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### **P4.20: ASSOCIATION OF A SINGLE NUCLEOTIDE POLYMORPHISM IN CYP2C8 WITH MYOCARDIAL INFARCTION IN BULGARIAN POPULATION**

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Hemodynamic variables by tertiles of HOMA index*				
Variable	T1 (<0.94) (n=32)	T2 (0.94-1.90) (n=28)	T3 (>1.90) (n=30)	P value
Peripheral SBP (mmHg)	111.7 ± 2.0	114.3 ± 1.8	123.2 ± 2.0	<0.0001
Peripheral DBP (mmHg)	76.8 ± 1.4	79.8 ± 1.3	84.7 ± 1.5	0.001
Peripheral PP (mmHg)	33.5 ± 1.0	35.0 ± 0.9	38.4 ± 1.0	0.004
Central SBP (mmHg)	103.7 ± 1.7	106.7 ± 1.5	115.3 ± 1.6	0.001
Central DBP (mmHg)	77.8 ± 1.5	81.1 ± 1.3	86.1 ± 1.5	0.001
Central PP (mmHg)	25.5 ± 1.5	25.1 ± 1.3	29.2 ± 1.0	0.071
MBP (mmHg)	92.5 ± 1.5	95.7 ± 1.3	102.3 ± 1.5	<0.0001
HR (bpm)	61.3 ± 1.9	65.0 ± 1.7	66.0 ± 1.9	0.212
PWV (m/s)	5.64 ± 0.17	5.71 ± 0.10	6.34 ± 0.9	0.012
Augmentation Index (%)	6.7 ± 3.2	6.1 ± 3.8	6.9 ± 2.2	0.082

\*Values are expressed as means ± SEM

#### P4.17

##### INFLUENCE OF ESTIMATED WALL SHEAR RATE INDICES ON CAROTID ARTERY INTIMA-MEDIA THICKNESS AND INTIMA-MEDIA COMPLEX ECHOGENICITY

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**Introduction:** Grey scale median of the carotid artery intima-media complex (IM-GSM) is a recently introduced measurement to characterise the arterial wall. Wall shear stress is thought to influence intima-media thickness (IMT) and to play a major role in the development of atherosclerosis. However, the relationship between wall shear stress and IM-GSM is not well understood. This study examined the relationship between estimated wall shear rate (WSR) indices and IMT as well as estimated WSR indices and IM-GSM.

**Methods:** Data from 156 middle-aged and older individuals (66.1±9.5yrs, 58F) were included in this analysis. Common carotid artery diameter, IMT, and blood velocity data were obtained using a Doppler ultrasound machine. Three estimates of WSR were calculated: peak, mean and diastolic WSR. IMT and IM-GSM were analyzed using a semi-automated edge-detection programme.

**Results:** IMT was inversely associated with all WSR indices (peak:  $r=-0.16$ , mean:  $r=-0.22$ , diastolic:  $r=-0.25$ , all  $p<0.05$ ). IM-GSM was positively associated with mean ( $r=0.20$ ) and diastolic WSR ( $r=0.17$ , both  $p<0.05$ ). Peak and mean WSR were independent determinants of IMT, and mean and diastolic WSR were independent determinants of IM-GSM after adjustments for age, sex and traditional cardiovascular risk factors.

**Conclusion:** These results show that estimated WSR indices were associated with IMT and IM-GSM, suggesting that WSR may, in part, determine the extent of IMT and the composition of the arterial wall in our cohort.

#### P4.18

##### OSTEOPROTEGERIN AND ARTERIAL STIFFNESS IN POSTMENOPAUSAL WOMEN

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**Background:** Many recent data support the hypothesis that circulating osteoprotegerin (OPT) levels are associated with arterial calcification and may serve as a potential predictor of cardiovascular disease and mortality. Matrix Gla Protein (MGP) is considered an inhibitor of vascular calcification. However, the role of these molecules in the arterial wall is still unclear. Arterial stiffness increases in postmenopausal women. The aim of our study was to determine the relation between circulating OPT and MGP and vascular parameters of arterial stiffness in postmenopausal women.

**Materials and Methods:** One hundred forty-four postmenopausal women, aged (61.4±10.6 years) were included in the study. PWV was measured using an oscillometric device. OPT, MGP, C-reactive protein and parameters of lipid and glucose metabolism were also determined.

**Results:** OPT correlated with aortic PWV ( $r=0.32$ ,  $p=0.006$ ), and C-reactive protein ( $r=0.37$ ,  $p=0.02$ ). In multiple regression models, after adjustment for potential confounders, OPT was independently associated with aortic PWV. No correlation was found between MGP and aortic PWV. There were 61% hypertensives, 34% patients with diabetes, 35.4% with hyperlipemia and 41.6% with obesity or overweight, in this study.

**Conclusions:** These results support the relationship between serum OPT and arterial stiffness in postmenopausal women, independent of the traditional cardiovascular risk factors and inflammation. At the same time, MGP was not found to be a predictor of arterial stiffness.

#### P4.19

##### AORTIC STIFFNESS, REFLEXION WAVE AND ARTERIAL HYPERTENSION UNDER ANTI-ANGIOGENIC DRUGS

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**Objective:** Sorafenib and Sunitinib are anti-angiogenic drugs (AAD) used in an increasing number of cancers. The most common side effect is arterial hypertension. We hypothesize that AAD lead to an early damage of large arteries which can be translated by an increase of aortic stiffness determined by the pulse wave velocity measurement (PWV).

**Material and Method:** In a longitudinal study, 32 patients have been treated with Sorafenib or Sunitinib. Subjects have been explored during a visit before the introduction of the treatment and then every two weeks for 2 months. Measured parameters are blood pressure, PWV, central pressure, augmentation index (Alx).

**Results:** 38% of the subjects have developed an early arterial hypertension requiring anti-hypertensive treatment. The initial values of brachial SBP was predictive from SBP changes under AAD while PWV and Alx was not. Furthermore, in patients who developed hypertension and required treatment with 5 to 10 mg amlodipine has been effective at decreasing SBP and MBP by -13 [-21;-4] et -8 [-14;-1] mmHg ( $p<0,01$ ) respectively, and Alx, -10% [-16;-4] ( $p<0,001$ ).

**Conclusion:** This study suggests that blood pressure at inclusion increases the risk of developing acute hypertension with AAD. It also shows that effective vasodilatation could be achieved despite small vessels disruption by AAD.

#### P4.20

##### ASSOCIATION OF A SINGLE NUCLEOTIDE POLYMORPHISM IN CYP2C8 WITH MYOCARDIAL INFARCTION IN BULGARIAN POPULATION

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Cytochrome P450 2C8 is a polymorphic enzyme responsible for the biosynthesis of vasoactive substances from arachidonic acid. Inter-individual differences in the action of these substances might be important in the pathogenesis of cardiovascular diseases such as acute myocardial infarction (AMI).

In the present study we analyzed the association of a genetic variant in CYP2C8 and the morbidity of AMI in Bulgarian population.

The study included 99 AMI patients and 370 control subjects. To determine the genotypes of the samples real time PCR with predesigned TaqMan SNP Genotyping Assays (Applied Biosystem) was used.

The rare allele (C) was found in 16% of the affected and 10% of the non affected cases and it showed statistical significance [OR (95% CI): 1.64 (1.00-2.56),  $P = 0.03$ ]. The TT genotype occurred more often in the control group compared with the patients with AMI [OR (95% CI): 0.58 (0.35-0.96),  $P = 0.039$ ]. The heterozygous genotype of CYP2C8 was found to be significantly associated with a risk of myocardial infarction [OR (95% CI): 2.25 (1.06-4.75),  $P = 0.036$ ] in women.

Possession of the rare genetic variant of CYP2C8 gene in Bulgarian population is associated with a modestly increased risk of AMI.

**Key words:** CYP2C8, risk, association

#### P4.21

##### CAROTID ELASTICITY BEHAVIOR DURING EXERCISE IS ALTERED IN PATIENTS WITH KNOWN OR SUSPECTED CORONARY ARTERY DISEASE

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**Objective:** The behavior of cardiovascular parameters during exercise remains unsettled. Our aim was to evaluate carotid elasticity during graded bicycle semi-supine exercise test, in patients with known or suspected coronary artery disease (CAD) and to compare it with a control group.

**Methods:** 36 consecutive patients (20 men, 61±8years), and 18 healthy volunteers (9 men, 34±3 years) were recruited. Right carotid diameter (D) and distension (ΔD) were estimated by ultrasound B-mode image processing, and central pulse pressure (PPa) by radial tonometry; then, carotid cross-sectional distensibility coefficient (DC) was obtained. All measurements were performed at rest and peak of age-dependent maximal heart rate.

**Results:** At rest, D and PPa were higher in patients than in controls (7.8±1.1 vs 6.2±0.6mm and 49±11 vs 27±5mmHg,  $p<0.05$ ), whereas no significant differences were observed in ΔD and mean blood pressure (0.50±0.21 vs 0.54±0.24mm and 98±7 vs 97±5mmHg,  $p=ns$ ); DC was lower in patients than in healthy volunteers (22.1±8.5 vs 59.7±20.6 10<sup>-3</sup>/KPa,  $p<0.05$ ). At peak, D (8.1±1.3 and 6.4±0.7mm) and ΔD (0.65±0.31 and 0.79±0.24mm) were similar to rest in both groups; PPa (67±17 and 45±12mmHg) and mean blood pressure (128±9 and 123±13mmHg) increased both in patients and controls ( $p<0.05$  vs rest); DC significantly decreased in healthy subjects (39.7±14.5 10<sup>-3</sup>/KPa,  $p<0.05$  vs rest), but not in patients (21.2±7.9 10<sup>-3</sup>/KPa,  $p=ns$  vs rest).

**Conclusions:** In patients with known or suspected CAD, carotid distensibility, which at rest is lower than in healthy controls, remains unchanged during maximal exercise, despite a similar increase in mean blood pressure in the two populations.

#### P4.22

##### GUIDELINE BASED CARDIOVASCULAR RISK MANAGEMENT VERSUS IMAGING ATHEROSCLEROSIS

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**Purpose:** We wanted to compare the outcome of a newly implemented Dutch Cardiovascular Risk Management guideline (so called Prevention Consult) with the non-invasive measurement of Carotid Intima Media Thickness and Plaque visualization (CIMT+P) in a group of 313 employees (170 men and 143 women, mean age 42.9 ± 0.5 years range 22 – 65 years) in one organization.

**Methods:** At one and the same measure point we performed the Prevention Consult short questionnaire with 7 questions ([www.testuwrisico.nl](http://www.testuwrisico.nl)), measuring weight, height, waist circumference, blood pressure, total/HDL-cholesterol, glucose and made a CIMT + P.

Table 1 shows results:

The Pearson correlation between risk test and the CIMT + P was significant ( $r = 0.248$ ,  $p < 0.01$ ). The risk test identified only 17 people at a high risk level and the CIMT + P showed for 70 people distinct atherosclerotic lesions.

**Conclusions:** Although there is a significant correlation between the outcome of the PreventionConsult and the CIMT + P, the CIMT + P is far more sensitive for atherosclerotic lesions than the Prevention Consult. Especially, in a middle age population with intermediate risk, a CIMT +

P offers more signs to warrant early prevention and effective intervention.

**Table 1**

		CIMT + P(A,normal risk, B 25% increased risk, C 50% increased risk and D 100% increased risk)				Total
		A	B	C	D	
Risk test	Low risk	17	10	3	1	31
	Intermediate risk	112	70	51	1	234
	High risk	1	2	12	2	17
Total		130	82	66	4	282

#### P4.23

##### HYPOECHOGENIC CAROTID PLAQUES ARE MORE MOBILE IN COMPARISON WITH HYPERECHOGENIC ONES

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**Background:** Speckle Tracking Technology allows to assess multi-dimensional regional mechanics of carotid wall and carotid plaques. We hypothesized that hypoechoic plaques are more mobile in comparison with hyperechoic ones.

**Objective:** The objective of this study was to investigate the mechanical properties of carotid plaques using ultrasound speckle tracking.

**Methods:** Study population consisted of 43 patients with carotid atherosclerosis (aged 53-89, median-69). In total, 48 carotid plaques were analyzed. For each plaque, maximal circumferential strain (S) and strain rate (SR) were measured (in several points separately for plaque cap, core and base). According to grey scale median analysis all plaques were divided into hyperechoic and low- and moderately echogenic ones. Degree of stenosis and plaque length were also assessed.

**Results:** S and SR were higher for all parts of hypo- and moderately echogenic plaques in comparison with hyperechoic ones and for cap and core the difference was significant (table 1). Spearman correlation analysis revealed significant negative associations between echogenicity and S and SR values (table 2). Multivariate linear regression confirmed that echogenicity is an independent determinant of S and SR after adjusting for potential confounders (degree of stenosis, plaque length). Univariate analysis found significant negative association between degree of stenosis and S and SR values (table 2).

**Conclusion:** Hypo- and moderately echogenic carotid plaques are more mobile in comparison with hyperechoic ones. Degree of stenosis is negatively associated with increased mobility and this may explain the fact that many vulnerable, symptomatic plaques have relatively moderate degree of stenosis.

**Table 1** S and SR values of hypo- and moderately echogenic and hyperechoic carotid plaques.

	Hypo- and moderately echogenic plaques	Hyper- echogenic plaques	p
cap			
S	5.42±3.71	3.78±2.25	$p=0.0006$
SR	0.52±0.31	0.43±0.27	$p=0.02$
core			
S	6.3±3.55	4.22±2.60	$p=0.0003$
SR	0.59±0.28	0.46±0.25	$p=0.008$
base			
S	4.78±3.2	3.61±3.14	$p=0.034$
SR	0.47±0.27	0.42±0.37	$p=0.32$

Data are expressed as mean ± SD