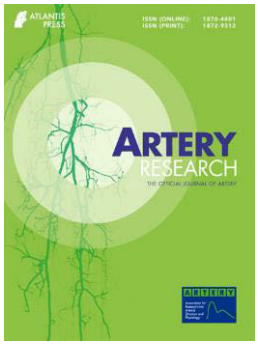

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P1.10: CIMT MEASUREMENT IS MORE RELIABLE THAN WEIGHT REDUCTION IN OVERWEIGHT YOUNG ADULTS TO ASSESS LIFESTYLE IMPACT

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P1.07
ROSUVASTATIN INCREASES EXTRACELLULAR ADENOSINE IN HUMANS IN VIVO: A NEW PERSPECTIVE ON CARDIOVASCULAR PROTECTION

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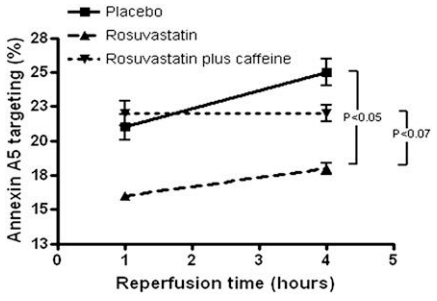
Background: Increased extracellular adenosine formation provides a cholesterol-independent explanation for the therapeutic benefit of statins. This theory was tested in humans in-vivo using dipyridamole-induced vasodilation as a read out for local adenosine formation. Its relevance was explored using a foream model of ischemia-reperfusion injury.
Methods: Twenty-one healthy volunteers were randomly allocated to receive either rosuvastatin (20 mg/day for eight days) or placebo in a double-blind parallel design. The vasodilator response to the nucleoside transport inhibitor dipyridamole was determined in the absence and presence of the adenosine antagonist caffeine. In two additional studies, healthy volunteers were randomly divided in four groups to receive either placebo (n=10), rosuvastatin (20 mg/day for 7 days; n=22), or rosuvastatin combined with intravenous caffeine (4 mg/kg, single dose; n=12). Subsequently, volunteers performed ischemic exercise of the non-dominant forearm. At reperfusion, Tc-99m-labeled annexin A5 was infused intravenously and scintigraphic images were acquired using a gamma camera, providing an early marker of injury.
Results: Rosuvastatin treatment significantly increased the vasodilator response to dipyridamole. This effect was completely abolished by caffeine. Rosuvastatin increased tolerance to ischemia-reperfusion injury, an effect which was attenuated by adenosine receptor blockade.
Conclusion: Rosuvastatin increases extracellular adenosine formation and protects against ischemia-reperfusion injury in humans in-vivo. Our observations prove the concept that statins and dipyridamole interact synergistically whereas caffeine consumption hinders the therapeutic action of statins.



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P1.08
EFFECTS OF ANTIOXIDANTS ON SERUM URIC ACID AS A MARKER OF VASCULAR FUNCTION

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Introduction: Serum uric acid is linked to vascular nitric oxide activity and therefore can blunt endothelium-dependent vasodilation. Antioxidants may increase nitric oxide activity and endothelial function and this might result in decreased uric acid levels.
Aim: The objective was to investigate if supplementation with antioxidants has a beneficial effect on uric acid.
Method: 74 borderline hypertensive Caucasian men participated (aged 45-65 years) in a randomized double-blind, cross-over intervention trial receiving either an antioxidant cocktail (vitamin C, E and folic acid) or placebo. Cardiovascular parameters were recorded with the Finometer. The Complior SP was used to measure the carotid-radialis PWV.
Results: Folic acid (as an indicator of compliance to antioxidant intake) increased significantly with 30% (P=0.005) with no changes in the placebo group. Uric acid was lower after the antioxidant intervention (changed from 0.53 mmol/L to 0.49 mmol/L (p=0.007), with no change in the placebo group. No significant differences were found between the pre and post intervention values for blood pressure, total peripheral resistance and PWV for both interventions . Significant correlations were found between uric acid and total cholesterol (placebo r=0.54: P< 0.001; antioxidant r=0.25: P=0.04).
Conclusion: With antioxidant intervention the lowered uric acid level point to a improvement in vascular function and oxidative stress. The weaker correlation between uric acid and cholesterol also points to improved vascular function since uric acid is strongly linked to cholesterol in vascular disease.

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P1.09
THE EFFECTS OF RIMONABANT-INDUCED WEIGHT LOSS ON ARTERIAL FUNCTION AND GLYCAEMIA IN OBESE ADULTS WITH TYPE 2 DIABETES

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Premature large artery stiffening is a major contributor to the development of cardiovascular disease in type 2 diabetes. Intentional weight loss through lifestyle intervention is associated with a reduction in arterial stiffness. Rimonabant is a cannabinoid-1 receptor blocker that reduces body weight and improves the cardiovascular risk profile in obese subjects. The purpose of this study was to examine the effects of rimonabant therapy on arterial function in obese subjects with type 2 diabetes.
Twenty-nine obese subjects (age range 30-72yrs) (13 male, 16 females) with type 2 diabetes (13 insulin-treated) were studied. Twenty subjects were studied before, during and after 6 months therapy with rimonabant in conjunction with dietary and lifestyle advice. Nine subjects received dietary and lifestyle advice only without rimonabant. Arterial function was assessed by measuring aortic and brachial pulse wave velocity (PWV) and augmentation index (Sphygmocor).
After 6 months, Rimonabant therapy led to significant weight loss (mean weight loss 5±4Kg, p<0.0001), improved glycaemia (HbA1c reduction 0.6±1.1%, p<0.05) and lipid profile (HDL cholesterol increase of 0.1±0.1mmol/L, p<0.01). Aortic systolic pressure was lowered by 5±9mmHg (p<0.05) but there were no changes to peripheral blood pressure, augmentation index or aortic PWV.
In conclusion, rimonabant therapy in association with dietary and lifestyle change leads to significant weight loss and improved glycaemic control in obese adults with type 2 diabetes. However, these clinical benefits do not appear to be accompanied by a reduction in arterial stiffness or wave reflection.

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P1.10
CIMT MEASUREMENT IS MORE RELIABLE THAN WEIGHT REDUCTION IN OVERWEIGHT YOUNG ADULTS TO ASSESS LIFESTYLE IMPACT

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The Insulin Resistance Syndrome is characterized by decreased tissue sensitivity to the action of insulin, obesity and a thick Carotid Intima Media Thickness (CIMT). Homeostasis Model Assessment (HOMA) remains an excellent to assess the level of insulin resistance. We studied the impact of a healthy lifestyle modification in young overweight BMI >27 and non-overweight adults BMI <22 m/kg2. The intervention consisted of a 16 weeks dietary consultation, exercise and a personalized vascular image.
Results:

overweight	BMI>27	(n=18)	normal weight	BMI <22 (n=10)
age	8-12 years		8-12 years	
HOMA glucose x Insulin/22.5	4.6	2.4	1.9	1.8
glucose mg/dl	92	88	78	77
insulin µU/ml	21	17	9.7	9.5
CIMT µ	539	530	522	520
Cholesterol mg/dl	160	162	148	143
HDL-C mg/dl	38	41	57	59
BP mmHg	130/76	126/72	110/68	108/70

Discussion: Both groups lost some weight and showed an improvement in different parameters. The relative change in CIMT was significantly more in the obese group A positive correlation between HOMA and CIMT was observed, (r= 0.717, p< 0.02). in the overweight cases increasing significantly (r=0.832, p<0.01) (delta change p<0.05).

What aspect contributed the most to these results(diet, exercise or possession of a personal vascular image) needs further larger early detection study.

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P1.11
DIURNAL AND GENDER VARIATION OF ARTERIAL STIFFNESS IN YOUNG HEALTHY VOLUNTEERS

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Objective: The augmentation index (AIx) is a measure of arterial stiffness, and is an autonomous determinant independent of other cardiovascular risk factors.
Methods: We examined whether the peripheral and central blood pressure (BP), pulse rate, AIx of healthy volunteers, measured at three different times of the day (8 AM, 12 PM, 5 PM), would show any difference. The measurements were carried out using SphygmoCor device.
Results: 52 healthy volunteers were included into the study. The average age and BMI of the 23 males were 24.4±2.5 years and 24.0±2.9 kg/m2, while it was 23.0±1.4 years and 20.5±3.6 kg/m2 at the 29 females, respectively. During the three different times of measurement, the actual peripheral and central systolic and diastolic BP and pulse rate did not show any significant difference either for males, or females. In contrast, the AIx of the males was significantly reduced over the course of the day: 8 AM: 13.1±10.2%; 12 PM: 5.3±9.8%; 5PM: 3.4±8.2% ($p<0,01$). We observed a similar trend in the case of the females as well: 8 AM: 17.0±9.1%; 12 PM: 13.3±10.2%; 5 PM: 11.3±7.5% ($p<0,01$). The females AIx were higher than that of males ($p<0,01$).
Conclusion: We conclude that augmentation index shows a considerable diurnal variation and gender difference. There is a gradual decrease from morning values over the course of the day along. Our data suggest to take period of the day at which the measurement was taken and gender into account, while determining physiological and pathological values or interpreting test results.

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P1.12
COMPARISON OF ARTERIAL RELAXATION TIME IN NORMOTENSIVE AND HYPERTENSIVE SUBJECTS

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Arterial stiffening is emerging as an important determinant of increased systolic blood pressure (SBP) and pulse pressure in the aging population. The relation of the brachial artery was studied in both normotensive and hypertensive volunteers. The test subjects include six healthy, normotensive (SBP/DBP $<$ 120/80 mm Hg) subjects (control group, four in the age range 19 to 23 years, and two in the older subjects, 57 and 60 years) and four subjects (48 to 58 years) with elevated SBP (ranging from 130-168 mm Hg) and who are currently on hypertensive medications (hypertensive group). Temporal measurements of the pressure and volume waveforms were recorded in both hands with one arm at heart level and the other initially at heart level and then raised a distance of 35 cm above heart level. Upon raising the arm, a delay is observed in the pulse measurement of the raised arm relative to the hand at heart level. The delay has previously been shown to decay exponentially with time. For the normotensive subjects, the average values of the pressure and volume relaxation times τ_P and τ_V were 75 s and 41 s for the younger-age group and 86 s and 68 s for the older-age group. The delay times for subjects in the hypertensive group were assumed to approach the baseline asymptotically. The validity of this assumption has been demonstrated in the control group. The average value of τ_P in the hypertensive group was found to be 581 s, significantly larger than the control group.

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P1.13
ENHANCED VASCULAR REACTIVITY TO COLD PRESSOR TEST IN AFRICAN NORMOTENSIVE SUBJECTS

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Background: Cold exposure increases arterial wave reflection to the aorta mainly through adrenergic vasoconstriction. Normotensive blacks exhibit heightened sympathetic response to cold as compared to Whites controls. We therefore decided to test the hypothesis that cold exposure would elicit a greater increase in arterial wave reflection in normotensive Africans when compared to normotensive Caucasian subjects. In addition we sought to investigate whether this would be accompanied by a higher increase in aortic pulse wave velocity (PWV) and by a more pronounced vasoconstriction of the skin microcirculation.
Methods: 17 young normotensive Africans and 17 age and weight matched Caucasians were recruited for the study. All underwent assessment of PWV and Augmentation Index corrected for heart rate (AIx) at rest, during and after hand immersion in ice water (cold pressor test, [CPT]). Concomitantly, skin microvascular blood flow response to cold was continuously monitored by laser Doppler flowmetry method.
Results: At rest, Africans exhibited higher values of PWV than Caucasians (7.3±0.3 vs 6.4±0.2 m/sec respectively, $p=0.04$). During CPT the magnitudes of increases in SBP and PWV were greater in Africans than Caucasians (26±3 mmHg vs 15±3 mmHg and 0.8±0.2 m/sec vs 0.4±0.2 m/sec respectively, $p<0.05$ for all). Additionally, CPT induced a more pronounced skin microvascular vasoconstriction in Africans as compared to Caucasians (-45±7 % vs -25±7 %, $p=0.01$). Finally, Africans exhibited higher AIx values during CPT (12.6±2.4 vs 5.5±2.4 %, $p=0.04$) when compared to Caucasian subjects.
Conclusions: Normotensive Africans exhibit intensified wave reflection to the aorta as response to CPT when compared to Caucasians. This is accompanied by a greater increase in PWV and a more pronounced vasoconstriction of the microcirculation.

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P1.14
CORRELATION BETWEEN AORTIC PULSE WAVE VELOCITY AND ASYMPTOMATIC CAROTID ATHEROSCLEROSIS

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Background: It seems that traditional risk factors are not sufficient predictors of the atherosclerosis and cardiovascular disease (CVD). Although the carotid ultrasonography is a gold standard of the detection of asymptomatic atherosclerosis, the correlation between aortic pulse wave velocity (PWVao) and the presence of preclinical carotid plaques was poorly investigated. The aim of this study was to examine this correlation and determine the most sensitive cut-off value of the aortic PWV for carotid atherosclerosis by using ROC (Receiving Operating Characteristic) analysis.
Methods: 557 asymptomatic subjects were included without known CVD. Arterial stiffness parameters (PWVao) were measured with non-invasive oscillometric device (Arteriograph) and carotid scan was performed with carotid ultrasonography in both side by a ''blinded'' investigator who was unaware of the stiffness-parameters in all subjects as well.
Results: We have found 283 carotid negative subjects and 274 carotid positive subjects. The carotid ultrasonography was positive when the IMT $>$ 1.3mm or calcificated plaque $\geq$ 1mm was detected. The mean values were: age 57, BP 134/82 mmHg, HR 72/min, Aix −8,7%, PWVao 9,9 m/s. In data analysis the SPSS software and the ROC curve were used. The most sensitive PWVao was 9.62m/s. The sensitivity of increased PWVao was 77.7%, the specificity 65.4%, the positive predictive value (PPV) 68,5%, the negative predictive value (NPV) 75,2%. The significance between these values was very good.
Conclusion: The increased ($>$9,62 m/s) PWVao shows a strong association with the asymptomatic carotid plaques and seems to be a suitable method to detect preclinical atherosclerosis.

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P1.15
ASSOCIATION BETWEEN CAROTID AND FEMORAL ATHEROSCLEROTIC BURDEN AND VASCULOGENIC ERECTILE DYSFUNCTION

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Background: Vasculogenic erectile dysfunction (ED) may be considered a clinical manifestation of a generalized arterial disease. We attempted to evaluate the association between penile vascular dysfunction and extent of