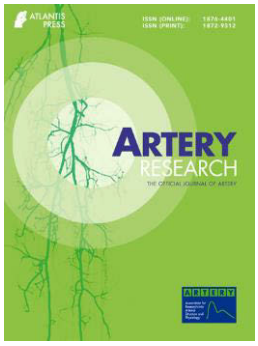

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# P2.34: THE PRESENCE OF CIRRHOSIS AMELIORATES THE ARTERIAL STIFFNESS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS

K. Baou, C. Vlachopoulos, E. Manesis, P. Xaplanteris, A. Bratsas, A. Archimandritis, C. Stefanadis

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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.

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**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**

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**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.

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

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**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.

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

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**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.

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

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**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

from the changes in neurohormonal regulatory systems, kidney function and cardiovascular system, such as the decreased overall systemic vascular resistance and the reduced arterial blood pressure.

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**P2.35**
**ROLE OF SYMPATHETIC ACTIVATION ON BRACHIAL ARTERY ENDOTHELIAL FUNCTION DURING HYPERINSULINEMIA IN HEALTHY SUBJECTS**

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**Aim:** Hyperinsulinemia worsens brachial artery endothelial function in healthy subjects, while in vitro and in vivo (in other vascular districts) evidence show that insulin facilitates nitric oxide release and endothelium-dependent dilatation. We evaluated role of sympathetic activation during hyperisulinemia on brachial artery endothelial function.
**Methods:** In 20 healthy male volunteers (age: 27±5 yrs), endothelium-dependent (flow-mediated dilation, FMD) and -independent (sublingual 25 μg glyceryl trinitrate, GTN) dilation were evaluated by ultrasound and computerized analysis of brachial artery diameter. Measures were taken at -60, -10, 120 and 240 minutes during euglycemic hyperinsulinemic clamp (insulin infusion at 0.25 mU.min-1.kg-1 and 20% glucose at variable rates), in absence (n=10) or presence (n=5) of infusion of clonidine (0.0052 μg.min-1.kg-1).
**Results:** Insulin infusion raised plasma concentrations from 63±4 to 210±22 pmol/l, without changes in blood pressure or heart rate. Insulin raised plasma noradrenaline (from 260±40 to 333±62 pg/ml, $p<0.05$). This increase was not observed in the presence of clonidine infusion. No change in FMD was observed during insulin infusion (from 7.2+-0.7 to 7.2±0.5%), while response to GTN was decreased (from 9.1±1.0 to 6.8±0.8%; $p<0.05$). Infusion of clonidine alone did not modify blood pressure, heart rate, FMD and response to GTN. During insulin clamp in the presence of clonidine infusion, FMD did not change (from 7.4±1.8 to 6.9 ±2.9%, p=n.s.), while response to GTN was increased (from 9.4±1.0 to 12.2±0.8, $p<0.05$).
**Conclusions:** In healthy subjects, a modest 4-hour hyperinsulinemia does not alter brachial artery endothelial function, but impairs endothelium-independent response. This effects disappears blocking sympathetic nervous system.

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**P2.36**
**INTERRELATIONSHIPS OF URIC ACID LEVELS, ARTERIAL STIFFNESS, PERIPHERAL AND CENTRAL PRESSURES IN HEALTHY, NORMOTENSIVE INDIVIDUALS**

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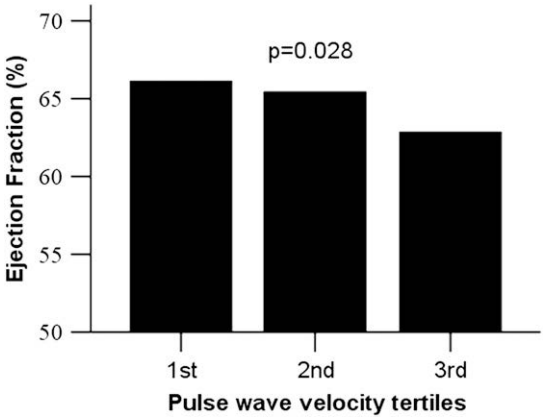
**Purpose:** Uric acid (UA) has been associated with cardiovascular disease, hypertension and endothelial dysfunction. The relationship between UA and arterial stiffness, peripheral/central pressures in normotensive individuals has not been addressed.
**Methods:** The study included 120 normotensive individuals (79 males, mean age 40.9 years). UA levels were determined from blood samples; peripheral pressures were measured by an electronic sphygmomanometer; aortic pressures were measured using a validated device, while carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness. The distribution of serum uric acid (UA) was split by the median (4.5 mg/dL) and subjects were divided in low (n=59) and high (n=61) UA group. Comparisons were performed using the independent samples t-test.
**Results:** UA levels were positively correlated with peripheral systolic (pSP, $r=0.373$, $p<0.001$) and diastolic (pDP, $r=0.362$, $p<0.001$) blood pressures, as well as central systolic (cSP, $r=0.296$, $p<0.001$), and diastolic (cDP, $r=0.359$, $p<0.001$) pressures. When compared to low UA subjects, high UA subjects demonstrated significantly higher levels of pSP (110.9±12.3 vs 118.5±8.7 mmHg, $p<0.001$), pDP (66.5±11 vs 74.05±7 mmHg, $p<0.001$), cSP (100.6±12.4 vs 107.2±8.9 mmHg, $p=0.001$) and cDP(67.6±10.9 vs 75.1±7.3 mmHg, $p<0.001$). As regards to PWV, it was positively correlated with UA levels ($r=0.242$, $p<0.01$), with significantly higher levels observed in the high UA group (6.03±1.06 vs 6.55±1.18 m/sec, $p=0.01$).
**Conclusion:** Increased levels of UA are associated with higher levels of peripheral/central pressures and herald arterial stiffening, as estimated by PWV, even in healthy, normotensive individuals. Our findings further elucidate the interplay of UA and arterial function.

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**P2.37**
**HUMAN-SPECIFIC GRAVITATIONAL DAMAGE OF VASCULAR SYSTEM**

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**Objectives:** To present a concept of human-specific gravitational damage of vascular system.
**Methods:** Application of Newton theory of gravitation to Guytońs cardio-vascular(CV) physiology supported by analysis of published research.
**Results:** In upright posture gravitation creates significant gradient of gravitational potential(GP) across human body. This gradient moves blood downward within CV system. CV system must actively respond to emptying of the upper body in upright posture. Guytońs CV physiology with passively filling heart determines two basic ways to prevent gravitation-induced downward blood shift: 1)low body vasoconstriction squeezing blood to the upper parts — well demonstrated in tilt studies by powerful increase of peripheral vascular resistance during head up tilt(precisely, feet-to-head gradient of GP requires exactly opposite head-to-feet gradient of additional vasoconstriction), 2)water retention to indirectly increase intravascular volume in the upper body — shown in space crews during postflight adaptation. The price is significant elevation of intravascular pressure and mechanical stress on vascular walls. This stress, however, is naturally prevented during walk when activated calf muscle pumps effectively return blood into upper body. From this analysis modern lifestyle with reduced walking and prolonged high upright sitting causes excessive gravitation-induced mechanical stress in vascular system. Mechanical wall stress has been widely shown to promote atherosclerosis in large arteries and hypertrophy/remodeling in small arteries while in severe cases also may cause wall rupture/dissection.
**Conclusion:** Gravitation may seriously damage human vascular system in modern sitting lifestyle.

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**P2.38**
**THE ANRIL LOCUS ON CHROMOSOME 9P21 AFFECTS STIFFNESS OF THE ABDOMINAL AORTA**

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Coronary artery disease (CAD) is the leading cause of death worldwide. Recently, several genome wide association studies have reported associations between a region on chromosome 9p21 and a broad range of arterial diseases, including CAD and intracranial aneurysms. However, no clear associations with intermediate phenotypes have been described. In order to investigate the possible influence of the CAD-associated SNPs on arterial wall integrity, we analyzed associations between SNPs and stiffness of the abdominal aorta.
400 subjects, 212 men and 188 women (70-88 years) were studied. The pulsatile diameter of the abdominal aorta was examined at the midpoint between the renal arteries and the bifurcation, using a wall track system. Blood pressure was taken from the brachial artery (Dinamap). Two CAD- and aneurysm-associated SNPs (rs10757274 and rs2891168) and one T2D-