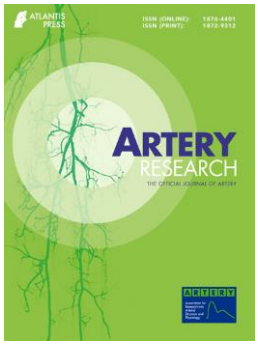

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P10.01: EFFECTS OF VEGFR-1 (FLT-1) INHIBITION DURING PREGNANCY ON THE UTERINE CIRCULATION OF THE MOUSE

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p< 0.05), augmentation index (AIx, 22.0±7.0 vs 13.1±5.2%, p<0.01) and pressure-dependent elastic modulus. After barnidipine, in hypertensive patients, office BP fell from 159±14/95±11 to 138±16/81±9 mmHg (p<0.001), due to a significant reduction in forward and backward pressures, and AIx decreased to 17.0±8.0% (p<0.01), without changes in arterial stiffness indices. A significant direct relationship between AIx and pulse pressure observed in hypertensive patients at baseline disappeared after therapy (r=0.45 before and 0.25 after therapy).
Conclusions. These data suggest that a reduced wave reflection during therapy with the calcium antagonist barnidipine is depending on its effects on muscular artery tone rather than on large artery stiffness.

P9.08
THE L-ARGININE/ASYMMETRIC DIMETHYLARGININE (ADMA) RATIO IS IMPROVED DURING ANTI-TUMOR NECROSIS FACTOR−α THERAPY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES: ASSOCIATION WITH AORTIC STIFFNESS

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Background: Anti-Tumor Necrosis Factor (TNF)-α therapy seems to improve cardiovascular risk in patients with inflammatory arthropathies such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide synthase (NOS). ADMA competes with L-arginine as a substrate for NOS, and the L-arginine/ADMA ratio is suggested to be important for modulation of NOS activity. **Objective:** To examine the effect of anti-TNF-α therapy on ADMA and L-arginine/ADMA, and the associations between ADMA, L-arginine/ADMA and aortic stiffness in patients with inflammatory arthropathies.
Methods: Fifty-five patients with RA, AS or PsA and a clinical indication for anti-TNF-α therapy were included. 36 patients started with a TNF-α antagonist and were compared with a non-treated group of 19 patients. Plasma ADMA, L-arginine and aortic stiffness (aortic pulse wave velocity, aPWV) were assessed at baseline and after 3 and 12 months.
Results: Baseline aPWV was associated with ADMA (P=0.02) and L-arginine/ADMA (P=0.02) in multiple linear regression analyses. One-year anti-TNF-α therapy improved the L-arginine/ADMA ratio (median [interquartile range]) in the treatment group compared to the control group (5 [-4, 16] vs. -10 [-20, 2], respectively; P=0.04), but did not affect ADMA (0.01 [-0.03, 0.04] μmol/L vs. 0.00 [-0.05, 0.06] μmol/L, respectively; P=0.78). The L-arginine/ADMA ratio was longitudinally associated with aPWV in a multivariable mixed analysis (P=0.03).
Conclusion: Plasma ADMA levels were associated with aortic stiffness in patients with inflammatory arthropathies. Anti-TNF-α therapy improved the L-arginine/ADMA ratio. The L-arginine/ADMA ratio was associated with aortic stiffness over time.

P9.10
COMPARATIVE EVALUATION OF VASCULAR AND METABOLIC EFFECTS OF PERINDOPRIL COMBINATION WITH INDAPAMIDE-RETARD OR HYDROCHLOROTHIAZIDE IN HYPERTENSIVE PATIENTS

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Our aim was to compare the changes of arterial stiffness (AS), endothelial function (EF) and metabolic parameters in patients with essential hypertension on treatment with combination of perindopril with either indapamide-retard or hydrochlorothiazide. The study involved 40 patients (mean age 52,4±7,1 years) who were randomly assigned to perindopril 5-10 mg o.d. in combination with indapamide-retard (P+IR) 1.5 mg o.d. (n=20) or with hydrochlorothiazide (P+HT) 25 mg o.d. (n=20). EF determined as the change of resistance index after inhalation of 400 mcg of salbutamol, AS measured as mean stiffness index after 500 mcg of sublingual trinitroglycerin (SI_{tng}), blood lipids and glucose were evaluated at baseline and 6 months thereafter. Vascular responses were calculated from digital pulse waves registered using photoplethysmography. Dynamics of BP after 6 months did not differ significantly between groups (-19.3% versus -19,2% and -16.2% versus -14.1% for systolic and diastolic BP on P+IR and P+HT, respectively, p<0.001 for all). Changes of vascular and metabolic parameters are depicted in the table.

	P+IR	P+HT
EF	+2.0% (p=0.64)	-24.3% (p<0.01)
SI_{tng}	-13.4% (p<0.001)	-9.8% (p<0.01)
Total cholesterol	-2.7% (p=0.54)	-6.4% (p=0.19)
LDL cholesterol	-4.9% (p=0.36)	-7.3% (p=0.22)
HDL cholesterol	-1.0% (p=0.83)	-4.6% (p=0.36)
Triglycerides	+3.8% (p=0.58)	+12.1% (p<0.05)
Glucose	+1.8% (p=0.63)	+9.4% (p<0.05)

Arterial stiffness significantly decreases on both regiments of treatment with the trend in favor of P+IR. Treatment with combination of P+HT resulted in significant decrease of EF accompanied by negative changes of triglycerides and glucose levels, whereas combination of P+IR did not affect endothelial function and was metabolically neutral.
Thus, despite the similar BP reduction the combinations of ACE-inhibitor − perindopril with two different diuretics significantly differ in vascular and metabolic effects. Worsening of endothelial function on P+HT combination may be attributed to negative metabolic effects of hydrochlorothiazide.

P9.11
STABILIZATION OR REGRESSION OF ATHEROSCLEROSIS BY LIFESTYLE MODIFICATION USING MOTIVATIONAL INTERVIEWING AND CAROTID ULTRASOUND

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Purpose: The preventive use of noninvasive measurement of carotid intima media thickness and plaque visualization (CIMT+P) is in the Netherlands a relatively new method to detect subclinical atherosclerosis of employees. The aim of the use of CIMT+P is to archive endurable lifestyle modification in employees without cardiovascular disease.
Methods: In one and the same Dutch company (a Steel Mill) we did CIMT+P measurements in 2008, 2009 and 2011 to follow the progression of atherosclerosis of the employees. With motivational interviewing and health advice by a dedicated occupational health physician we have been stimulating the employees to modify their lifestyle (quit smoking, eat a healthy life style, increase exercise, relaxation techniques in addition to treat hypertension). With a longitudinal analysis we investigate the effects of our intervention using both CIMT and plaque formation images as end-points and as additional substitute modifiers
Results: The mean thickness of the common carotid arteries right and left in 169 cases average age 49 years range 39-64 y. were combined plaque formation was measured in the bulb when these were present. A distinction was made between soft plaques and calcified plaques.
The results were the following: 2008 2009 2011
Mean value of CIMT (mm) was 0.7104 0.7023 0.7001
Number of cases with soft plaques 26 13 11
Number of cases with all plaques 46 43 36
Conclusions: CIMT+P can be used as a preventive method for lifestyle modification in healthy Dutch employees. In a longitudinal follow up of 3 years a stabilization or even regression of subclinical atherosclerosis can be archived as an effect of lifestyle modification. It is noteworthy that cases that were smoking and quit smoking were the ones were the soft plaque disappeared or calcified. Hypertension treatment was another significant risk factor that correlated well with plaque formation whereas LDL-cholesterol control and a HDL-c increase was significant correlated to the change on the average CIMT. Motivational interviewing may have played an important role.

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P10.01
EFFECTS OF VEGFR-1 (FLT-1) INHIBITION DURING PREGNANCY ON THE UTERINE CIRCULATION OF THE MOUSE

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Recent attention has focused on the role of soluble VEGFR-1 (sFlt-1) in the genesis of preeclampsia; less is known about the role of the non-soluble form

of this receptor in the maternal uteroplacental circulation during pregnancy. To investigate this question, mice were injected with an anti-VEGFR-1 antibody (35 mg/kg i.p.) every other day beginning on day 8 (n= 9) or 12 (n=11) of gestation; vehicle-only injected mice were used as controls (n=12). All animals were killed late in pregnancy (day 19), prior to onset of parturition for determination of average pup number, resorption rate, and fetal and placental weights. Gestational vascular remodeling was evaluated by measuring the unstressed diameter and length of the main uterine artery and vein, as well as segmental artery diameter and length. Day 8 Ab injection resulted in a reduction in the average number of viable pups from 10 $\pm$ 1.2 to 3 $\pm$ 1.0 ($p<0.01$) and a high rate of fetal resorption (75 $\pm$ 7% vs. <5% in controls; $p<0.05$). Reproductive performance was also compromised in the day 12 group, although to a lesser extent. Placental and pup weights were similar throughout. Main and segmental uterine artery diameters were unchanged in either Ab group, although the diameter of the main uterine vein was reduced by 38 and 33% in both 8- and 12-day Ab-injected mice, respectively ($p<0.05$), Main uterine and segmental artery lengths were also significantly reduced. These results indicate that VEGFR-1 inhibition significantly compromises both reproductive performance and uterine vascular remodeling during murine pregnancy.

P10.02
INSTABILITY PHENOMENA IN THE MECHANICAL BEHAVIOR OF THE ANEURYSM ARTERY

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This study proposes a mathematical model to investigate stability of arteries. The artery is considered as a prestressed thick-walled tube subjected to dynamical pressure and made of a hyperelastic and composite material [1]. To model the mechanical contributions of the different arterial components, the here considered constitutive law of the wall takes into account the isotropic part due to the elastin-dominated matrix and the anisotropic due to the collagen fibers [2]. In this context, the purpose of this work focuses on the initial formation of aneurysms in human arteries which may be modelled as instability phenomena. For that, a perturbation technique is used on the equations of motion to highlight possible instabilities of the artery. This instability interpretation provides a theoretical approach under which different biological mechanisms leading to the risk of aneurysm formation can be assessed.
The proposed approach shows the influence of disturbances on the time variation of the radial deformation at the inner surface of the arterial wall. This means that the stress distributions are very sensitive to disturbances and may explain the aneurysm formation and its growth.
[1] E. Diouf, M. Zidi, *Finite azimuthal shear motions of a transversely isotropic compressible elastic and prestressed tube*, International Journal of Engineering Science 43, 262-274, 2005.
[2] I. Masson, C. Fassot, M. Zidi, *Finite dynamic deformations of a hyperelastic, anisotropic, incompressible and prestressed tube. Applications to in vivo arteries*, European Journal of Mechanics - A/Solids 29, 523-529, 2010.

P10.03
EVALUATION OF ARTERIAL STIFFNESS IN ATHEROSCLEROTIC RABBITS IN VIVO VIA ECHOTRACKING

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Objectives: We have shown that large artery stiffening, a major risk factor in cardiovascular diseases, can be evaluated in hypertensive rats by echotracking, analysing arterial compliance and also the arterial pulsatile diameter distension. We aimed to analyze similarly arterial stiffness in a model of atherosclerosis.
Methods: Male 9 week-old rabbits were fed 0.3 % cholesterol diet (ATH) or standard diet (CON) during 28 weeks. Then, under anaesthesia, blood pressure was recorded by catheterization and diameter via an ArtLab device, in a motion mode to detect pulsatile displacement of aortic walls (distension).
Results: Compliance, distension and distension/pressure loop were greatly decreased in ATH aorta versus CON, without mean diameter or blood pressure alteration. Basal femoral artery parameters were lower than aortic parameters. In ATH femoral artery, compliance, distension and the distension/pressure loop were reduced when recorded at a plaque level but increased at the upstream adjacent site; mean diameter was increased at both sites versus CON. Aortic endothelial function, assessed by ACh relaxation ex vivo was abolished in aorta and reduced in femoral artery; the lesions area in aorta (55 %) was 4x that observed in femoral artery.
Conclusions: This study analysed for the first time the in vivo dynamic arterial compliance in atherosclerotic rabbit. The data indicate a reduced arterial compliance and pulsatile distension and also show that the upstream adjacent site of a plaque is submitted to a higher stress and increased distension, in agreement with human data, which may participate to the plaque progression.

P10.04
ELASTIN AND COLLAGEN DEGRADATION REDUCES THE MECHANICAL STABILITY OF ARTERIES

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Arteries with elastin deficiency demonstrate tortuosity in human and animals, but the underlying mechanism has not been clearly elucidated. Our previous studies suggested that mechanical instability is a mechanism that leads to vessel tortuosity [1]. The objective of this study was to determine the role of extracellular matrix proteins in maintaining the mechanical stability of arteries. To this end, two groups of porcine carotid arteries were treated with elastase (8U/ml) and collagenase (2000 U/ml) respectively and tested before and after the treatments. The arteries were tested for pressurized inflation and the data were fitted with a Fung strain energy function to determine their stress-strain relationship. The critical pressures, at which the arteries became unstable and started to bend, were determined by a buckling test. The specimens were then processed for elastin staining and collagen staining and microscopy examinations. Our results demonstrated that elastase and collagenase treatment led to significant decreases in wall stiffness and critical buckling pressure of arteries. For example, the pre- and post- elastase treatment critical pressures of arteries are 19.9$\pm$5.3 kPa and 9.1$\pm$3.6 kPa, respectively, at *in vivo* length (n=6. $p<0.05$, see Figure 1). These results suggested that elastin and collagen degradation reduced the stability of arteries making them more susceptible to buckling and that mechanical buckling could initiate vessel tortuosity.
Acknowledgment: Supported by the NSF CAREER award 644646 and NHLBI grant HL095258 and NO1-HV-00244.
Reference: 1. Han HC: Blood vessel buckling within soft surrounding tissue generates tortuosity. J Biomech 2009;42:2797-2801.

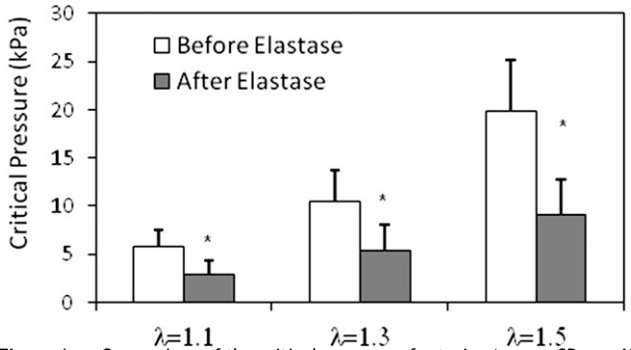

Figure 1 Comparison of the critical pressure of arteries (mean$\pm$SD, n=6) measured before and after elastase treatment. * $p < 0.05$.

P10.05
DOES THE AORTIC VALVES CORRESPOND TO A STABLE ANATOMICAL LANDMARK?

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Purpose: In order to determine if the height of a subject could be a reliable surrogate variable to determine the pulse wave travelling distance within the aorta, we investigated the anatomical distance between the aortic valve nidus and the hyoid bone.
Methods: Using 28 patient's chest CT-scans. From MPR reconstructed oblique plans we measured 1) the length of the aortic arch from the aortic valve (AV) to the intercept of an horizontal line passing through the aortic valves