

## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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### **P.001: ACUTE EFFECTS OF NICOTINE ON PERIPHERAL AND CORONARY VASCULAR FUNCTION IN YOUNG NON-SMOKERS**

D. Adamopoulos, J.F. Argacha, M. Gujic, C. Garcia, N. Preumont, J.P. Degaute, S. Goldman, P. van de Borne

**To cite this article:** D. Adamopoulos, J.F. Argacha, M. Gujic, C. Garcia, N. Preumont, J.P. Degaute, S. Goldman, P. van de Borne (2007) P.001: ACUTE EFFECTS OF NICOTINE ON PERIPHERAL AND CORONARY VASCULAR FUNCTION IN YOUNG NON-SMOKERS, Artery Research 1:2, 53–53, DOI: <https://doi.org/10.1016/j.artres.2007.07.058>

**To link to this article:** <https://doi.org/10.1016/j.artres.2007.07.058>

Published online: 21 December 2019

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Age-related changes in arterial stiffness are ascribed to collagen and elastin content in the aorta (Ao) which is modulated by the matrix metalloproteinases (MMPs). However, no study has directly compared arterial stiffness and arterial structure in man.

Aortic and internal mammary artery (IMA) tissue were obtained from 10 patients ( $62 \pm 1$  years, 2 female) undergoing coronary artery bypass grafting (CABG). Aortic pulse wave velocity (PWV) was measured prior to CABG. Collagen content was assessed in tissue sections using Sirius Red staining and elastin by ACCUSTAIN. Elastin fragmentation in the Ao media was graded; increasing in severity from 1 to 4. MMP-2 and MMP-9 activity was quantified in the Ao using gelatine zymography. Results are expressed as mean  $\pm$  SEM,  $p < 0.05$  considered significant.

The collagen concentration was 50% (intima), 42% (media) and 76% (adventitia) in the Ao but was lower in the IMA. PWV was significantly associated with Ao medial ( $r = 0.79$ ,  $p = 0.03$ ) but not intimal or adventitial collagen concentrations. Aortic intimal thickness was related significantly with age ( $r = 0.70$ ,  $p < 0.05$ ) but not PWV. There was no relationship between age and Ao collagen concentration. There was a significant association ( $p < 0.001$ ) between increasing elastin fragmentation in the aortic media and PWV but not age. There was no relationship between collagen concentration in the IMA and either PWV or age. Neither latent nor active MMP-2 activity was related with PWV or age. Latent MMP-9 expression was significantly associated with PWV ( $r = 0.66$ ,  $p < 0.05$ ) but not age.

Aortic stiffness is associated with Ao medial collagen content and the degree of elastin fragmentation in man.

#### 10.02

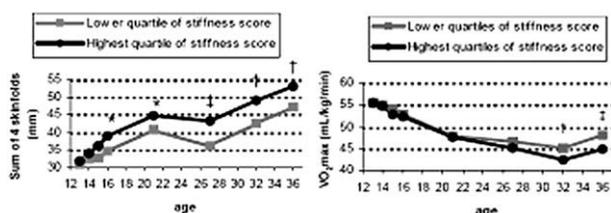
##### LONGITUDINAL DEVELOPMENT OF FITNESS AND FATNESS FROM ADOLESCENCE TO ADULTHOOD: IMPACT ON ARTERIAL STIFFNESS AT THE AGE OF 36 YEARS. THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY (AGAHLS)

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**Introduction:** Body fatness (BF) and low levels of cardiopulmonary fitness (CF) during adolescence have been associated with arterial stiffness (AS) later in life. How the development over time (i.e. from adolescence to adulthood) of BF and CF impact on AS in adulthood is not known.

**Methods:** Longitudinal data on BF (sum of 4 skinfolds – SSKF) and CF (VO<sub>2</sub>max) were derived from the AGAHLS ( $n = 372$ , 197 women; 8 follow-up measures at the ages of 13, 14, 15, 16, 21, 27, 32 and 36 yrs). Arterial stiffness (i.e. carotid, brachial and femoral distensibility and compliance coefficients) was assessed by non-invasive ultrasonography when subjects were 36-yrs-old; a stiffness score (average of the z-scores of these 6 estimates) was calculated. We used generalized estimating equations to compare the patterns of development of SSKF and VO<sub>2</sub>max levels (adjusted for each other and for potential confounders) over the 24-yr follow-up period between those subjects with 'higher' (i.e. lowest sex-specific quartile) vs. 'normal' (higher 3 quartiles) levels of stiffness score at the age of 36 yrs.

**Results:** In all subjects, SSKF increased and VO<sub>2</sub>max decreased between the ages of 13 and 36 ( $p < 0.001$ ); higher increases in SSKF during adolescence and decreased levels of VO<sub>2</sub>max in recent but not early years characterized individuals with higher arterial stiffness at the age of 36 as compared to their 'normal' counterparts (Figure).



**Conclusion:** Increases in body fatness rather than decreases in cardiopulmonary fitness during adolescence impact on arterial stiffness later in life; lifestyle interventions in the young should therefore target weight control.

#### 10.03

##### EARLY REFLECTION OBSERVED IN THE PULSE WAVE IN THE COMMON CAROTID ARTERY ORIGINATES FROM EITHER THE CIRCLE OF WILLIS OR THE CAPILLARY BED OF THE FACIAL MUSCULATURE

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**Introduction:** Arterial wave reflections augment pulse pressures at heart level and manifest as an inflection point in the blood pressure waveform. However, the origin of reflection is still partly unresolved and can not be derived using the waveform from a single location.

**Method:** Two distension waveforms, spaced at 16.4mm, were simultaneously obtained in the left CCA of 12 young subjects with dual M-line ultrasound. The second derivatives of the distension waveforms were calculated to identify the opening of the aortic valve (AVO) and the inflection point before systolic peak pressure (IP). The time-delay ( $\Delta T$ ) between both time points, either AVO or IP, in the proximal and distal waveform was calculated to obtain the direction of propagation.

**Results:** Mean time difference between AVO and IP was  $38 \pm 8$ ms. There was a significant time difference in AVO ( $p < 0.0001$ ) and IP ( $p = 0.0012$ ) between proximal and distal waveform. AVO had a positive delay  $\Delta T_{AVO} = 3.3 \pm 1.0$ ms. In contrast IP had a negative delay  $\Delta T_{IP} = -3.6 \pm 3.1$ ms.

**Discussion:** Time-delay of AVO and IP are comparable but opposite in sign. Measurements were performed on the CCA, which is a small straight arterial segment without branches, therefore the effect of dispersion or tapering can be ignored and the direction of propagation of IP can only be explained by reflections. Using the time difference between AVO and IP and assuming constant wave-speed, the distance between reflection and measurement site was estimated at 12cm, pointing at the circle of Willis or the capillary bed of the facial musculature as distal reflection sites.

#### 10.04

##### LARGE AND SMALL ARTERY STRUCTURE & STIFFNESS IN RELATION TO GLYCAEMIA AND BLOOD PRESSURE IN PRE-MENOPAUSAL WOMEN

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**Introduction:** Diabetes and Hypertension affect large and small artery structure and function. We investigated the relationship between large artery structure (common carotid intima-medial thickness: cIMT), function (aortic pulse wave velocity-aPWV) and structure and stiffness index of small subcutaneous arteries in a group of pre-menopausal women who had undergone an oral glucose tolerance test (OGTT) during pregnancy.

**Patients and Methods:** 29 pre-menopausal women (age 36.2 years, 95% CI 35.1-37.2) underwent an OGTT and under standardised conditions, assessment of aPWV and biopsy of subcutaneous fat to assess the small arterial structure and function.

**Results:** cIMT was related to aPWV ( $r = 0.58$ ,  $p = 0.001$ ) and media cross-sectional area of small arteries (McxA,  $r = 0.43$ ,  $p = 0.023$ ); the latter correlated with small artery stiffness index (saSI,  $r = 0.34$ ,  $p = 0.01$ ). After adjustment for smoking, these independent parameters influenced vascular indices:

Multiple regression Beta (p value)	aPWV	cIMT	saSI	McxA
Age	0.16 (0.046)			0.49 (0.034)
BMI	0.23 (0.018)			
SBP	0.16 (0.01)			
Fasting glucose	-1.4 (0.03)	-0.004 (0.03)		
Total cholesterol	1.26 (0.034)			
Medial thickness cIMT	264.1 (0.003)			
McxA			2.42 (0.04)	

**Conclusion:** In young women, even without overt diabetes or hypertension, large and small vessel structure & function but not stiffness are closely related. These vascular properties are modulated by degree of current glycaemia and other cardiovascular risk factors.

## Poster Presentations

P.001

### ACUTE EFFECTS OF NICOTINE ON PERIPHERAL AND CORONARY VASCULAR FUNCTION IN YOUNG NON-SMOKERS

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**Background:** Despite overwhelming evidence associating cigarette smoking with arterial stiffening, the precise mechanisms involved in this relationship are not fully understood. The aim of this study was to test the hypothesis that nicotine could increase aortic wave reflection and that this would be accompanied by an alteration in skin blood flow reactivity and a reduction in myocardial perfusion.

**Materials and methods:** We conducted a prospective study, divided into two experimental settings, in 21 healthy, non-smoker, male subjects. In the first setting (n=11), subjects received a placebo and a 2 mg nicotine tab, according to a randomized, double-blind, cross-over design. Each subject underwent measurements at baseline and for 1 hour post-nicotine or placebo, using the augmentation index (AIx) of the aortic pressure waveform to assess wave reflection. Endothelial function was evaluated twice, at baseline and 40 minutes after nicotine or placebo intake, using two hyperemic tests: skin heating (SkBF-H) and acetylcholine iontophoresis (SkBF-Ach). In the second experimental setting (n=10), subjects underwent an N-13 positron emission tomography (PET) study before and 60 minutes after 2 mg of nicotine, in order to quantify myocardial perfusion.

**Results:** Nicotine administration was associated with an increase in heart rate (HR) ( $P < 0.001$ ) and AIx corrected for HR ( $p = 0.013$ ) throughout the study. No microcirculatory effects of nicotine were observed on endothelial function as assessed by SkBF-h or SkBF-Ach. The subendocardial viability ratio was decreased ( $p = 0.006$ ), suggesting an impairment in myocardial perfusion induced by nicotine. This was confirmed by the N-13 PET studies, which revealed a reduction in resting myocardial perfusion (from  $0.96 \pm 0.07$  to  $0.84 \pm 0.06$  ml/min/g,  $p < 0.05$ ).

**Conclusions:** Nicotine does not impair endothelium-dependent microvascular vasomotricity. Nevertheless, exposure to small amounts of nicotine increase aortic wave reflection and reduces resting myocardial perfusion in non-smokers.

P.002

### HABITUAL ANTIOXIDANT VITAMIN INTAKE, AUGMENTATION INDEX AND FLOW MEDIATED DILATION IN HYPERTENSIVE PATIENTS AND NORMOTENSIVE CONTROLS

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**Objective:** We evaluated the association of daily dietary intake of antioxidants vitamins C and E with augmentation index and endothelial function in untreated essential hypertensive (HT) patients and normotensive (NT) subjects.

**Methods:** Dietary intake of major nutrients, total caloric intake and antioxidant vitamins were assessed with the Italian EPIC questionnaire in 200 untreated HT patients and 130 NT subjects. Augmentation index (AIx) was determined with radial applanation tonometry. Endothelium-dependent response was assessed as flow mediated dilation (FMD) of the brachial artery by high resolution ultrasounds and computerized analysis (automatic edge detection system) of brachial artery diameter modifications.

**Results:** AIx was significantly higher in HT patients ( $26.9 \pm 9.6\%$ ) as compared to NT subjects ( $20.4 \pm 11.3\%$ ), whereas FMD resulted significantly lower ( $5.0 \pm 2.5$  vs  $6.2 \pm 2.7$ ;  $p < 0.001$ ). Calculated intake of vitamin C and E was similar in HT patients and in NT subjects (Vitamin C median  $146.4 \pm 68.7$  mg/day and  $149.1 \pm 84.0$  mg/day, Vitamin E median  $8.68 \pm 2.7$  mg/day and  $8.63 \pm 2.9$  mg/day, respectively). Multivariate analyses were controlled for smoking, physical activity status and total caloric intake. In both groups, levels of Vitamin C or E intake were not significant predictors for AIx. Finally, in both groups, levels of Vitamin C or E intake were not significant predictors for FMD.

**Conclusions:** No association exists between normal levels of regular food antioxidant intake, augmentation index and endothelial function in untreated essential hypertensive patients and normotensive subjects. This

suggests that supplementation with vitamin C and E is necessary to show an effect on vascular function in this population.

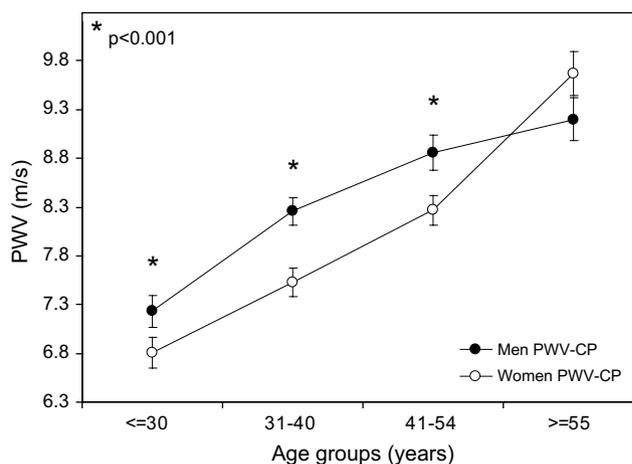
P.003

### EFFECTS OF AGING ON PULSE WAVE VELOCITY IN AFRICAN MEN AND WOMEN

A.E. Schutte, H.W. Huisman, M. Reimann, J.M. Van Rooyen, L. Malan, N.T. Malan. North-West University, Potchefstroom, South Africa

**Background:** The pulse wave velocity (PWV) in Caucasian men and women is similar and show similar increases with aging. But women develop a greater pulse pressure (PP) with aging due to smaller body size (since the height, weight and DBP are higher in men)[1]. Africans have a smaller body size than Caucasians, and African women are shorter and usually more obese than men. **Aim:** To compare age-related changes in PWV of African men and women. **Methods:** In 182 African men and 192 women (aged 20 to 77 years), carotid-radialis (C-R) and carotid-dorsalis pedis (C-P) PWV determined with the Complior SP. Anthropometric measurements were also done.

**Results:** As expected women weighed significantly more than men and were shorter than men ( $p < 0.001$ ). Similar SBP, DBP and PP were shown for men and women (whole group), and in all age groups (except 31-40 yrs). PWV (adjusted for BP, obesity) was overall higher ( $p < 0.001$ ) in men than women, also in most age groups. Only the eldest female group showed a trend to have higher C-P PWV than men.



**Conclusion:** Africans show contrasting results compared to Caucasians, namely significant gender differences in distensibility of the peripheral arterial tree, which seems to disappear after menopause. [1] Smulyan et al. JACC 2001; 37:1374-80.

P.004

### ETHNIC DIFFERENCES IN PULSE WAVE VELOCITY AND ITS RELATION TO BLOOD PRESSURE

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**Introduction:** It is known that African men suffer from high BP and vascular dysfunction. Normally a correlation exist between PWV and BP. However some studies show changes in PWV, independent of BP, possibly as a result of vascular remodeling [1].

**Aim:** To compare PWV in subjects of African and Caucasian ethnicity and its relation to BP.

**Method:** The study included 74 Caucasian and 64 African men from South Africa (aged 45-65 years). Cardiovascular parameters were recorded with the Finometer. The Complior SP was used to measure the carotid-radialis PWV.

**Results:** DBP and MAP were significantly higher in the Africans. SV and arterial compliance were significantly lower in the Africans but the TPR was significantly higher- an indication of vascular dysfunction. In the Africans the PWV was significantly higher than in the Caucasians ( $11.2$  m/s vs  $10.6$  m/s). With the Bonferroni test (corrected for BP) the same results were found. In the