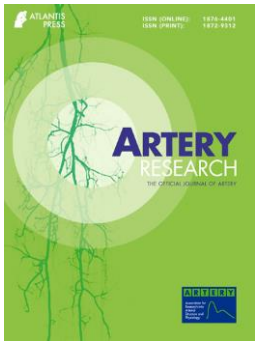

Artery Research

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

P2.30: SERUM FATTY ACID COMPOSITION AS MEDIATORS OF AORTIC PULSE WAVE VELOCITY'S IMPACT ON MORTALITY

S.G. Anderson, T.A.B. Sanders, J.K. Cruickshank

To cite this article: S.G. Anderson, T.A.B. Sanders, J.K. Cruickshank (2008) P2.30: SERUM FATTY ACID COMPOSITION AS MEDIATORS OF AORTIC PULSE WAVE VELOCITY'S IMPACT ON MORTALITY, Artery Research 2:3, 113–114, DOI: https://doi.org/10.1016/j.artres.2008.08.396

To link to this article: https://doi.org/10.1016/j.artres.2008.08.396

Published online: 21 December 2019

Experiments were performed on a Bruker 4T NMR system using a custom-developed setup adapted to small animal investigations.
Tissue perfusion quantification in *gastrocnemius* of mice was performed with a NMR sequence combining fast imaging with ASL[1]. It uses magnetically-labeled blood water as an endogenous tracer to quantify perfusion.
NMR method to determine BP is based on the sphygmomanometric principle: the caudal artery of the mouse was subjected to an external pressure from a tail air cuff. Arterial inflow signal was collected by single-slice dynamic NMR angiography and analyzed by reference to air pressure in the tail cuff.
These hemodynamics parameters were measured during reactive hyperemia after arterial occlusion in 10-week-old male db/db diabetic mice (n=17) and controls (n=14).
Using our dynamic NMR approach, we found both decreases in mean BP (68±9 vs 91±15 mmHg; $p<0.05$) and maximal perfusion (82±19 vs 105±38 $ml.min^{-1}.100g^{-1}$ $p<0.05$) in young db/db mice. However, we found that their maximal vascular conductance was not altered (1.22±0.3 vs 1.27±0.7 $ml.min^{-1}.100g^{-1}.mmHg^{-1}$), hence the relevance of our integrated approach.
1-Raynaud MRM 2001

doi:10.1016/j.artres.2008.08.392

P2.27
MECHANICAL MODELING OF IN VIVO HUMAN CAROTID ARTERIES FROM NON-INVASIVE CLINICAL DATA

I. Masson [1], P. Boutouyrie [2], S. Laurent [2], J.D. Humphrey [3], M. Zidi [1].
[1] *CNRS UMR 7054, University Paris 12, Créteil, France*
[2] *HEGP Department of Pharmacology & INSERM UMRS 872, Paris, France*
[3] *Department of Biomedical Engineering, Texas A&M University, College Station, USA*

Background: For mechanical modeling, in vivo data are relatively incomplete in comparison to in vitro results. However, identification of mechanical properties from human clinical data to compute wall stress fields can play an important role in understanding better pathological evolutions.
Aim: Demonstrate the feasibility of material identification and stress computation from clinical data.
Methods: In vivo human common carotid arteries (CCAs) were explored non-invasively. During several cardiac cycles, medial diameter, intimal-medial thickness and blood pressure were measured by a high-resolution echotracking (Art.Lab®) and applanation tonometry (SphygmoCor®), respectively. To study the wall mechanical behavior, the CCA was assumed to be a thick-walled, three-dimensional cylinder subjected to dynamical intraluminal pressure and perivascular constraints. We also assumed a nonlinear, hyperelastic, fiber-reinforced, incompressible material with smooth muscle activity and residual stresses. We included wall mechanical contributions by micro-constituents: an elastin-dominated matrix, collagen fibers, and vascular smooth muscle. We solved the in vivo boundary value problem semi-analytically to compute the intraluminal pressure during a cardiac cycle. Minimizing the difference between computed and measured inner pressures over the cardiac cycle provided the identification of optimal model parameters employing a nonlinear regression. Illustrative data were from two healthy subjects.
Results: The fit-to-data gave very good results. The predicted radial, circumferential, and axial stretches and stresses within the wall during the cardiac cycle were sensible.
Conclusion: We were able to identify experimentally unknown geometric and material parameters directly from in vivo human data. We can extend the proposed approach to pathological cases such as hypertension.

doi:10.1016/j.artres.2008.08.393

P2.28
DEVELOPMENT AND VALIDATION IN FLOW-PHANTOMS OF A SIMPLE ULTRASOUND-BASED METHOD FOR ESTIMATION OF WALL SHEAR STRESS IN-VIVO

P.R. Hoskins, J. Blake, W.J. Easson.
University of Edinburgh, Edinburgh, United Kingdom

Background: Wall shear stress (WSS) is an important measure of endothelial function however there are few clinical studies due to lack of a widely available measurement technique.
Aim: To develop and validate a simplified technique for estimation of WSS.
Methods: The Womersley equations were used; these describe pulsatile blood flow. With input of the vessel diameter (from B-mode ultrasound) and the centre-line blood velocity waveform (from Doppler ultrasound), the equations provided velocity profile as a function of time. Wall shear rate was estimated from the velocity gradient at the vessel wall. WSS was estimated from WSR*(viscosity), with an assumed viscosity of 4mPas. The technique was validated in a pulsatile flow phantom for vessels of physiological depth, diameter and flow-waveform.
Results: Estimated mean WSS was in error by 9±1% for brachial, 7±1% for carotid, 22±4% for femoral and 17±10% for fetal aorta.
Discussion: The errors are comparable with those obtained using dedicated WSS measuring systems. The method assumes that the vessel is rigid, straight and that flow is fully developed. There are several arteries where these flow conditions might hold, in health and in early disease where lumen diameter is preserved through outward remodelling. In-vivo validation is needed, possibly against a 'gold-standard' of MRI and computational fluid dynamics.
Conclusion: A simple method for estimation of WSS has been developed which is suitable for clinical studies.
Acknowledgement: The work has been published (Ultrasound Med Biol 2008, 34, 760-774) and previously presented (British Medical Ultrasound Society meeting, UK, December 2007)

doi:10.1016/j.artres.2008.08.394

P2.29
AN IN SILICO MODEL OF THE ROLE OF ELASTIN ON GEOMETRY AND BIOMECHANICAL PROPERTIES OF ARTERY IN WILLIAMS BEUREN SYNDROME

L. Hua, V. Louvet, E. Grenier, F. Gueyffier, B. Kassai.
EPICIM/HCL, Centre d'Investigation Clinique 201/INSERM, UCB Lyon I/ UMR5558, Lyon, France

Arteriopathy in Williams-Beuren syndrome (WBS) patients with elastin gene deletion represents the most important mortality and mobidity causes and seems directly correlated with elastin quantity. There is a need for a comprehensive model that accounts for the quantity of elastin and its role in the geometry and biomechanical properties of artery. Such model might improve our understanding of the pathophysiology and improve innovation in drug development for WBS. We present an *in silico* model for the adaptation of human carotid artery in response to elastin deficiency. The model is based on the hypothesis that elastin deficiency-induced growth and remodelling occurs via the excessive production of vascular smooth muscle cells (VSMCs), change in collagen engagement, and increased laminar units to ensure that the average stress of lamina unit in the homeostatic state is unchanged under normal condition. Using an elastin-stress driven model and a constituents-based model, which considers the contributions of elastin, collagen, and VSMCs in an explicit form, we illustrate capabilities of the model in predicting the arterial thickness and biomechanical properties with varying elastin quantity before and after elastin restoration. Alternatively, the model has the potential to estimate, indirectly, the fraction of remaining elastin using the values of arterial thickness and mechanical properties. Our model provides a new approach for mathematically assessing the arterial growth and remodelling in human vascular disease with insight into the importance of constituent distributions.

doi:10.1016/j.artres.2008.08.395

P2.30
SERUM FATTY ACID COMPOSITION AS MEDIATORS OF AORTIC PULSE WAVE VELOCITY'S IMPACT ON MORTALITY

S.G. Anderson [1], T.A.B. Sanders [2], J.K. Cruickshank [1].
[1] *The University of Manchester, Manchester, United Kingdom*
[2] *King's College London, London, United Kingdom*

Aims/Hypothesis: Aortic stiffness predicts all-cause and cardiovascular mortality in essential hypertension, diabetes and the community. Potential intermediaries in this relationship include serum fatty acids (FA). We examined whether serum FA influenced aortic stiffness, measured as pulse wave velocity (aPWV), and its impact on mortality.
Methods: After randomly sampling population registers, 174 nondiabetic participants had fasting blood samples and a 75g glucose challenge (GTT), measures of doppler-derived aortic PWV and then serum FA composition determined by HPLC. Mortality data over 18 years' follow-up were obtained via the national registry and principal component (PC) analysis used for statistical modelling.
Results: Docosahexaenoic acid (DHA; $\rho = -0.22$; $p = 0.02$) and Arachidonic acid (AA; $\rho = -0.25$; $p<0.001$) were inversely related to PWV. PC analyses, including 10 measured serum FAs, ethnicity, age and sex, identified five

components. SBP, PWV, smoking or central adiposity was directly related to Component 1 and inversely to component 4, whose pattern was higher AA, eicosapentaenoic (EPA) and DHA and lower oleic, palmitic (PA) and linoleic (LA) levels. Component 4 was associated with a decreased risk of mortality (HR 0.49 (0.39, 0.62) independent of PWV. Component 1, associated with increased mortality (HR = 1.13, 1.01-1.27), included people with higher levels of the saturated FAs (myristic and PA) but lower levels of poly-unsaturated FAs (LA, dihomo-gamma-linolenic (DGLA) & AA).
Conclusion: Patterns of serum fatty acids, partially reflecting diet, are associated with mortality, perhaps by modulating large vessel vascular function.

doi:10.1016/j.artres.2008.08.396

P2.31
AORTIC STIFFNESS IS AN INDEPENDENT PREDICTOR OF MILDLY ELEVATED DIASTOLIC BLOOD PRESSURE IN YOUNG PATIENTS WITH WELL CONTROLLED, EARLY ONSET, TYPE 1 DIABETES

C. Morizzo [1], C. Palombo [1], L. Gnesi [2], F. Massart [2], M. Kozakova [1], E. Malshi [1], F. Santini [1], G. Federico [2].
[1] *Department of Internal Medicine, University of Pisa, Pisa, Italy*
[2] *Department of Pediatrics, University of Pisa, Pisa, Italy*

Background: few data are available on cardiovascular (CV) involvement in young DM1 subjects with disease onset in pediatric age.
Aim: to assess preclinical CV changes in young patients with early onset DM1.
Methods: Thirty DM1 normotensive subjects (age =19.4±3.2 years, BMI=22.1±2.7 kg/m^2, disease duration=10.7±5.4 years, HbA1c=7.8±1.4%) without macro- and microvascular complications, and 14 controls (C) of comparable age and BMI. Common carotid artery (CCA) IMT, local stiffness (ß and Ep) and wave speed (WS) were obtained by echo-tracking (Aloka Alpha10). Aortic stiffness was assessed by carotid-femoral pulse wave velocity (PWV). Myocardial tissue velocities, LV geometry and function were evaluated by echocardiography.
Results: DM1 had, compared to C, higher ($p<0.05$) diastolic BP (DBP: 68±7 vs 62±4 mmHg), interventricular septum thickness (IVS) (0.76±0.11 vs 0.65±0.10 cm) and LV relative wall thickness (RWT: 0.31±0.4 vs 0.28±0.03). No differences between groups were found for pulse pressure, LV mass index, midwall shortening, transmitral E/A, myocardial velocities, CCA IMT and stiffness, WS and PWV. In the entire population, DBP increased with age, BMI, WS and PWV (r from 0.33 to 0.38, $p < 0.05$), and IVS increased with SBP and BMI (r=0.35 and 0.49, $p<0.05$). Independent predictors of DBP were WS and DM1 ($R2=0.23$, $p<0.005$), whereas predictors of IVS were sex, BMI and DM1 ($R2=0.53$, $p<0.0001$). RWT was independently related to DM1 ($R^2=0.12$, $p<0.05$).
Conclusions: well controlled young DM1 subjects show mildly elevated DBP and a trend towards LV concentric remodelling. Whether arterial stiffness is mechanism or result of increased DBP remains to be established.

doi:10.1016/j.artres.2008.08.397

P2.32
NON ALCOHOLIC FATTY LIVER IS RELATED TO IMPAIRED ARTERIAL FUNCTION AND SUBCLINICAL ATHEROSCLEROSIS

K. Baou [1], C. Vlachopoulos [1], E. Manesis [2], I. Dima [1], P. Pietri [1], Terentes-Printzios D [1], N. Ioakeimidis [1], A. Archimandritis [1], C. Stefanadis [1].
[1] *1st Cardiology Department;Hippokration general Hospital, Athens, Greece*
[2] *2nd Department of Internal Medicine;Hippokration general Hospital, Athens, Greece*

Background: Non-alcoholic fatty liver disease (NAFLD) is associated with metabolic syndrome, a marker of increased cardiovascular risk. Aortic stiffness, flow-mediated dilation (FMD) and intima-media thickness (IMT) are markers of cardiovascular disease and independent predictors of the corresponding risk. We investigated whether the presence and the histological activity of NAFLD are associated with arterial function and early vascular changes.
Methods: A total of 51 subjects participated in this study, 23 patients (mean age 55±14 yrs, 48% males) with biopsy evidence of NAFLD but without cirrhosis, and 28 control subjects adjusted for age, gender and other cardiovascular risk factors. Carotid-femoral pulse wave velocity (PWV) was measured as index of aortic stiffness. FMD of the brachial artery, an index of endothelial function, and mean IMT of common carotid arteries, a marker of subclinical atherosclerosis, were measured using B-mode ultrasound imaging.
Results: NAFLD subjects had significantly higher PWV (8.2±1.3 m/sec vs. 6.9±1.3 m/sec, P=0.001), and higher carotid IMT (0.78±0.17 mm vs. 0.67±0.13 mm, P=0.01) compared to controls. NAFLD subjects had significantly reduced FMD (1.92±2.11% vs. 4.8±2.43%, P<0.001) compared to controls. Multivariable regression analysis, showed that histological activity was associated independently with FMD ($\beta=-0.388$, P=0.037). Leptin was an independent determinant of PWV ($\beta=0.384$, P=0.003). FMD was independently associated with both leptin ($\beta=-0.294$, P=0.035) and adiponectin ($\beta=0.366$, P=0.008).
Conclusions: Patients have higher PWV and IMT and lower FMD compared to controls, indicating both functional and structural impairment in large arteries. The histological activity of NAFLD and levels of adipokines predict the degree of arterial impairment.

doi:10.1016/j.artres.2008.08.398

P2.33
ADIPONECTIN HORMONE, HYPERTENSION AND ENDOTHELIAL DYSFUNCTION IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS

K. Baou, C. Vlachopoulos, E. Manesis, I. Dima, N. Alexopoulos, K. Aznaouridis, A. Archimandritis, C. Stefanadis.
Hippokration General Hospital, Athens, Greece

Background: Non-alcoholic fatty liver disease (NAFLD) is a component of metabolic syndrome, which is a marker of increased cardiovascular risk. Flow-mediated dilation (FMD) is an independent prognostic factor of cardiovascular risk. Adiponectin is an adipose − tissue hormone and has vasculoprotective effects. We investigated whether NAFLD is associated with impaired arterial function and the role of adiponectin in this relation.
Methods: We studied 19 hypertensive patients (age 57±12 years, 9 males) with biopsy evidence of NAFLD, and 14 hypertensive control subjects adjusted for classical risk factors. The changes in the diameter of the brachial artery were measured in response to reactive hyperemia and also in response to nitroglycerin. Adiponectin levels were measured by ELISA kit.
Results: NAFLD subjects had significantly reduced flow-mediated vasodilation (2.07±2.26% vs 5.57± 2.8%, $p<0.01$), while nitroglycerin-mediated vasodilation did not differ among the two groups. Systolic, diastolic and pulse pressure were not different among the two groups. NAFLD subjects had significantly reduced levels of adiponectin (8.98±6.32 μg/ml vs 17.08±8.57 μg/ml, $p<0.01$) compared to controls. Interestingly enough, adiponectin levels were associated with flow-mediated dilation ($r=0.403$, $p<0.05$).
Conclusion: Although the initiating events that trigger the impaired arterial function in NAFLD patients cannot be ascertained, the role of adipocytokines may identify a potential basis.

doi:10.1016/j.artres.2008.08.399

P2.34
THE PRESENCE OF CIRRHOSIS AMELIORATES THE ARTERIAL STIFFNESS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS

K. Baou, C. Vlachopoulos, E. Manesis, P. Xaplanteris, A. Bratsas, A. Archimandritis, C. Stefanadis.
Hippokration general Hospital, Athens, Greece

Background: Non-alcoholic steatohepatitis (NASH) is linked with metabolic syndrome and is associated with increased cardiovascular risk. NASH is characterized by steatosis, inflammation, and fibrosis and may progress to cirrhosis. Aortic stiffness and wave reflections are independent markers and predictors of cardiovascular risk. We investigated the arterial stiffness in NASH patients with or without cirrhosis.
Methods: The study population consisted of 34 subjects (mean age: 62.2 ± 10.2 yrs, 9M/25F). In particular, 19 had bioptical evidence of NASH, cirrhosis was present in 7 of them and 12 NASH patients had no bioptical or biochemical evidence of cirrhosis. 14 subjects without liver disease were recruited in this study. The three groups did not differ in classical risk factors. Carotid-femoral pulse wave velocity (PWV) was measured as index of aortic stiffness. Augmentation index (AIx) of the central (aortic) pressure waveform was measured as an index of wave reflections.
Results: PWV was significantly increased in NASH patients without cirrhosis compared to controls (9.3 ± 1.6 vs 7.7 ± 1.3 m/s, $p<0.05$), but cirrhotic patients had significantly reduced PWV compared to NASH patients without cirrhosis (7.2 ±1.2 vs 9.3 ± 1.6 m/s, $p<0.05$), while AIx did not differ.
Conclusions: The transition of NASH to cirrhosis is followed by the paradoxical improvement of the stiffen arteries, which may be explained