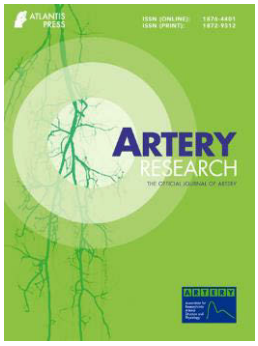

Artery Research

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

10.01: ARTERIAL STIFFNESS IS ASSOCIATED WITH ELASTIN DEFRAGMENTATION AND MEDIAL COLLAGEN CONTENT IN THE HUMAN AORTA

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To cite this article: A. Mahmud, M. McNulty, E. McGovern, V. Young, M. Tolan, J. Feely (2007) 10.01: ARTERIAL STIFFNESS IS ASSOCIATED WITH ELASTIN DEFRAGMENTATION AND MEDIAL COLLAGEN CONTENT IN THE HUMAN AORTA, Artery Research 1:2, 51–52, DOI: https://doi.org/10.1016/j.artres.2007.07.054

To link to this article: https://doi.org/10.1016/j.artres.2007.07.054

Published online: 21 December 2019

06.05
AORTIC STIFFNESS AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Background: Patients with COPD have increased aortic stiffness which may contribute to the excess cardiovascular risk in this group. Increased aortic stiffness increases left ventricular (LV) afterload and may contribute to impaired LV relaxation and diastolic dysfunction. We investigated LV diastolic function and its relationship to aortic stiffness in patients with COPD.
Methods: 36 COPD patients (19 male) and 14 age and gender matched healthy smokers (HS), both groups free of cardiovascular disease, were studied at clinical stability. The degree of airways obstruction was assessed using spirometry. Measures of LV diastolic function — mitral E/A, isovolumetric relaxation time (IVRT) and E/Ea were determined using echocardiography with myocardial velocity imaging. Aortic pulse wave velocity (APWV) was determined as a measure aortic stiffness using the Sphygmocor system.
Results: Patients, mean (SD) age 66.5(8.9) years exhibited airways obstruction across a wide spectrum of severity. Patients had a longer mean (SD) IVRT, 125(15.2) ms, compared with HS, 98.2(21.1) ms, $p<0.01$. E/Ea was also greater in patients than controls ($p<0.01$), while mitral E/A was similar between groups. APWV was higher in patients (11.5(2.9) m/s) than HS (9.45(1.3) m/s), $p<0.001$. In patients APWV was related to E/E_A ($r=0.55$, $p<0.01$), mitral E/A ($r=-0.38$, $p<0.05$) and IVRT ($r=-0.46$, $p<0.01$). APWV was the only significant predictor of IVRT in a mf aortic PWV may be useful in the assessment of LV diastolic dysfunction.y with myocardial velocity imaging. VIVionultiple regression analysis that included age and mean arterial pressure (r sq=0.22).
Conclusions: COPD patients have LV diastolic dysfunction which is related to aortic stiffness. Aortic PWV may be a useful marker of LV diastolic function in patients with COPD.

06.06
ARTERIAL STIFFNESS AND ENLARGEMENT IN MILD TO MODERATE CHRONIC RENAL FAILURE: ROLE OF VITAMIN D

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Background: Chronic kidney disease (CKD) is associated with arterial abnormalities characterized by an increase in arterial stiffness and an enlargement of carotid artery. Non classical cardiovascular risk factors such as abnormalities of mineral metabolism are associated with an increase risk in cardiovascular disease in end stage renal disease patients. The aim of this cross-sectional study is to evaluate the relationship between arterial phenotype and mineral metabolism parameters, serum parathormone (PTH), 25(OH) vitamin D and $1.25(OH)_2$ vitamin D, in 95 CKD patients (58.4 ± 14.9 years, GFR ^{51}Cr-EDTA 36 ± 16mL/min/1.73m^2).
Methods: Common carotid artery diameter, intima-media thickness, carotid stiffness, Young's elastic modulus were determined with an echotracking system. Aortic stiffness was evaluated by the measurement of carotid-to-femoral pulse wave velocity (Complior^R).
Results: After adjustment for mean blood pressure, age and GFR, 25 (OH) vitamin D level is significantly and negatively correlated with carotid stiffness ($P=0.005$) and Young elastic modulus ($P=0.003$) and explains respectively 4.1% and 5.3% of the variance. After adjustment for mean blood pressure, age and GFR, $1.25(OH)_2$ vitamin D level is significantly and positively correlated with carotid diameter ($P=0.002$), with carotid stiffness ($P=0.03$) and young elastic modulus ($P=0.04$). PTH is significantly and negatively correlated with aortic stiffness ($P=0.01$) and explains 3.7% of the variance.
Conclusion: Vitamin D status is associated with an increase in arterial stiffness and enlargement in mild to moderate chronic renal failure, 25 (OH) D3 is associated with favourable arterial phenotype whereas $1.25(OH)_2$ D3 and PTH are associated with adverse arterial phenotype.

06.07
EVALUATION OF A METHOD OF WAVE REFLECTION ASSESSMENT VIA TRIANGULAR FLOW WAVE APPROXIMATION

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Introduction: Wave reflections affect the aortic pressure and flow wave and play a role in systolic hypertension. Accurate quantification of pressure wave reflection requires separation of pressure in its forward (P_f) and backward (P_b) components, which requires aortic flow measurement. This limitation can be overcome by replacing the unknown flow wave by a triangular estimate of arbitrary amplitude, as recently proposed. We verified this technique using pressure and flow data measured in the Asklepios study (>2500 participants, 35 to 55 years).
Method: Wave separation analysis using measured pressure and flow yielded the reference reflection magnitude ($RM=P_b/P_f$). Then, RM was estimated using three triangular approximations of the flow wave, each with duration equal to the ejection time but with peak at (i) the shoulder point of the pressure wave (F^{tSP}); (ii) 30% of the ejection time (F^{t30}) and (iii) the moment of real peak flow (F^{tQm}).
Results: The correlation between measured and estimated RM's was highly significant ($P<0.001$) but overall disappointingly poor ($R^2=0.21$ to 0.25), the highest correlation coefficient being obtained when using (F^{tQm}). Overall, the approximation overestimated RM_{ref} by 10 to 12%. Interestingly, we found the accuracy of all estimations to depend highly on age ($P<0.001$), with the accuracy improving with age.
Conclusion: In healthy middle-aged subjects, quantification of wave reflection by estimating a triangular flow wave shows limited accuracy, even when timing of the peak is obtained directly from the flow waveform. This seems to imply that the triangular shape may be a too simple waveform approximation in this population.

06.08
RELATIONSHIP BETWEEN PULSE WAVE VELOCITY AND DIFFERENT BLOOD PRESSURE PATTERNS: THE VOBARNO STUDY

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Aim of this study: Was to assess the relationships between pulse wave velocity and different BP patterns (sustained normotension NT, isolated clinical hypertension ICH, ambulatory hypertension AHT and sustained hypertension HT) in a general population sample.
Design and methods: In 198 untreated subjects (age 55.7 ± 9.5, BMI 25.7 ± 4.0, 46.5% males) participating in our population study PWV was measured. Subjects underwent laboratory examinations and clinic and 24 hours BP measurement. Subjects were divided into subgroups: NT (office BP<140/90 and 24 h BP<125/80 mmHg), ICH (office BP≥140/90 and 24h BP<125/80 mmHg), AHT (office BP<140/90 and 24h BP≥125/80 mmHg) and HT (office BP≥140/90 and 24h BP≥125/80 mmHg).
Results: Patient with ICH and HT were older than NT (58.6 ± 10.2 and 58.1 ± 10.0 vs 52.7 ± 8.2, respectively $p<0.01$). The prevalence of male gender was higher in HT and AHT than NT and ICT (69% and 73% vs 29% and 34% respectively, $p<0.01$). BMI was higher in HT than in NT and ICH (26.9 ± 4.3 vs 24.7 ± 3.7 and 25.9 ± 4.0, respectively, $p<0.01$). PWV was significantly higher in AHT and HT in comparison to NT (11.9 ± 2.4 and 12.3 ± 2.8 vs 10.0 ± 1.6, respectively $p<0.01$); this difference remained statistically significant after adjustment for age, BMI, height, glycemia, uric acid, HDL and triglycerides ($p<0.05$).
Conclusions: In a general population arterial stiffness is increased in patients with sustained hypertension and with ambulatory hypertension in respect to subject with clinic and 24 hours normal BP values. The use of BP monitoring may be useful for the identification of patients with more pronounced vascular target organ damage.

10.01
ARTERIAL STIFFNESS IS ASSOCIATED WITH ELASTIN DEFRAGMENTATION AND MEDIAL COLLAGEN CONTENT IN THE HUMAN AORTA

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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 metalloprotienases(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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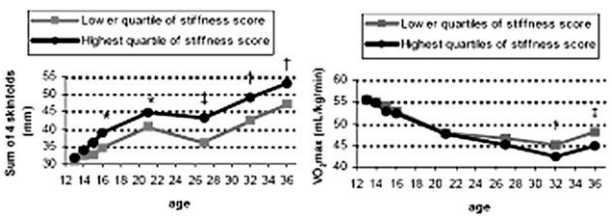
Introduction: Body fatness (BF) and low levels of cardiopulmonary fitness (CF) during adolescence have been associated with arterial stiffness (AS) later in life. How the development over time (i.e. from adolescence to adulthood) of BF and CF impact on AS in adulthood is not known.
Methods: Longitudinal data on BF (sum of 4 skinfolds — SSKF) and CF (VO2max) 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 VO2max 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 VO2max decreased between the ages of 13 and 36 ($p<0.001$); higher increases in SSKF during *adolescence* and decreased levels of VO2max *in recent but not early years* characterized individuals with higher arterial stiffness at the of age 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 (ΔT) 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 $\pm$ 8ms. 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 $\Delta T_{AVO}=3.3\pm1.0$ms. In contrast IP had a negative delay $\Delta T_{IP}=-3.6\pm3.1$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.