



## Artery Research

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### **P7.16: ASSESSMENT OF CENTRAL HAEMODYNAMICS AND ARTERIAL STIFFNESS IN THE COMMUNITY – ARE WE THERE YET?**

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sphygmomanometry, central BP and aortic pulse wave velocity (PWV) were estimated by applanation tonometry. Stepwise multiple regression analysis (corrected for multiple covariates related to cardiovascular risk) was used to determine independent predictors of central and peripheral haemodynamics.

**Results.** Results from the multiregression analysis of gender-specific associations with height are presented in the table. Height was not significantly associated with aortic PWV in men or women. Height was (borderline) associated with brachial SBP in women ( $r=0.27$   $p=0.051$ ), but not in men ( $r=0.19$   $p=0.087$ ). Conversely, central SBP, augmentation index (AIx) at 75 bpm and time of reflected wave ( $T_R$ ) were independently associated with height in both men and women. Moreover, both men and women of above median height were less likely to be taking vasoactive medication (38% vs 56%;  $p<0.001$ ) or have hypertension (40% vs 53%;  $p=0.002$ ) compared to participants of below median height.

**Conclusions.** After correcting for conventional cardiovascular risk factors, taller individuals have more favourable central haemodynamics and reduced prevalence of hypertension and antihypertensive therapy compared with shorter men and women. These findings may help explain the decreased cardiovascular risk associated with being taller and have important clinical consequences regarding therapy.

Dependant variable	Gender	Beta	p-value	Adjusted R <sup>2</sup>
Brachial SBP (mmHg)	Women	-0.115	0.051	0.84
	Men	-0.096	0.087	0.82
Central SBP (mmHg)	Women	-0.172	<0.001	0.88
	Men	-0.139	0.002	0.89
AIx@75 bpm (%)	Women	-0.224	<0.001	0.33
	Men	-0.189	<0.001	0.52
Aortic PWV (m/s)	Women	0.025	0.067	0.34
	Men	0.014	0.148	0.39

#### P7.13

##### WHICH ARTERIAL STIFFNESS PARAMETER IS THE BEST PREDICTOR OF CARDIOVASCULAR MORTALITY IN HEMODIALYSIS PATIENTS?

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According to previous studies different parameters characterize arterial stiffness relate to cardiovascular mortality in patients on haemodialysis. However, its relative prognostic value and the optimal time of measurement have not previously been examined in one cohort.

The carotid-femoral pulse wave velocity (PWV), the carotid augmentation index (AI), the carotid pulse pressure (CPP) and the carotid-brachial pulse pressure amplification (AMP) were determined in 98 patients before and after haemodialysis procedure. Patients were followed for 29 months (median; range 1–34) and the association of these parameters with the risk of cardiovascular mortality was assessed using log-rank tests and Cox proportional hazards regression.

During follow-up, 25 patients died of cardiovascular causes. Increasing pre- and postdialysis PWV tertiles and decreasing predialysis AMP tertiles were significantly related to cardiovascular mortality ( $p = 0.012$  and  $0.011$  for PWV, respectively; and  $<0.001$  for AMP). Neither the AI nor CPP was related to cardiovascular mortality. The adjusted hazard ratios for 1 m/s higher pre- and postdialysis PWV were 1.24 (1.07–1.44) and 1.17 (1.06–1.28), respectively. The hazard ratio for 10% lower predialysis AMP was 1.41 (1.03–1.92). When included in the same model, both predialysis PWV and AMP remained significantly associated with cardiovascular mortality.

Among different stiffness parameters, PWV is consistently related to cardiovascular mortality, irrespectively of the timing of measurement. Predialysis AMP seems to provide additional prognostic information.

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#### P7.14

##### C-REACTIVE PROTEIN AND MARKERS OF ARTERIAL STIFFNESS IN HIGH CARDIOVASCULAR RISK PATIENTS

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**Introduction:** The aim of the study was to investigate the relationship between C-reactive protein (CRP) and markers of arterial stiffness.

**Methods:** We have analyzed the data of 3163 high cardiovascular risk patients selected from a larger cohort of patients inspected in Vilnius University Hospital Santariskiu Klinikos primary prevention cardiovascular unit. The criteria for inclusion was low value of CRP ( $<5$  mg/l). The mean age of the selected sample was  $54.03 \pm 6.10$ . Almost two thirds of them were females (65.7%). We divided all patients into two groups. The first group consisted of patients having CRP below 2 mg/l ( $n=2041$ ), whereas the second group consisted of patients having CRP no less than 2 mg/l ( $n=1122$ ). After that, these groups were compared with respect to the following markers of arterial stiffness: augmentation index (AIx), flow mediated dilatation (FMD), femoral and brachial pulse wave velocities (PWV (femoral), PWV (brachial)). Only femoral PWV significantly differed between the groups: ( $8.69 \pm 2.68$  (CRP $<2$  mg/dl) vs  $9.00 \pm 1.59$  (CRP $\geq 2$  mg/dl);  $p=0.003$ ), and there were no differences with respect to other markers. Division of patients into groups with CRP $<3$  mg/l ( $n=2623$ ) and CRP $\geq 3$  mg/l ( $n = 540$ ) yielded the same results. There was a significant difference only with regard to femoral PWV ( $8.74 \pm 2.45$  (CRP $<3$ ) vs.  $9.12 \pm 1.56$  (CRP $\geq 3$ );  $p=0.004$ ).

**Results:** Our study suggests that there is a moderate relationship between CRP and arterial stiffness and it is best diagnosed by alterations of femoral PWV.

#### P7.15

##### MEASUREMENT OF ARTERIAL STIFFNESS IN THE PORTUGUESE

##### POPULATION: THE GUIMARÃES STUDY (STUDY TO DETERMINE THE CARDIOVASCULAR RISK OF THE POPULATION OF GUIMARÃES/VIZELA: PREVALENCE OF ARTERIAL STIFFNESS AND EARLY VASCULAR AGING SYNDROME)

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We observed 1104 subjects of the Portuguese population coming from two adjacent cities in the north: Guimarães and Vizela. They were randomly selected from the population to be included in a cohort representative of the age and gender distribution. We evaluated their age, sex, clinical history, blood pressure (BP) (mean of three measurements), height, weight, lipidic profile, fasting glucose, HbA1c, serum creatinine, microalbuminuria (occasional sample); we also performed Pulse Wave Velocity (PWV) measurements (Sphygmocor®).

These 1104 subjects (56,4% females), had a mean global age of 47,6 years (18 – 94); 42% had hypertension, 10,7% had Diabetes, 80% had lipidic profile abnormalities, 3,1% had GFR  $< 60$  ml/min and 16,1% had microalbuminuria. The mean brachial systolic BP was 131,3 mmHg (84 to 243) and the mean brachial diastolic BP was 76,7 mmHg (44 to 128); The average BMI was 26,8 kg/m<sup>2</sup> (16,8 to 46,2).

The mean PWV value recorded in the population was 7,4 m/sec (4,1 to 18); mean PWV values were distributed as follows, according to the different age classes: 18 to 30 years – 6,1 m/sec (4,1 to 9,7); 31 to 40 years – 6,6 m/sec (4,2 to 13,6); 41 to 50 years – 7,5 m/sec (4,7 to 14,1); 51 to 60 years – 7,5 m/sec (4,6 to 12,3); 61 to 70 years – 9,0 m/sec (4,5 to 18); 71 to 80 years – 9,4 m/sec (5 to 15,4); 81 to 90 years – 10,5 m/sec (6,7 to 15,7). These are, to our knowledge, the first arterial stiffness measurements performed on a population based cohort in Portugal.

#### P7.16

##### ASSESSMENT OF CENTRAL HAEMODYNAMICS AND ARTERIAL STIFFNESS IN THE COMMUNITY – ARE WE THERE YET?

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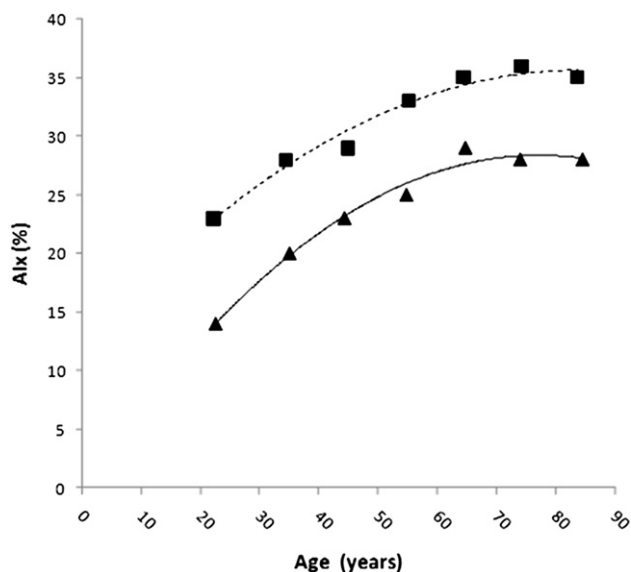
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**Background:** The assessment of arterial stiffness and central pressures has been limited to specialised techniques and settings. New, more practical methods (ARCSolver) allow assessment using a standard brachial cuff. The objective was to assess the feasibility of central haemodynamics and surrogates of arterial stiffness from the ARCSolver in a community based setting.

**Methods:** Peripheral and central systolic and diastolic blood pressure (BP) and wave reflection parameters (augmentation index) were obtained from a 1,903 volunteers in an Austrian community setting. We assessed for known differences and associations according to gender and each age deciles from <30 years to ≥80 years in the whole population and a subset with a systolic BP < 140 mmHg.

**Results:** Age and gender associations with central haemodynamic and augmentation parameters reflected those previously established from gold-standard non-invasive techniques under specialised settings (Fig. 1). Findings were the same for patients with a systolic BP below 140 mmHg (i.e. normotensive). Differences in actual values for augmentation index are likely due to lower numbers of volunteers in these age groups and method differences.

**Conclusion:** One-off measures of central haemodynamics and pulse wave augmentation from the ARCSolver demonstrated known age and gender associations which were not limited to normotensive individuals. Using ARCSolver to obtain estimates of central pressure and augmentation appears robust and feasible in a community setting. Further validation is now possible in large cohort studies, particularly in primary care settings.



**Figure 1** Regression curves for the effect of age on augmentation index in males (▲) and females (■)

## P8 – Endothelium and Small Arteries 2

### P8.01

#### ENDOTHELIAL DYSFUNCTION AND LOW-GRADE INFLAMMATION ARE ASSOCIATED WITH ARTERIAL STIFFNESS IN HEALTHY ADULTS OVER A 6-YEAR PERIOD

#### THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY (AGAHLS)

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Endothelial dysfunction and low-grade inflammation are associated with cardiovascular disease. Arterial stiffening plays an important role in cardiovascular disease and thus may be a mechanism through which endothelial dysfunction and/or low-grade inflammation lead to cardiovascular disease. We investigated the associations between, on the one hand, biomarkers of endothelial dysfunction (soluble endothelial selectin, thrombomodulin and both vascular- and intercellular adhesion molecules 1 and von Willebrand factor) and of low-grade inflammation (C-reactive protein, serum amyloid A, interleukin 6, interleukin 8, tumour necrosis factor  $\alpha$  and soluble intercellular adhesion molecule 1) and, on the other hand, arterial stiffness over a 6-year period, in 293 healthy adults (155 women). Biomarkers were combined into mean Z-scores. Carotid, femoral and brachial arterial stiffness and carotid-femoral pulse wave velocity were determined by ultrasonography. Measurements were obtained when individuals were 36 and 42 years of age. Associations were analysed with generalised estimating equation and adjusted for sex, height and mean arterial pressure. The endothelial dysfunction Z-score was inversely associated with femoral distensibility [ $\beta$ (95%CI)-0.51(-0.95;-0.06)] and compliance coefficients [-0.041(-0.076;-0.006)], but not with carotid or brachial stiffness or carotid-femoral pulse wave velocity. The low-grade inflammation Z-score was inversely associated with femoral distensibility [-0.51(-0.95;-0.07)] and compliance coefficients [-0.050(-0.084;-0.016)], and with carotid distensibility coefficient [-0.91(-1.81;-0.008)], but not with brachial stiffness or carotid-femoral pulse wave velocity. Biomarkers of endothelial dysfunction and low-grade inflammation are associated with greater arterial stiffness. This provides evidence that arterial stiffening may be a mechanism through which endothelial dysfunction and low-grade inflammation lead to cardiovascular disease.

### P8.02

#### CHARACTERIZATION OF THE VASORELAXANT MECHANISMS OF ENDOCANNABINOID OLEOYLETHANOLAMIDE IN THE BOVINE OPHTHALMIC ARTERY

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**Background:** Numerous studies show the potential therapeutic effect of different endocannabinoids and in particular the vasorelaxant effects in several vascular beds

**Aim:** To evaluate the vasorelaxant effect of oleoylethanolamide on isolated bovine ophthalmic arteries and to evaluate the possible mechanisms involved in relaxant responses.

**Methods:** Ophthalmic arteries were isolated from bovine eyes and mounted in a wire miograph for isometric tension recording. The effects time- and concentration-dependent were assayed by addition of the oleoylethanolamide to the organ bath.

**Results:** Oleoylethanolamide (0.1 - 10  $\mu$ M) produced a significant concentration- and time-dependent vasorelaxation in the bovine ophthalmic artery pre-contracted with 5-HT (1  $\mu$ M). The removal of endothelium provoked a slight reduction of the relaxant effects. Interestingly, a pre-treatment with antagonist PPAR $\alpha$  GW6471 (1  $\mu$ M) inhibited the concentration- and time-dependent oleoylethanolamide-induced vasorelaxation.

**Conclusion:** The present study shows that oleoylethanolamide relaxed the isolated bovine ophthalmic artery in the concentration- and time-dependent manner. The candidate responsible of the vasorelaxant response to oleoylethanolamide appear to be the PPAR $\alpha$ . This relaxant effect is an exciting tool to prevent ischemic injury because it improves the blood supply to the retina.

### P8.04

#### DIFFERENT EFFECTS OF PLASMA MEMBRANE CALCIUM ATPASE 4 (PMCA4) ABLATION AND ACUTE INHIBITION ON CONTRACTILITY OF ISOLATED MOUSE MESENTERIC ARTERIES

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Plasma Membrane Calcium ATPases (PMCA's) are calcium extrusion pumps which may also modulate signal transduction. The most abundant PMCA