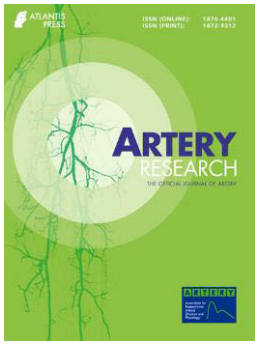

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06.05: AORTIC STIFFNESS AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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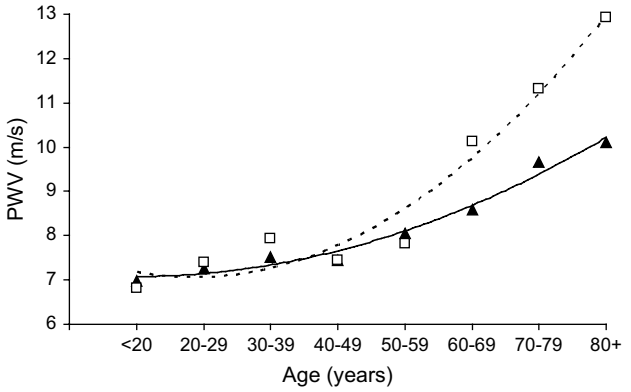
pressure. In multivariate analyses, hypertension, diabetes, smoking and the presence of cardiovascular disease were independently associated with aortic PWV (R^2=0.65, P<0.001). In conclusion, aortic PWV appears to be a sensitive marker of cardiovascular risk in individuals aged over 50 years.



Age-related changes in aortic PWV in healthy controls (▲) versus diabetics (□)

† Anglo-Cardiff Collaborative Trial.

06.02

AORTIC AND CAROTID STIFFNESS IN OLDER ADULTS. THE ROTTERDAM STUDY

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The purpose of this study is to describe aortic (aPWV) and carotid stiffness (DC) in older adults according to age, gender and blood pressure. Information on both measures was available for 2766 subjects. The mean value of both aPWV and DC was lower in women than in men. The difference (95% CI) in aPWV was -0.99 (-0.81 to -1.18) (m/s) and the difference in DC was -1.62 (-1.35 to -1.82) (10^{-3}/kPa) for women as compared for men. With aging, both aorta and carotid artery become stiffer but the increase attenuates at high age. Women under 80 years of age had a less stiff aorta and a stiffer common carotid artery as compared to men of the same age. The relations of both measures of arterial stiffness with SBP and PP were non-linear, flattening off at higher levels, whereas the relation with DBP was non-linear and resembled a J-shape. We found a quadratic relationship between DC and aPWV: DC = 27.4 - 1.9 * (aPWV) + 0.04 * $(aPWV)^2$ [p total model ≤ 0.001], (R^2= -0.41, P<0.001). Subjects with increased aortic stiffness had a 30-fold increased risk of also having increased carotid stiffness, OR 31.2 (95% CI 20.9-46.4) (Figure 1).

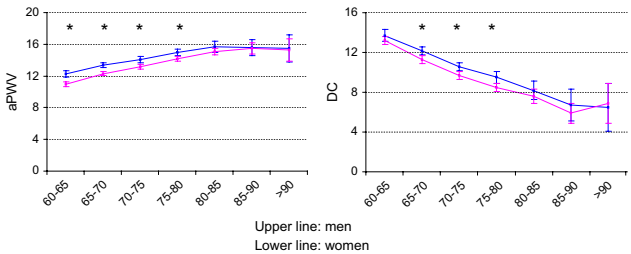

Figure 1. Mean (95% CI) aPWV and DC per 5-years age category in strata of gender. *p < 0.05 for difference between men and women.

06.03

NITRIC OXIDE AND ENDOTHELIUM-DERIVED HYPERPOLARIZING FACTOR REGULATE THE ADAPTATION OF HUMAN CONDUIT ARTERY MECHANICS TO CHANGES IN SHEAR STRESS

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The role of NO and endothelium-derived hyperpolarizing factor (EDHF), synthesized by cytochrome epoxygenases and acting through calcium-activated potassium (KCa) channels, in the flow-mediated regulation of human conduit artery mechanics has never been investigated.

In 11 healthy volunteers, whole blood viscosity, arterial pressure, radial artery diameter, wall thickness and flow (echotracking) were measured during hand skin heating in the presence of saline and the NO-synthase inhibitor, L-NMMA, infused alone and combined with the inhibitors of KCa channels, tetraethylammonium, and cytochrome epoxygenases, fluconazole. Wall shear stress, the flow-dependent stimulus, was calculated (Poiseuillean model). Arterial compliance, elastic wall modulus were calculated and fitted as functions of midwall stress (wall loading conditions) to suppress the confounding influence of changes in geometry.

Heating induced in all cases an increase in radial artery flow, diameter, shear stress and midwall stress and a decrease in wall thickness without change in arterial pressure. The increase in diameter with shear stress was reduced by L-NMMA and, in a more extent, by both combinations. Heating induced an upward shift of the compliance-midwall stress curve and a downward shift of the modulus-midwall stress curve under saline demonstrating an associated decrease in smooth muscle tone and wall stiffness with the shear stress increase. The shifts of these curves were decreased by L-NMMA and abolished by both combinations.

These results demonstrate that NO and EDHF regulate the adaptation of conduit artery mechanics to shear stress variations in humans suggesting the major role of the endothelium in maintaining arterial conductance and adjusted cardiac load.

06.04

NON-ALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED WITH IMPAIRED SECRETION OF FAT PRODUCED HORMONES AND INCREASED CARDIOVASCULAR RISK

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Purpose: Adipocytokines may provide a link between metabolic syndrome, inflammation and cardiovascular disorder in non-alcoholic fatty liver disease (NAFLD) patients. We investigated whether NAFLD is associated with fat produced hormones and if this relation can affect the impaired endothelial structure and function.

Methods: We studied 34 patients (age 55 ± 13 years, 20M) with biopsy evidence of NAFLD, and 34 control subjects adjusted for classical risk factors. The changes in the diameter of the brachial artery were measured in response to reactive hyperemia and nitroglycerin. Mean IMT of common carotid arteries and carotid-femoral PWV were determined as markers of atherosclerosis and aortic stiffness respectively. Adipocytokines were measured by ELISA kit.

Results: NAFLD subjects had significantly reduced flow-mediated vasodilation (1.1 ± 1.9% vs 4.3± 3%, p<0.05), and mean value of carotid IMT (0.98 ± 0.3 vs 0.77 ± 0.2 mm, p<0.05) and PWV (8.4 ± 1.6 vs 7.3 ± 1.7 m/s, p<0.01) were increased compared to controls. NAFLD subjects had increased levels of leptin (21.81± ng/ml vs 12.12 ± 10 ng/ml, p<0.01), and resistin (5.174 ± 1.6 ng/ml vs 3.5 ± 1.28 ng/ml, p<0.01) and reduced levels of adiponectin (7.96 ± 5.19 μg/ml vs 13.17 ± 12.4 μg/ml, p<0.05) compared to controls. After adjustment for confounding factors, resistin levels were independently associated with impaired endothelial function (p<0.05, t=7.53, coefficient st=0.883) and leptin levels were independently associated with the increased mean IMT (p<0.01, t=6.92, coefficient st=0.888), and PWV (p< 0.05, t=2.258, coefficient st=0.32) in NAFLD patients.

Conclusion: Although the initiating events that trigger the development of atherosclerosis in NAFLD patients cannot be ascertained, the role of adipocytokines may identify a potential basis.

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

A. Mahmud [1], M. McNulty [1], E. McGovern [2], V. Young [2], M. Tolan [2], J. Feely [1]. *[1]Department of Pharmacology & Therapeutics, Trinity College*