)	-0.426	-0.6, -0.2	-0,344	<0,0001	0,14
Sex (male)	-4.373	-8.4, -0.3	-0,212	0,029	0,04
Age (48±11 yrs)	-0.187	-0.7, 0,3	-0.187	0,547	-
MAP (97.9±8.8 mmHg)	-0.019	-0.4, 0.2	-0.077	0,759	-
R-Squared for the model including only significant variables (PWV, sex, HR)					**0,342**

P4.16
INSULIN RESISTANCE IS ASSOCIATED WITH INCREASED LARGE ARTERY STIFFNESS IN NORMOTENSIVE HEALTHY ADULTS

J. E. Ochoa [1,3], M. M. Correa [2], A. M. Valencia [2], J. G. McEwen [2], J. A. Gallo [2], G. Bilo [3], P. Salvi [3], D. Aristizabal [2], G. Parati [1,3]
[1]*Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Milan, Italy*
[2]*Corporación para Investigaciones Biologicas, Clinical and Research Center, SICOR, Medellin, Colombia*
[3]*Department of Cardiology, S. Luca Hospital, Istituto Auxologico Italiano, Milan, Italy*

Aim: At present there is limited evidence on the relationship between insulin resistance (IR) and measures of large artery stiffness (AS) and wave reflections in normotensive healthy adults. Aim of the present study was to explore this issue in 90 normotensive (Systolic(S) blood pressure(BP) 107.1±9.3; diastolic (D) BP 69.6±7.7 mmHg), normoglycemic, non-obese, otherwise healthy adults (mean age 48 ± 10 yrs, 50% female).
Methods: IR was assessed with HOMA-Index and subjects were classified into IR tertiles, based on the distribution of HOMA-index values. Recordings of pulse waveform were obtained by means of a validated oscillometric device (Mobil-O-Graph NG, IEM, Stolberg, Germany) for ambulatory BP monitoring with in-built transfer-function like method. Aortic pulse wave velocity (PWV, m/s) and other measures derived from pulse wave analysis such as augmentation index (AIx, %), central SBP (cSBP), central DBP (cDBP) and central pulse pressure (cPP) were computed. Peripheral SBP and DBP, and heart rate (HR) were recorded and pulse pressure (PP) calculated as the difference between SBP and DBP.
Results: After multiple regression analysis adjusting for age, sex, HR and BMI, there was a significant overall effect of IR on measures of large artery stiffness and in central and peripheral BP levels. IR was associated with increased aortic PWV, and with higher central and peripheral SBP and DBP levels. See table.
Conclusion: our results indicate that in normotensive, healthy adults, IR may induce significant increases in large artery stiffness (as assessed with aortic PWV) and in central and peripheral BP levels.

Hemodynamic variables by tertiles of HOMA index*				
Variable	**T1 (<0.94) (n=32)**	**T2 (0.94-1.90) (n=28)**	**T3 (>1.90) (n=30)**	**P value**
Peripheral SBP (mmHg)	111.7 ± 2.0	114.3 ± 1.8	123.2 ± 2.0	<0.0001
Peripheral DBP (mmHg)	76.8 ± 1.4	79.8 ± 1.3	84.7 ± 1.5	0.001
Peripheral PP (mmHg)	33.5 ± 1.0	35.0 ± 0.9	38.4 ± 1.0	0.004
Central SBP (mmHg)	103.7 ± 1.7	106.7 ± 1.5	115.3 ± 1.6	0.001
Central DBP (mmHg)	77.8 ± 1.5	81.1 ± 1.3	86.1 ± 1.5	0.001
Central PP (mmHg)	25.5 ± 1.5	25.1 ± 1.3	29.2 ± 1.0	0.071
MBP (mmHg)	92.5 ± 1.5	95.7 ± 1.3	102.3 ± 1.5	<0.0001
HR (bpm)	61.3 ± 1.9	65.0 ± 1.7	66.0 ± 1.9	0.212
PWV (m/s)	5.64 ± 0.17	5.71 ± 0.10	6.34 ± 0.9	0.012
Augmentation Index (%)	6.7 ± 3.2	6.1 ± 3.8	6.9 ± 2.2	0.082

*Values are expressed as means ± SEM

P4.17
INFLUENCE OF ESTIMATED WALL SHEAR RATE INDICES ON CAROTID ARTERY INTIMA-MEDIA THICKNESS AND INTIMA-MEDIA COMPLEX ECHOGENICITY

K. Aizawa, S. Elyas, D. D. Adingupu, A. C. Shore, W. D. Strain, P. E. Gates
Peninsula Medical School, Peninsula NIHR Clinical Research Facility, University of Exeter, Exeter, United Kingdom

Introduction: Grey scale median of the carotid artery intima-media complex (IM-GSM) is a recently introduced measurement to characterise the arterial wall. Wall shear stress is thought to influence intima-media thickness (IMT) and to play a major role in the development of atherosclerosis. However, the relationship between wall shear stress and IM-GSM is not well understood. This study examined the relationship between estimated wall shear rate (WSR) indices and IMT as well as estimated WSR indices and IM-GSM.
Methods: Data from 156 middle-aged and older individuals (66.1±9.5yrs, 58F) were included in this analysis. Common carotid artery diameter, IMT, and blood velocity data were obtained using a Doppler ultrasound machine. Three estimates of WSR were calculated: peak, mean and diastolic WSR. IMT and IM-GSM were analyzed using a semi-automated edge-detection programme.
Results: IMT was inversely associated with all WSR indices (peak: r=-0.16, mean: r=-0.22, diastolic: r=-0.25, all $p<0.05$). IM-GSM was positively associated with mean (r=0.20) and diastolic WSR (r=0.17, both $p<0.05$). Peak and mean WSR were independent determinants of IMT, and mean and diastolic WSR were independent determinants of IM-GSM after adjustments for age, sex and traditional cardiovascular risk factors.
Conclusion: These results show that estimated WSR indices were associated with IMT and IM-GSM, suggesting that WSR may, in part, determine the extent of IMT and the composition of the arterial wall in our cohort.

P4.18
OSTEOPROTEGERIN AND ARTERIAL STIFFNESS IN POSTMENOPAUSAL WOMEN

A. Albu, D. Fodor, C. Bondor, L. Poanta, M. Porojan
University of Medicine and Pharmacy, Cluj-Napoca, Romania

Background: Many recent data support the hypothesis that circulating osteoprotegerin (OPT) levels are associated with arterial calcification and may serve as a potential predictor of cardiovascular disease and mortality. Matrix Gla Protein (MGP) is considered an inhibitor of vascular calcification. However, the role of these molecules in the arterial wall is still unclear. Arterial stiffness increases in postmenopausal women. The aim of our study was to determine the relation between circulating OPT and MPG and vascular parameters of arterial stiffness in postmenopausal women.
Materials and Methods: One hundred forty-four postmenopausal women, aged (61.4±10.6 years) were included in the study. PWV was measured using an oscillometric device. OPT, MGP, C-reactive protein and parameters of lipid and glucose metabolism were also determined.
Results: OPT correlated with aortic PWV (r=0.32, p=0.006), and C- reactive protein (r=0.37, p=0.02). In multiple regression models, after adjustment for potential confounders, OPT was independently associated with aortic PWV. No correlation was found between MGP and aortic PWV. There were 61% hypertensives, 34% patients with diabetes, 35.4% with hyperlipemia and 41.6% with obesity or overweight, in this study.
Conclusions: These results support the relationship between serum OPT and arterial stiffness in postmenopausal women, independent of the traditional cardiovascular risk factors and inflammation. At the same time, MGP was not found to be a predictor of arterial stiffness.

P4.19
AORTIC STIFFNESS, REFLEXION WAVE AND ARTERIAL HYPERTENSION UNDER ANTI-ANGIOGENIC DRUGS

M. A. Alivon [1], J. G. Giroux [2], P. B. Boutouyrie [1], F. G. Goldwasser [2], S. L. Laurent [1]
[1]*Inserm U970-Hôpital Européen Geroges Pompidou, Paris, France*
[2]*Onclogy Service- Hôpital Cochin, Paris, France*

Objective: Sorafenib and Sunitinib are anti-angiogenic drugs (AAD) used in an increasing number of cancers. The most common side effect is arterial hypertension. We hypothesize that AAD lead to an early damage of large arteries which can be translated by an increase of aortic stiffness determined by the pulse wave velocity measurement (PWV).
Material and Method: In a longitudinal study, 32 patients have been treated with Sorafenib or Sunitinib. Subjects have been explored during a visit before the introduction of the treatment and then every two weeks for 2 months. Measured parameters are blood pressure, PWV, central pressure, augmentation index (AIx).
Results: 38% of the subjects have developed an early arterial hypertension requiring anti-hypertensive treatment. The initial values of brachial SBP was predictive from SBP changes under AAD while PWV and AIx was not. Furthermore, in patients who developed hypertension and required treatment with 5 to 10 mg amlodipine has been effective at decreasing SBP and MBP by -13 [-21;-4] et -8 [-14;-1] mmHg ($p<0,01$) respectively, and AIx, -10% [-16;-4] ($p<0,001$).
Conclusion: This study suggests that blood pressure at inclusion increases the risk of developing acute hypertension with AAD. It also shows that effective vasodilatation could be achieved despite small vessels disruption by AAD.

P4.20
ASSOCIATION OF A SINGLE NUCLEOTIDE POLYMORPHISM IN CYP2C8 WITH MYOCARDIAL INFARCTION IN BULGARIAN POPULATION

G. A. Atanasova [1], R. T. Tzveova [2], M. T. Tzekova, assoc.prof[3], R. K. Kaneva, assoc.prof[4], V. M. Mitev [5]
[1]*Galya Naydenova, Pleven, Bulgaria*
[2]*Reni Tzveova, Sofia, Bulgaria*
[3]*Maria Tzekova, Pleven, Bulgaria*
[4]*Radka Kaneva, Sofia, Bulgaria*
[5]*Vanyo Mitev, Sofia, Bulgaria*

Cytochrome P450 2C8 is a polymorphic enzyme responsible for the biosynthesis of vasoactive substances from arachidonic acid. Inter-individual differences in the action of these substances might be important in the pathogenesis of cardiovascular diseases such as acute myocardial infarction (AMI).
In the present study we analyzed the association of a genetic variant in CYP2C8 and the morbidity of AMI in Bulgarian population.
The study included 99 AMI patients and 370 control subjects. To determine the genotypes of the samples real time PCR with predesigned TaqMan SNP Genotyping Assays (Applied Biosystem) was used.