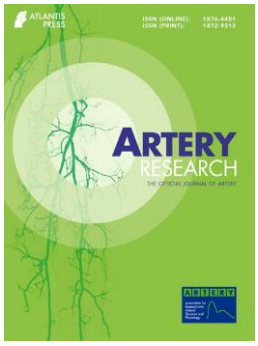

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P3.09: TREATMENT WITH TOCILIZUMAB IMPROVES ARTERIAL FUNCTION IN RHEUMATOID ARTHRITIS: A 6-MONTHS PILOT STUDY

A.D. Protogerou, E. Zampeli, K. Fragiadaki, K. Stamatelopoulos, S. Panopoulos, C.M. Papamichael, P.P. Sfikakis

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P3.06
RELATION BETWEEN HAPTOGLOBIN PHENOTYPE AND ARTERIAL STIFFNESS IN NEWLY DIAGNOSED UNTREATED HYPERTENSIVE PATIENTS

C. Strandhave [1], M. Svensson [2], K. Holdensen [1], C. M. Skov [1], H. Krarup [3], J. H. Christensen [1]
[1]*Dept. of Nephrology, Aalborg Hospital, Aarhus University Hospital, Aalborg, Denmark*
[2]*Dept. of Nephrology, Skejby Hospital, Aarhus University Hospital, Aarhus, Denmark*
[3]*Dept. of Clinical Biochemistry, Aalborg Hospital, Aarhus University Hospital, Aalborg, Denmark*

Arterial stiffness is a valuable predictor of cardiovascular risk in essential hypertension. Arterial stiffness is affected by several factors including genetic polymorphisms. Moreover, increased arterial stiffness has been associated with oxidative stress. Haptoglobin (Hp) is an innate antioxidant which due to molecular heterogeneity forms three phenotypes: 1-1, 2-1, and 2-2. The antioxidant ability is phenotype dependent. In diabetes mellitus Hp 2-2 is a predictor of vascular complications but whether Hp 2-2 predicts vascular complications in essential arterial hypertension has not previously been examined.
The aim of the study was to investigate if Hp 2-2 was positively associated with aortic pulse wave velocity (aPWV) and central systolic blood pressure (sysBP).
We examined 94 newly diagnosed untreated hypertensive patients. aPWV and central sysBP were measured using the SphygmoCor device. Hp phenotype was determined using high-performance liquid chromatography. The cohort consisted of 42 men and 52 women with an average age of 48 ± 11 years. The median aPWV was 7.6 (6.0; 9.7) m/s in Hp 1-1, 8.0 (5.3; 11.0) m/s in Hp 2-1, and 8.3 (5.5; 10.6) m/s in Hp 2-2. The difference was non-significant ($p=0.5$, ANOVA). The median central sysBP was 147 (123; 163) mmHg in Hp 1-1, 151 (123; 187) mmHg in Hp 2-1, and 155 (124; 195) mmHg in Hp 2-2. Also, these differences were non-significant ($p=0.4$, ANOVA).
This study showed a potential yet non-significant difference in aPWV and in central sysBP between Hp phenotypes with the highest levels in Hp 2-2 hypertensive patients.

P3.07
THE INFLUENCE OF ANTIHYPERTENSIVE TREATMENT ON ARTERIAL STIFFNESS AND ARTERIAL WALL SHEAR STRESS

M. W. Rajzer, W. Wojciechowska, M. Klocek, K. Kawecka-Jaszcz
[1]*st Dept. of Cardiology and Hypertension, Jagiellonian University, Krakow, Poland*

The aim of the study was to compare the effects of 5 drugs representing different antihypertensive classes on arterial wall shear stress (WSS) and arterial stiffness in patients with essential arterial hypertension (HT).
Material and methods: 95 pts. with HT (stage 1 and 2) were divided into 5 groups, ($N=19$) and treated for 6 months by: quinapril 20-40 mg/d (group-1), amlodipine 5-10mg/d (group-2), hydrochlorothiazide 12,5-25mg/d (group-3), losartan 50-100 mg/d (group 4), bisoprolol 5-10 mg/d (group-5). Before and then after 1,3 and 6 months of treatment WSS in common carotid artery (CCA) was calculated using blood viscosity measured by Brookfield DV-III pro and maximal blood flow velocity measured ultrasonographically. At the same visits carotid femoral pulse wave velocity (PWV) was measured using 3 devices Complior®, Sphygmocor® and Arteriograph™ , office BP was measured using Omron M5-I device.
Results: At the baseline no differences between groups were observed in BP, PWV, CCA- WSS. ANOVA for repeated measurements revealed for all groups during treatment period significant decrease in SBP ($p<0.001$), DBP ($p<0.001$) and PWV measured by three different devices ($p<0.001$). CCA-WSS increased significantly ($p<0.001$). No between treatment groups differences were observed in above mentioned effects. In multiple regression analysis decrease of PWV was in significant relation to its baseline value ($B=0.567$, $p=0.00032$ and increase of CCA- WSS ($B=0.232$, $p=0.0074$).
Conclusion: Antihypertensive treatment reduces arterial stiffness proportionally to its baseline value and independently of the used drug. This effect could be partially explained by increase of arterial wall shear stress.

P3.08
NITROGLYCERIN EFFECT ON AORTAL AUGMENTATION AND CENTRAL AUGMENTATION INDEX

M. Berzina [1,2], A. Krallisa [1,2], G. Latkovskis [1,2], M. Zabunova [1,2], I. Mintale [1,2], A. Erglis [1,2]
[1]*Paul Stradins Clinical University Hospital, Riga, Latvia*
[2]*University of Latvia, Riga, Latvia*

Background: Nitroglycerin (NG) reduces the systolic blood pressure, pulse pressure and augmentation index. The aim of our study was to evaluate the effect of NG on aortal augmentation (AA) and central augmentation index (CAI) in patients with different significance of the angiographically proved coronary artery disease (CAD).
Methods. The group of 66 patients referred for scheduled coronary angiography at Paul Stradins Clinical University Hospital Latvian Centre of Cardiology was analyzed. The mean age of patients was 62.8±11.9 years, 48.5% of them were male. The data about case history, cardiovascular risk factors, previous and concomitant therapy were collected. The applanation tonometry with Sphygmocor device, including radial pulse wave analysis (PWA), carotid PWA, carotid-femoral PWV before and after NG, was done. Coronary angiography was done for determination of presence and degree of coronary artery stenoses (CAS).
Results. Aortal augmentation and central augmentation index before and after nitroglycerin are seen in the Table 1.

Table 1 PWA before and after NG test and CAS.

PWA	No CAS	CAS<50%	CAS 50-70%	CAS>70%	p value
AA before NG, mmHg	12.7 ± 10.9	17.4 ± 7.2	15.3 ± 6.4	22.0 ± 9.9	0.012
AA after NG, mmHg	4.3 ± 6.4	2.3 ± 8.1	2.6 ± 4.7	11.5 ± 9.9	0.003
CAI before NG, %	25.2 ± 16.3	36.0 ± 17.9	28.6 ± 6.8	37.0 ± 10.0	0.019
CAI after NG, %	9.8 ± 15.3	6.3 ± 19.9	4.3 ± 9.7	21.0 ± 15.3	0.014
AA decrease after NG, %	86.0 ± 62.9	80.8 ± 39.0	89.1 ± 25.5	48.4 ± 47.8	0.061
CAI decrease after NG, %	89.6 ± 73.9	71.4 ± 45.4	87.7 ± 34.2	46.5 ± 38.6	0.055

Conclusions. There is a tendency of less decrease of the aortal augmentation and central augmentation index after the nitroglicerine test in patients with significant CAS. Additive prognostic value of nitroglicerine test should be further explored in future studies.

P3.09
TREATMENT WITH TOCILIZUMAB IMPROVES ARTERIAL FUNCTION IN RHEUMATOID ARTHRITIS: A 6-MONTHS PILOT STUDY

A. D. Protogerou [1], E. Zampeli [1], K. Fragiadaki [1], K. Stamatelopoulos [2], S. Panopoulos [2], C. M. Papamichael [2], P. P. Sfikakis [1]
[1]*First Department of Propaedeutic and Internal Medicine, Laikon Hospital, Athens, Greece*
[2]*Vascular Laboratory, Department of Clinical Therapeutics, Alexandra Hospital,, Athens, Greece*

Background: Endothelial function and arterial stiffness are significantly worse in rheumatoid arthritis (RA) compared to healthy controls in part due to the high-grade inflammation. In non-RA subjects, elevated serum levels of interleukin (IL)-6 are associated with accelerated atherosclerosis. Objectives: To examine whether therapeutic blockade of IL-6 receptor by tocilizumab in patients with active RA improves endothelial dysfunction and increases arterial elasticity.
Methods: In 11 non-diabetic women with RA (aged 44.5±9.9 years, mean±SD) without concomitant cardiovascular disease, who had documented endothelial dysfunction (defined by flow mediated dilatation (FMD) of the brachial artery: <5%), we assessed (i) endothelial function by FMD and (ii) central arterial stiffness (by carotid-femoral pulse wave velocity (PWV)) at baseline after 3 and 6 months of treatment with tocilizumab (8mg/kg IV/28 days).
Results: FMD improved significantly after 3 months and this improvement was sustained at 6 months [FMD (%) from 3.3±0.8 to 6.4±1.3 and 5.2±1.9, respectively, $p=0.003$ for trend by Friedman test]. PWV showed significant progressive amelioration after each trimester of TCZ treatment [PWV (m/sec) from 8.2±1.2 to 7.7±1.3 and 7.0±1.0, respectively: $p<0.001$ for trend by Friedman test] without alteration of the mean arterial blood pressure. High sensitivity reactive protein (hs-CRP) decreased dramatically from

20.4±23.2 to 5.9±5.9 and 3.9±3.20 mg/dl, whereas the atheromatic index, defined as total cholesterol/high density cholesterol, remained unchanged (from 3.4±1.1 to 3.1±0.8 and 3.0±0.6).
Conclusions: Short-term treatment with tocilizumab reversed endothelial dysfunction and improved arterial elasticity in a pilot study of RA patients, possibly via decreases of the systemic inflammatory burden.

P3.10
EFFECTS OF NITROGLYCERIN TO REDUCE AORTIC PRESSURE AUGMENTATION MAY NOT BE MEDIATED BY DILATION OF MUSCULAR ARTERIES

H. Fok [1], M. Li [1,2], B. Jiang [1], P. Chowienczyk [1]
[1]*King's College London BHF Centre, Department of Clinical Pharmacology, St Thomas' Hospital, London, United Kingdom*
[2]*Miao Li, Department of Ultrasound, the Second Affiliated Hospital of Xi 'an Jiaotong University, Xi'an, China*

Nitroglycerin (NTG) reduces aortic pressure augmentation (AP) and index (AIx), by a mechanism thought to involve a reduction in pressure wave reflection by selective dilation of muscular arteries. We examined this assumption by comparing effects of NTG with those of phentolamine (PHT) a vasodilator with little action on muscular arteries. Seven healthy subjects aged 35-62 were studied receiving PHT (1.12, 2.25 and 4.5 mg bolus/infusion i.v.) and NTG (90, 300, 900 μg i.v. infusion over 30 min) on separate occasions in a cross-over study. Central pressures (from radial tonometry) and carotid-femoral pulse wave velocity (cfPWV) were assessed using the SphygmoCor system. Brachial, carotid and abdominal aortic diameter were recorded by ultrasound. NTG (90 μg) reduced AIx from 22.2±5.5 to 13.7±5.7% ($P<0.05$) and PHT (4.5 mg) produced a similar reduction from 24.6±5.1 to 15.6±5.7% ($P<0.05$). These changes in AIx were observed in the absence of any significant fall in mean arterial blood pressure (MAP) or cfPWV. NTG (90 μg μg/min) produced a greater dilation of the brachial artery than of the carotid or aorta and vasodilation of the brachial artery by this dose of NTG was significantly greater than that by PHT (4.5 mg): 11±0.19 vs. 2.6±0.13% ($P<0.01$). These results suggest that, although actions of NTG are associated with dilation of muscular arteries, this is not necessarily the action leading to a reduction in AIx. Actions on other parts of the vascular tree and/or on ventricular ejection may be responsible for the reduction in AIx by NTG and PHT.

P4 — Basic science and modelling 1

P4.01
STRESS CALCULATIONS IN 3D RECONSTRUCTIONS OF ARTERIES: THE INFLUENCE OF AXIAL IMAGE RESOLUTION

H. A. Nieuwstadt [1], A. Akyildiz [1], L. Speelman [1], J. J. Wentzel [1], R. Virmani [2], T. van der Steen [1], F. Gijsen [1]
[1]*Biomedical Engineering, Erasmus MC, Rotterdam, Netherlands*
[2]*CVPath Institute Inc., Gaithersburg, United States of America*

Computational modeling of the stress distribution in vulnerable atherosclerotic plaques facilitates identification of high stress locations which can be related to plaque rupture. The first step in doing 3D biomechanical stress simulations is to accurately re-create the artery geometry from histology or in-vivo imaging. This research investigated the influence of the axial sampling resolution of histology on the stress distribution in plaques.
A 3D reference geometry of a diseased human coronary artery was constructed based on 7 histological images with an axial spacing of 0.5 mm. Three under sampled models were generated: a 3D model based on four slices (1 mm spacing) and two 2D models based on one slice only (Figure 1). The stress distribution was calculated using the Finite Element Method (FEM).
The under sampled 3D model underestimates the peak stress by approximately 3% (Figure 2). The peak stress in the 2D models is 6% higher in one case and 12% lower in the other case. It can be concluded that a lower axial sampling resolution leads to a lower stress estimation due to smoothing of the geometry. Performing 2D simulations results in a more unpredictable stress distribution in that slice. However, approximate stress values and the location of peak stresses can be predicted well with a 3D under sampled geometry, indicating that 1 mm axial sampling might be sufficient for clinical FEM studies.
This research was supported by the Center for Translational Molecular Medicine and the Netherlands Heart Foundation (PARISk)

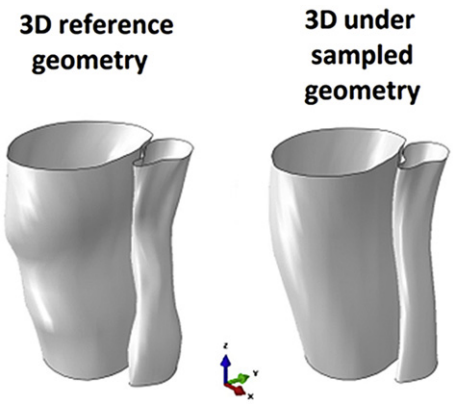

Figure 1 3D geometries (lumen and lipid surfaces shown)

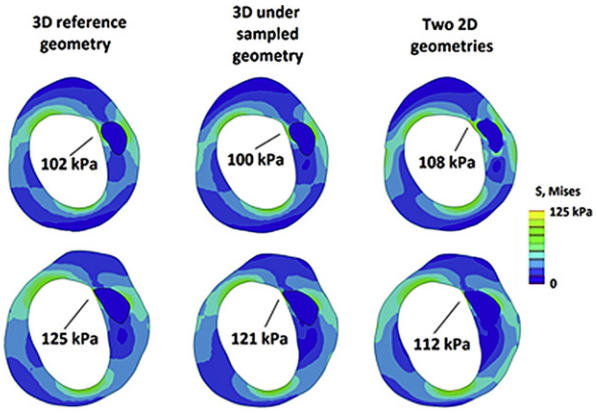

Figure 2 Von Mises stress distributions.

P4.02
INFLUENCE OF PLAQUE GEOMETRY ON PEAK CAP STRESS

A. C. Akyildiz, L. Speelman, H. Nieuwstadt, Steen A. Van Der, J. Wentzel, F. Gijsen
Biomedical Engineering Dept., Erasmus MC, Rotterdam, Netherlands

Introduction: Cap of an atherosclerotic plaque ruptures when mechanical stresses in the cap exceeds local strength. In this study, we investigated influence of plaque geometry on cap stresses.
Methods: Histology images of 30 cross-sections from 10 atherosclerotic human coronary vessels (perfusion fixed at 100 mmHg) were segmented. Mechanical stresses at 140 mmHg blood pressure were computed using finite element analysis after initial stresses were obtained using Backward Incremental Method [1]. Relation between cap stress and six geometric parameters (see Table) were evaluated. For each geometric parameter, two groups were created: the high group containing cross-sections with a value higher than the median value ($n=15$) and the low group ($n=15$). Mean values were compared for the two groups (Student's t-test).
Results: Thin cap cross-sections showed higher stresses than thick cap cross-sections (Table). Plaques with thinner necrotic core (NC) had larger stresses than the plaques with thick NC. Other geometric parameters were statistically insignificant.
Discussion: Higher peak cap stresses for thinner cap cross-sections confirm previous studies [2]. However, higher peak cap stresses for plaques with thin NC contradict an earlier study [2] with idealized geometries. Sharp corners at NC edges in realistic geometries might affect stress distribution in cap. Moreover, not only thickness but shapes of plaque components might influence peak cap stresses. In the near future, the analysis will be extended by incorporating other geometric parameters describing plaque component shapes and multivariate analysis to assess cross correlations between geometric parameters.

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