



## Artery Research

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### **P1.28: INFLUENCE OF AGE ON CAROTID ENDOTHELIAL FUNCTION AS DETERMINED BY HYPERCAPNIA INDUCED VASODILATATION**

N.P. Saeed, G. Esquivel, I.M. Graf, A.P.G. Hoeks

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adjustments, excepted on BP, HR for all-cause mortality risk associated with PWV was 1.12 (1.03-1.22), but after adjustment on all variables, relationship was no longer significant: HR=1.08 (0.98-1.18). Before 60 years, after adjustments, PWV-related risk was 1.09 (0.95-1.24), (NS), but it reached 1.22 (1.08-1.38),  $p<0.02$ , in patients  $>60$  years.

**Conclusion:** In a low to moderate risk population, aortic PWV was significantly and independently associated with all-cause mortality only among subjects after 60 years. In such population, the direct impact of BP on aortic stiffness overcomes the intrinsic stiffness alterations which are linked to all-cause mortality, at least in young, low risk, subjects.

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#### P1.25

##### ARTERIAL PROPERTIES IN RELATION TO GENETIC VARIATIONS IN THE ADDUCIN SUBUNITS IN A WHITE POPULATION

J. Seidlerova<sup>2</sup>, J.A. Staessen<sup>1</sup>, M. Bochud<sup>4</sup>, T. Nawrot<sup>1</sup>, N. Casamassima<sup>5</sup>, L. Citterio<sup>5</sup>, T. Kuznetsova<sup>1</sup>, Y. Jin<sup>1</sup>, P. Manunta<sup>5</sup>, T. Richart<sup>3</sup>, H.A. Struijker-Boudier<sup>6</sup>, R. Fagard<sup>1</sup>, J. Filipovsky<sup>2</sup>, G. Bianchi<sup>5</sup>.

<sup>1</sup> The Studies Coordinating Centre, Division of Hypertension and Cardiovascular Rehabilitation, Department of Cardiovascular Diseases, University of Leuven, Leuven, Belgium

<sup>2</sup> the Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

<sup>3</sup> Genetic Epidemiology Unit, Department of Epidemiology, Maastricht University, Maastricht, Netherlands

<sup>4</sup> Institute of Social and Preventive Medicine, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland

<sup>5</sup> Divisione di Nefrologia Dialisi e Ipertensione, Ospedale San Raffaele, Dipartimento di Scienze e Tecnologia Biomediche, Università Vita Salute, Milan, Italy

<sup>6</sup> the Department of Pharmacology and Toxicology, Cardiovascular Research Institute, University of Maastricht, Maastricht, Netherlands

**Background:** Adducin is a membrane skeleton protein, which consists either of  $\alpha$ - and  $\beta$ - or  $\alpha$ - and  $\gamma$ -subunits. We investigated whether arterial characteristics might be related to the genes encoding *ADD1* (*Gly460Trp*), *ADD2* (*C1797T*) and *ADD3* (*A386G*).

**Methods:** We randomly recruited 1126 Flemish subjects (mean age, 43.8 years; 50.3% women). Using a wall-tracking ultrasound system, we measured the properties of the carotid, femoral and brachial arteries. We studied multivariate-adjusted phenotype-genotype associations, using a population- and family-based approach.

**Results:** In single-gene analyses, brachial diameter was 0.15 mm ( $P=0.0022$ ) larger, and brachial distensibility and cross-sectional compliance were  $1.55 \times 10^{-3}$ /kPa ( $P=0.013$ ) and  $0.017 \text{ mm}^2/\text{kPa}$  ( $P=0.0029$ ) lower in *ADD3 GG* than *ADD3 AA* homozygotes with an additive effect of the *G* allele. In multiple-gene analyses, the association of brachial diameter and distensibility with the *ADD3 G* allele only occurred in *ADD1 GlyGly* homozygotes. Otherwise, the associations between the arterial phenotypes in the 3 vascular beds and the *ADD1* or *ADD2* polymorphisms were not significant. In family-based analyses, the multivariate-adjusted heritability was 0.52, 0.38 and 0.30 for brachial diameter, distensibility, and cross-sectional compliance, respectively ( $P<0.001$ ). There was no evidence for population stratification ( $0.07 \leq P \leq 0.96$ ). Transmission of the mutated *ADD3 G* allele was associated with smaller brachial diameter in 342 informative offspring ( $-0.12 \pm 0.04 \text{ mm}$ ;  $P=0.0085$ ) and in 209 offspring, who were *ADD1 GlyGly* homozygotes ( $-0.14 \pm 0.06 \text{ mm}$ ;  $P=0.018$ ).

**Conclusions:** In *ADD1 GlyGly* homozygotes, the properties of the brachial artery are related to the *ADD3* (*A386G*) polymorphism, but the underlying mechanism needs further clarification.

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#### P1.26

##### THE INFLUENCE OF ENDOTHELIAL NITRIC OXIDE SYNTHASE POLYMORPHISMS AND CURRENT SMOKING ON LARGE ARTERY STIFFNESS

J. Filipovsky<sup>1</sup>, Mayer Jr. O<sup>1</sup>, M. Pesta<sup>1</sup>, R. Cifkova<sup>2</sup>.

<sup>1</sup> Charles University Medical Faculty, Pilsen, Czech Republic

<sup>2</sup> Institute of Clinical and Experimental Medicine, Prague, Czech Republic

**Background:** Nitric oxide belongs to the most important factors influencing structural and functional properties of vessel wall. Both genetic and environmental factors may influence its metabolism. The aim of this study was to explore whether two common polymorphisms of endothelial nitric

synthase (eNOS) may, jointly with smoking, influence the stiffness of large arteries, quantified by pulse wave velocity (PWV).

**Methods:** One hundred ninety four subjects free of manifest atherosclerosis or chronic cardiovascular pharmacotherapy were selected from population-based post-MONICA study. PWVs were measured using Sphygmocor® device between carotid and femoral arteries (aortic PWV) and between femoral and tibialis-posterior arteries (peripheral PWV). Two common eNOS polymorphisms, T786C and G894T, were assessed.

**Results:** Among current smokers ( $n=70$ ), homo- or heterozygous carriers of T786C mutation ( $n=42$ ) showed significantly higher peripheral PWV than normal genotype carriers ( $14.0$  vs  $10.7 \text{ m/sec}$ ,  $p<0.002$ ); the same applied to the carriers of G894T mutation ( $n=41$ ;  $13.9$  vs  $11.0 \text{ m/sec}$ ,  $p<0.015$ ). No differences were found in non-smokers, and neither of the eNOS polymorphisms influenced aortic PWV in our setting.

**Conclusion:** Genetically determined disorder of nitric oxide metabolism was associated with increased stiffness of peripheral muscular-type arteries in generally healthy, untreated subjects, but only in interaction with active smoking.

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#### P1.27

##### INTERRELATIONSHIPS OF MONOCYTE COUNT WITH CAROTID INTIMA-MEDIA THICKNESS, AORTIC STIFFNESS AND PENILE DOPPLER FINDINGS, IN PATIENTS WITH VASCULOGENIC ERECTILE DYSFUNCTION

D. Terentes-Prinzios, C. Vlachopoulos, N. Ioakeimidis, N. Alexopoulos, A. Bratsas, I. Dima, K. Rokkas, C. Stefanadis.

1st Department of Cardiology, Athens Medical School, Athens, Greece

**Background:** Erectile dysfunction (ED) has been associated with both systemic inflammation and generalized vascular disease. Monocyte count (MNC) represents a sensitive marker of inflammatory activity in atherosclerosis. We examined the possible associations between MNC, penile vascular damage and early atherosclerosis.

**Methods:** 145 consecutive ED patients were divided into three groups according to pharmacologically stimulated peak systolic velocity (PSV) values of cavernous arteries: Group A (venous occlusive disease), group B (mild arterial insufficiency) and group C (severe arterial insufficiency,  $PSV<25 \text{ cm/s}$ ). PSV shows the greatest flow velocity detectable in an artery throughout the systole. Ultrasound-determined intima media thickness (IMT) of carotid arteries and carotid-femoral pulse wave velocity (PWV) as an index of aortic stiffness were used to assess subclinical atherosclerosis.

**Results:** Patients with severe arterial insufficiency ( $n=44$ ) compared to subjects in group B ( $n=41$ ) and A ( $n=60$ ) had increased IMT ( $0.96$  vs  $0.93$  vs  $0.87 \text{ mm}$ ,  $P<0.05$ ) and PWV ( $9.3$  vs  $8.9$  vs  $8.5 \text{ m/s}$ ,  $P<0.05$ ). They also exhibited higher MNC, compared to those of groups A and B ( $0.47$  vs  $0.44$  vs  $0.39 \times 10^9/\text{L}$ ,  $P<0.05$ ), whereas there were no significant differences between the 3 groups as regards white cell counts. Furthermore, MNC remained significantly different between groups after adjustment for CRP, fibrinogen and risk factors, ( $P<0.05$ ). MNC correlated with IMT ( $r=0.23$ ,  $P<0.05$ ), PWV ( $r=0.27$ ,  $P<0.01$ ) and PSV ( $r=-0.26$ ,  $P<0.01$ ).

**Conclusions:** Our study shows that there is an augmentation in MNC throughout increasing penile vascular damage and subclinical atherosclerosis. These findings may reflect the potential role of MNC as a marker of early atherosclerosis in ED patients.

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#### P1.28

##### INFLUENCE OF AGE ON CAROTID ENDOTHELIAL FUNCTION AS DETERMINED BY HYPERCAPNIA INDUCED VASODILATATION

N.P. Saeed<sup>1</sup>, G. Esquivel<sup>2</sup>, I.M. Graf<sup>1</sup>, A.P.G. Hoeks<sup>1</sup>.

<sup>1</sup> Maastricht University, Department of Biophysics, Maastricht, Netherlands

<sup>2</sup> Department of Psychiatry & Neuropsychology, Maastricht, Netherlands

**Background:** An increase in blood velocity-associated shear stress results in release of endothelial factors, causing endothelium-dependent flow mediated dilatation (FMD). Hypercapnia strongly stimulates cerebral blood flow velocity in the common carotid artery (CCA).

**Objective:** Test the reliability of hypercapnia induced FMD of the CCA and evaluate the stimulus response relationship (changes in blood velocity and diameter) for different age populations.

**Methods:** Hypercapnia was induced with inhalation of a gas mixture of 6.8% CO<sub>2</sub>, 74.5% N<sub>2</sub>, and 18.6% O<sub>2</sub> for a period of 2 minutes in 19 healthy young

(24±6y) and 11 old (60±12y) subjects. Continuous beat-to-beat changes in CCA diameter were used to determine FMD magnitude in percentage change in end diastolic diameter ( $\Delta D/D$ ) and mean centre stream blood velocity ( $\Delta V/V$ ). Endothelial function (EF) is estimated by the relative response of  $\Delta D/D$  to  $\Delta V/V$ . **Results:** Heart rate increases significantly during and post hypercapnia. No significant changes are seen in peripheral blood pressure. Hypercapnia stimulus induces significant increases in flow velocity and diameter in both populations, reaching a steady state after 3 minutes.  $EF = 0.6 \pm 0.03$  (young), and  $EF = 0.4 \pm 0.08$  (old).

**Conclusions:** CO<sub>2</sub> stimulated FMD response at the CCA exposes the dynamic interrelationship between blood velocity and diameter. It provides a direct and well-tolerated tool to quantify endothelial function in atherosclerotic prone arteries.

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#### P1.29

### ONE CLINIC MEASURE OF LIGHT EXERCISE CENTRAL BLOOD PRESSURE IS A STRONGER CORRELATE OF LEFT VENTRICULAR MASS THAN 24 HOUR AMBULATORY BLOOD PRESSURE MONITORING

J.E. Sharman, S. Thomas, J.L. Hare, R. Leano, C. Jenkins, T.H. Marwick.  
*The University of Queensland, Brisbane, Queensland, Australia*

**Background:** Twenty four hour ambulatory blood pressure (24ABPM) is the gold standard for assessing blood pressure (BP) control. However, central BP during daily activity may be a stronger determinant of cardiovascular risk. This study aimed to compare 24ABPM with light exercise central BP (mimicking daily activity) for predicting left ventricular (LV) mass.

**Methods:** Study population comprised 54 patients (aged 58±7 years; 20 men) including those with treated hypertension (n=16), untreated masked hypertension (n=23) and normotensive controls (n=15). Subjects underwent 2D echocardiography for determination of LV mass (indexed; g/m<sup>2.7</sup>), resting brachial BP, 24ABPM and estimated central BP by radial tonometry during graded cycle ergometry. Central systolic BP (SBP) was estimated from the radial second systolic peak (P2) as well as the derived central waveform.

**Results:** The range of LV mass index and 24ABPM SBP were 17.8-55.1 g/m<sup>2.7</sup> and 107-153 mmHg respectively. As expected, 24ABPM SBP was significantly associated with LV mass index ( $r=0.30$ ,  $p=0.02$ ), but not with clinic resting brachial ( $r=0.21$ ;  $p=0.14$ ) or central SBP ( $r=0.20$ ;  $p=0.14$ ). However, the strongest correlates of LV mass index were light exercise (50% heart rate reserve) radial P2 ( $r=0.54$ ,  $p<0.001$ ) and central SBP ( $r=0.47$ ;  $p<0.001$ ). On multiple regression analysis, radial P2, but not 24ABPM SBP, was independently associated ( $\beta=0.45$ ;  $p<0.01$ ) with LV mass index after accounting for other confounding variables.

**Conclusion:** A one-off clinic estimate of light activity central SBP outweighs 24ABPM for predicting LV mass. This rapid, noninvasive technique may provide a superior measure of BP control compared with the current gold standard.

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#### P1.30

### INDICES OF ARTERIAL STIFFNESS AND RAISED BLOOD PRESSURE AMONGST PUBLIC SCHOOL CHILDREN IN GUJARAT, INDIA

J.V. Patel<sup>1</sup>, R. Potluri<sup>2</sup>, A. Gunarathne<sup>1</sup>, J.K. Cruickshank<sup>3</sup>, Lip GYH<sup>2</sup>, D. Prabhakaran<sup>4</sup>, P.S. Gill<sup>2</sup>, E.A. Hughes<sup>1</sup>.

<sup>1</sup> Sandwell and West Birmingham Hospitals NHS Trust, West Midlands, United Kingdom

<sup>2</sup> University of Birmingham, Birmingham, United Kingdom

<sup>3</sup> University of Manchester, Manchester, United Kingdom

<sup>4</sup> All India Institute of Medical Sciences, Delhi, India

**Background:** Pediatric hypertension is increasing in prevalence with the global childhood obesity epidemic. The burden of paediatric hypertension and prehypertension are poorly understood in areas of the Indian subcontinent.

**Methods:** Using standardised methods for anthropometry (International Society for the Advancement of Kinanthropometry), and blood pressure (British Hypertension Society guidelines) - paediatric obesity, blood pressure and a marker of arterial stiffness (stiffness index using digital volume pulse analysis PCA Micromedical) were measured within 303 school children (4-14 years) in rural Gujarat, India.

**Results:** The prevalence of prehypertension was 13.3% in boys and 13.7% in girls, which were markedly higher those reported for the US (3.4%). Many of the Indian children were deemed not have reached their true growth potential, where 82.5% of children were below the 50th percentiles for height,

gender and age as advised by consensus US guidelines. On logistic regression, prehypertension was associated with waist to height ratio ( $P<0.001$ ) and body-mass index ( $P<0.001$ ). Median stiffness index was comparable in boys 6.89 m/s (IQR: 2.95-7.79) and girls - 6.62 m/s (5.58-7.72). Prehypertension was unrelated to indices of arterial stiffness, which were associated with waist to height ratio ( $r = -0.34$ ,  $P<0.001$ ).

**Conclusion:** Low birth weight and an early manifestation of aberrant endocrine activity are likely to be implicated in higher blood pressure for these children, for which further research is warranted given the impeding threat of over nutrition that looms with the rising epidemic of obesity across the Indian subcontinent. Given the healthcare challenge of cardiovascular morbidity that faces Asia, the assessment of paediatric hypertension and obesity amongst children is an important consideration for prevention strategies.

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#### P1.31

### DETERMINING PULSE WAVE VELOCITY USING MRI: A COMPARISON AND REPEATABILITY OF RESULTS USING SEVEN TRANSIT TIME ALGORITHMS

M. Butlin<sup>1</sup>, S. Hickson<sup>2</sup>, M.J. Graves<sup>3</sup>, C.M. McEnery<sup>2</sup>, A.P. Avolio<sup>1</sup>, I.B. Wilkinson<sup>2</sup>.

<sup>1</sup> The Australian School of Advanced Medicine, Macquarie University, Sydney, NSW, Australia

<sup>2</sup> Clinical Pharmacology Unit, University of Cambridge, Addenbrookes Hospital, Cambridge, United Kingdom

<sup>3</sup> Department of Radiology, University of Cambridge, Cambridge, United Kingdom

**Aim:** MRI provides a non-invasive method for assessing segmental aortic pulse wave velocity (aPWV). However, the best mathematical algorithm for transit time calculation using MRI flow waves is unclear.

**Methods:** 7 different algorithms were applied to aortic flow waveforms measured by MRI (10 subjects, 36±7 years, 4 male). Two measurements were recorded in each subject on different days for repeatability analysis. PWV was calculated between 5 sites along the aorta. Outlier PWV results were classed as a "failed" measurement and the success rate calculated. Bland-Altman plots were constructed for each algorithm, and repeatability calculated. Agreement between different methods was calculated using repeated measures analysis.

**Results:** The method of intersecting lines of fit during late diastole and early systole had the highest success rate followed by the Fourier analysis phase-slope method (99%; 98% respectively). Repeatability of measurement was highest using the phase-slope method followed by the method of intersecting lines (standard deviation 1.9; 2.2 m/s respectively). Methods of deviation of a systolic line of fit, maximum of second derivative, intersecting lines of fit, and the corner detection algorithm had the highest agreement, corrected for repeatability (corrected standard deviation range 1.8-1.9 m/s).

**Conclusions:** Whilst agreement between several PWV algorithms was high, no one algorithm was better in all categories. The intersection of lines of fit method was most robust. The phase-slope method showed the greatest repeatability. These findings are important in aPWV measurement, and for reliable and accurate PWV measurement in general.

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#### P1.32

### BRACHIAL-ANKLE PULSE WAVE VELOCITY: A NEW METHOD FOR CLINICAL EVALUATION OF ARTERIAL STIFFNESS COMPARED WITH CAROTID-FEMORAL PULSE WAVE VELOCITY

F. Santini<sup>1</sup>, C. Palombo<sup>1</sup>, C. Morizzo<sup>1</sup>, E. Malshi<sup>1</sup>, P. Spontoni<sup>2</sup>, M. Kozakova<sup>1</sup>, Di Stefano R<sup>2</sup>, A. Balbarini<sup>2</sup>.

<sup>1</sup> Department of Internal Medicine, University of Pisa, Pisa, Italy

<sup>2</sup> Cardiothoracic and Angiology Department, University of Pisa, Pisa, Italy

**Background:** Arterial stiffness (AS) reflects morfo-functional modifications of elastic arteries due to aging and atherosclerosis.

Carotid-femoral pulse wave velocity (PWVcf) represents an established marker of aortic stiffness and predictor of cardiovascular mortality.

Recently, a new method for evaluating arterial stiffness based on brachial-ankle pulse wave velocity (PWVba) and capable to provide a stiffness index, CAVI (cardio-ankle vascular index), has been proposed.

**Aim:** to compare PWVba with PWVcf and to evaluate the corresponding relationships with age and blood pressure in healthy subjects and patients with major risk factors for atherosclerosis.

**Methods:** 46 subjects (19 controls; 27 patients with risk factors but without clinical cardiovascular disease; 31 women; age 43±18) were studied. PWVcf