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 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 obtaining fast imaging with ASL. It uses magnetically-labelled blood water as an endogenous tracer to quantify perfusion.

**NMR method to determine BP** is based on the spin-echo monometric 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 after arterial occlusion in 10-week-old male db/db diabetic mice (n<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.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.100g−1.p<0.05) in young db/db mice.

**Methods:**
In vivo human common carotid arteries (CCAs) were explored non-invasively. During several cardiac cycles, medial diameter, intimal-medial thickness, and vessel area were measured using a high-speed cine-3D sequence (Art.Lab®) and application tonometry (SphyngmoCor®), respectively. To study the wall mechanical behavior, the CCA was assumed to be a thick-walled, three-dimensional cylinder subject 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.

**References:**


**Methods:** After randomly sampling population registers, 174 non-diabetic 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; p = -0.22; p = 0.02) and Arachidonic acid (AA; p = -0.23; p<0.001) were inversely related to PWV. PC analyses, including 10 measured serum FAs, ethnicity, age and sex, identified five 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)

**References:**


**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 I P. Boutouyrie S, Laurent J.D. Humphrey M, Zidi M.

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 vessel area were measured using a high-speed cine-3D sequence (Art.Lab®) and application tonometry (SphyngmoCor®), respectively. To study the wall mechanical behavior, the CCA was assumed to be a thick-walled, three-dimensional cylinder subject 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.

**References:**


**Methods:** After randomly sampling population registers, 174 non-diabetic 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; p = -0.22; p = 0.02) and Arachidonic acid (AA; p = -0.23; p<0.001) were inversely related to PWV. PC analyses, including 10 measured serum FAs, ethnicity, age and sex, identified five 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)

**References:**


**doi:** 10.1016/j.artres.2008.08.392
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 polyunsaturated 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/m², 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 (β 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, transmural E/A, myocardial velocities, CCA IMT and stiffness, WS and PWV. In the entire population, DBP increased significantly with SBP and BMI (r = 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 (R2 = 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 2, E. Manesis 1, N. Alexopoulos 2, K. Aznaouridis 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 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 adipokynes may identify a potential basis.

doi:10.1016/j.artres.2008.08.399

P2.33
ADIPONECtin hormone, hypertension and Endothelial Dysfunction in non-alcoholic Fatty Liver disease patients
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 adipoytokines 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 biopsy evidence of NASH, cirrhosis was present in 7 of them and 12 NASH patients had no biotical 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 (7.2±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