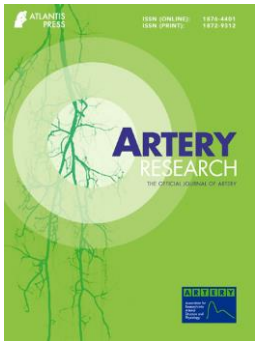

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P2.38: THE ANRIL LOCUS ON CHROMOSOME 9P21 AFFECTS STIFFNESS OF THE ABDOMINAL AORTA

H.M. Bjorck, T. Lanne, U. Alehagen, K. Persson, L. Rundkvist, A. Hamsten, U. Dahlstrom, P. Eriksson

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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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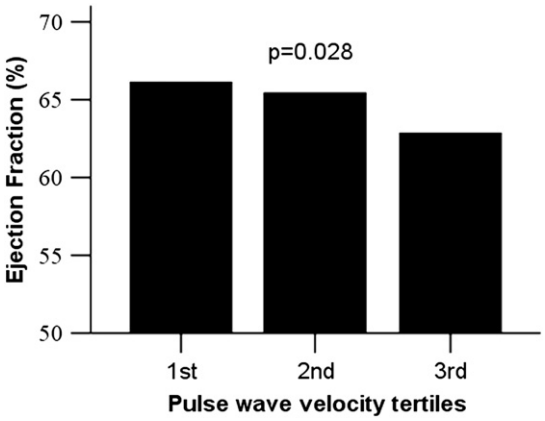
Purpose: Uric acid (UA) has been associated with cardiovascular disease, hypertension and endothelial dysfunction. The relationship between UA and arterial stiffness, peripheral/central pressures in normotensive individuals has not been addressed.
Methods: The study included 120 normotensive individuals (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 cardiovascular(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

H.M. Bjorck [1], T. Lanne [1], U. Alehagen [1], K. Persson [1], L. Rundkvist [1], A. Hamsten [2], U. Dahlstrom [1], P. Eriksson [2].
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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-

associated SNP (rs1081161) within the 9p21 region were genotyped. Aortic stiffness was decreased in male carriers of the rs10757274G and rs2891168G alleles. Accordingly, aortic compliance and distensibility were higher in men who carried the rs10757274G and rs2891168G alleles. Adjustment for age and mean arterial pressure had no effect on these associations. None of the SNPs were associated with either intima-media thickness or lumen diameter of the abdominal aorta. There were no associations between the T2D-associated rs10811661 SNP and any measure of aortic stiffness.
Impaired mechanical properties of the aortic wall may be a link between the association between chromosome 9p21 polymorphisms and vascular disease.

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P2.39
INCREASED CARDIOVASCULAR RISK IN PATIENTS WITH A HYPERTENSIVE RESPONSE TO EXERCISE MAY BE EXPLAINED BY MASKED HYPERTENSION

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Background: A hypertensive response to exercise (HRE; defined as normal clinic blood pressure [BP] and exercise BP >210/105mmHg in men or >190/105mmHg in women) independently predicts incident hypertension and cardiovascular mortality. The mechanisms remain unclear but may be related to masked hypertension. This study aimed to assess the prevalence of masked hypertension and cardiovascular risk factors, including aortic reservoir function, in patients with a HRE.
Methods: Comprehensive clinical and echocardiographic evaluation (including central BP, aortic reservoir pressure, aortic pulse wave velocity by tonometry) and 24 hour ambulatory BP monitoring (ABPM) were performed in 81 untreated patients with HRE (aged 54±9 years; 60% male; free from coronary artery disease). Masked hypertension was defined as ABPM systolic BP (SBP) ≥130 mmHg and clinic BP <140/90 mmHg.
Results: Masked hypertension was present in 50 patients (62%). These patients had higher left ventricular (LV) mass index (92.1±17.8 g/m^2 versus 77.2±17.9g/m^2; p=0.01) aortic reservoir pressure (104±9mmHg versus 97±10mmHg; p=0.001) and exercise SBP (226±15mmHg versus 210+15mmHg; p<0.001), despite no significant difference in aortic pulse wave velocity or central pulse pressure (p>0.05 for both). Aortic reservoir pressure was significantly correlated with peak exercise SBP (r=0.34; p=0.002). The strongest independent determinant of LV mass index was the pressure of masked hypertension (β=0.37; p=0.001) ,
Conclusions: Aortic reservoir pressure is significantly elevated, and masked hypertension highly prevalent in HRE patients with a normal resting office BP. This may help to explain increased risk in patients with a HRE and clinicians should suspect masked hypertension in this population.

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P2.40
CENTRAL AORTIC PRESSURE IS A BETTER DETERMINANT OF ANTI-HYPERTENSIVE RESPONSE THAN BRACHIAL PRESSURE IN YOUNG HYPERTENSIVE PATIENTS

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Aortic blood pressure (BP) has been shown as a stronger predictor of target organ damage than brachial BP. Whether pre-treatment aortic BP is a better determinant of early anti-hypertensive response than brachial BP is not known.
We analysed the pre and post treatment haemodynamic data on untreated hypertensive subjects (n=290) aged 51±0.6 years, who had received in random fashion ; ACE inhibitors, angiotensin receptor blockers, calcium antagonists & nebivolol (vasodilators) & non-vasodilating agents ; atenolol & thiazide diuretics. Data were analysed using JMP Version 7.1.
Baseline aortic systolic BP showed a better correlation with reduction in either brachial or aortic systolic BP compared with brachial systolic BP. In subjects < 50 years, baseline aortic systolic BP showed a stronger correlation with brachial systolic response(r=0.38, p<0.0001) than brachial systolic BP(r=0.28, p<0.001). Baseline brachial systolic BP showed a poor correlation with reduction in aortic systolic (r=0.19, p<0.05) compared with baseline aortic systolic BP(r=0.37, p<0.0001). In those >50 years, pre-treatment brachial(r=0.46, p<0.0001) and aortic (r=0.47, p<0.0001) systolic BP showed similar correlations. Baseline aortic systolic BP showed a better correlation with BP response to vasodilating anti-hypertensives (r=0.42, p<0.0001) than non-vasodilator agents(r=0.36, p<0.0001). In multiple regression analysis, gender, vasodilator agents and baseline aortic systolic BP emerged as independent determinants of brachial BP response with no significant contribution from brachial systolic BP.
Aortic BP is a better determinant of BP response than brachial BP, especially in young hypertensive patients and particularly to vasodilating antihypertensives and may guide choice of initial anti-hypertensive agent in the young patient.

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P2.41
PULSE WAVE VELOCITY CORRELATES WITH LEFT VENTRICULAR SYSTOLIC FUNCTION IN NEVER-TREATED ESSENTIAL HYPERTENSIVES

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Introduction: Hypertension is associated with increased arterial stiffness. Arterial stiffness, which is a predictor of cardiovascular risk, has been shown to correlate with diastolic dysfunction of left ventricle in hypertensive patients.
Hypothesis: We assessed the hypothesis that arterial stiffness is associated with left ventricular systolic function in never-treated hypertensive patients.
Methods: We enrolled 195 consecutive essential hypertensives (mean age 50±12 years) with preserved left ventricular ejection fraction (LVEF>45%). Arterial stiffness was determined with carotid-femoral pulse wave velocity (PWV). LVEF was measured echocardiographically and calculated using the Teichholz method.
Results: Subjects were divided into tertiles according to PWV. There was a correlation of PWV tertiles with age (44±13 vs 49±11 vs 57±9 years at the 1st, 2nd and 3rd tertile, respectively). Mean blood pressure was similar across the tertiles (p=NS). We observed a stepwise decrease of LVEF with increasing PWV. (Figure) Multivariable regression analysis showed that the inverse correlation of LVEF with PWV was independent of age, sex and mean blood pressure (p=0.028, adjusted R^2 of model=0.241).
Conclusion: Higher PWV is an independent predictor of a lower LVEF in never-treated essential hypertensives. This finding provides further insights into the role of arterial stiffness in left ventricular function.

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P2.42
POSTURAL CHANGES HAVE A DIFFERENTIAL RESPONSE ON BRACHIAL, COMPARED WITH CENTRAL, SYSTOLIC BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION

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Background: Clinic brachial blood pressure (BP) is typically recorded in the seated, supine and standing positions. However, it is unknown whether central BP may be differentially altered with postural changes, and this may have treatment implications. This study aimed to assess brachial and central BP during different postures in patients with hypertension compared with controls.
Methods: Study population comprised 41 patients with hypertension receiving medication (HTN; aged 60±7 years; 22 male), 26 untreated patients with masked hypertension (MaskHTN; 57±9 years; 19 male) and 36 normotensive controls (aged 54±9 years; 22 male). The average of two brachial and central BP's (by radial tonometry; SphygmoCor) were recorded in the seated, supine (after 3-5 minutes) and standing (after 2 minutes) positions.
Results: Supine brachial systolic BP (SBP) was significantly higher in patients with HTN (127±12 mmHg) and MaskHTN (130±10 mmHg) compared with controls (120±13 mmHg; p<0.05). As expected for the controls, seated brachial SBP was slightly, but non significantly (p>0.05), higher than both supine and standing positions. This non significant pattern was similar for central SBP in the controls and MaskHTN patients, but not patients with HTN, whose standing central SBP (109±12 mmHg) was significantly lower compared with the supine position (116±14 mmHg; p<0.05).
Conclusion: Posture has a differential effect on central, compared with brachial SBP in patients with treated hypertension. This highlights the importance of assessing central BP in these people, which may be particularly useful for managing patients with symptoms related to orthostatic hypotension.

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