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### **P1.07: RELATIONSHIP BETWEEN ECHOES FROM THE CAROTID MEDIA, CLINICAL VARIABLES AND ARTERIAL STIFFNESS: A CROSS-SECTIONAL ANALYSIS**

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using Sphygmocor Px device, calculated pulse wave velocity (PWV) and determined erythrocyte NKA activity before and after addition of spironolactone (50 mg/day) to the therapy.

In rat aortic explants, treatment with MBG resulted in a two-fold rise in the levels of collagen-1 and a marked reduction in the sensitivity to the vasorelaxant effect of sodium nitroprusside following endothelin-1-induced constriction ( $EC_{50} = 0.05 \text{ umol/L}$  vs.  $1.98 \text{ umol/L}$  in vehicle-treated rings;  $P < 0.01$ ). Canrenone blocked effects of MBG on collagen synthesis and restored sensitivity of vascular rings to sodium nitroprusside ( $EC_{50} = 1.7 \text{ umol/L}$ )

Patients with RH exhibited elevated plasma MBG concentration ( $0.18 \pm 0.02$  vs.  $0.37 \pm 0.05 \text{ nmol/L}$ ;  $P = 0.01$ ) and reduced NKA activity ( $1.9 \pm 0.15$  vs.  $2.8 \pm 0.1 \text{ umol Pi/ml/hr}$ ,  $P < 0.01$ ) vs. 16 healthy controls. Six-month administration of spironolactone was associated with a decrease in PWV ( $P < 0.01$ ) and systolic/diastolic BP ( $12 \pm 3/7 \pm 2 \text{ mmHg}$ ;  $P < 0.01$ ), and restoration of NKA activity ( $1.9 \pm 0.15$  to  $2.3 \pm 0.11 \text{ umol Pi/ml/hr}$ ,  $P < 0.01$ ). These results demonstrate that CS-induced vascular fibrosis is a likely target for aldosterone antagonists.

#### P1.04

##### PREDICTORS OF VASCULAR AGE IN A POPULATION WITH CARDIOVASCULAR RISK FACTORS

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**Background:** We aimed at evaluating determinants of the vascular age.

**Material and Methods:** 187 subjects [86 M and 101 W] with CV risk factors were classified into three categories of the Framingham CV Risk (FR). Their mean carotid intima media thickness (CIMT) and arterial stiffness (a.s.) parameters were assessed. The VA was calculated from the CIMT according to the nomograms from the ARIC Study. The subjects were divided into two groups: 1- VA exceeds the chronological age (CA) for at least 5 years and 2 – others.

**Results:** The VA > the CA in M and W (M:  $68.5 \text{ y}$  vs  $52.4 \text{ y}$ ,  $p < 0.001$ ; W:  $67.1$  vs  $55.00$ ,  $p < 0.001$ ). No relationship between the FR category and classification to group 1 or 2 was observed. In both sexes diabetes mellitus (DM) (M: OR 3.10, 95% CI 1.28 ÷ 7.50,  $p < 0.05$ ; W: OR 4.40, 95%CI 1.85 ÷ 10.47,  $p = 0.001$ ) and additionally in W BMI >25 kg/m<sup>2</sup> (OR 5.87, 95%CI 2.15 ÷ 15.99,  $p = 0.009$ ) differentiated group 1 from group 2. Increased  $\beta$  ( $9.36$  vs  $7.77$ ,  $p = 0.005$ ) and Ep ( $131.9$  vs  $110.1$ ,  $p < 0.05$ ) in M and Ep ( $132.3$  vs  $106.5$ ,  $p < 0.05$ ) in W distinguished group 1 from group 2. In the multivariate analysis, DM and elevated BMI in W and DM and increased  $\beta$  in M were proved to be independent predictors of VA > CA.

**Conclusions:** FR categories did not allow for prediction if the VA > CA. DM appeared as the strongest predictor of the VA > CA.

#### P1.05

##### SEDENTARY LIFESTYLE IS ASSOCIATED WITH INDICES OF ARTERIAL STIFFNESS, DIASTOLIC DYSFUNCTION AND OBESITY

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The aim of the present study was to examine the relationship between weekly physical activity patterns, obesity and early sub-clinical cardiovascular dysfunction.

For this study, 84 healthy lifelong non-smoking, normotensive subjects (54 male & 30 female) were recruited (age  $39 \pm 11$  years, BMI  $25.2 \pm 3.3 \text{ kg.m}^2$ ). Weekly physical activity levels were objectively measured over a five day period using triaxial accelerometry (RT3, Stayhealthy, USA). Activity data was categorized as relative time spent being sedentary, lightly active, moderately active and vigorously active<sup>1</sup>. Body fat composition was estimated using bioelectrical impedance (TBF410GS, Tanita, UK). Augmentation index (Alx, Sphygmocor, Skidmore Medical, UK) and pulse wave velocity (PWV, Vicorder, Skidmore Medical, UK), indices of arterial stiffness, were measured using applanation tonometry. Early/late mitral valve filling velocity (MV E/A) was used to assess cardiac diastolic function (Vivid 7 Dimension, GE, USA).

Mean Alx, PWV, MV E/A ratio, body fat composition were  $13.43 \pm 14.32 \%$ ,  $6.79 \pm 0.93 \text{ m.s}^{-1}$ ,  $5.11 \pm 13.23$  and  $24.54 \pm 7.70 \%$ . Spearman's correlation analysis identified significant correlations between relative time spent being sedentary and Alx  $r = 0.3008$   $p < 0.0054$ , PWV  $r = 0.2174$   $p < 0.0469$ , MV E/A ratio  $r = -0.3541$   $p < 0.027$  and % body fat  $r = 0.3440$   $p < 0.0017$ . The results of the study show that people who spend more time being sedentary have greater body fat, greater arterial stiffness and poorer diastolic function. These observations have important implications for public health.

1. Treuth MS, et al. Defining accelerometer thresholds for activity intensities in adolescent girls. *Med Sci Sports Exerc* 2004;**36**(7):1259-66.

#### P1.06

##### IS IMPAIRED FASTING GLUCOSE ASSOCIATED WITH SUBCLINICAL ARTERIAL DISEASE? THE STRONG HEART STUDY

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**Background:** Vascular disease is a leading cause of morbidity and mortality in diabetes mellitus (DM). It is uncertain whether pre-diabetes (impaired fasting glucose [IFG]) increases risk for subclinical vascular disease.

**Methods:** Cardiovascular disease (CVD) risk factors and carotid artery structure (wall thickness [IMT] and vascular mass) and presence and extent of atherosclerosis were compared in 2461 Strong Heart Study participants free of prevalent CVD: 1038 with normal fasting glucose (NFG), 254 with IFG (110-125 mg/dl), and 1169 with DM.

**Results:** Participants with IFG were more obese and had lower HDL cholesterol than those with NFG but were comparable in other CVD risk factors. Participants with DM were more likely to be female, hypertensive, non-smoking, and to have higher triglycerides than the other two groups. Following adjustment for differences in CVD risk factors, DM had greater carotid IMT (0.75 mm), mass (16.38 mm<sup>2</sup>) and presence (69.1%) and extent (log transformed plaque score: 0.78) of atherosclerosis compared to NFG and IFG. NFG and IFG had comparable adjusted IMT (0.73 vs. 0.73 mm), arterial mass (15.51 vs. 15.67 mm<sup>2</sup>), plaque (58.8 vs. 58.5 %) and plaque score (0.64 vs. 0.66).

**Conclusions:** Other than elevated fasting glucose, the distinguishing features of IFG are obesity and reduced HDL cholesterol (comparable to DM). Greater degrees of arterial hypertrophy and atherosclerosis are seen in DM but not IFG. These findings have implications for public health efforts to identify individuals with IFG and intervene to limit progression to the vascular disease associated with DM.

#### P1.07

##### RELATIONSHIP BETWEEN ECHOES FROM THE CAROTID MEDIA, CLINICAL VARIABLES AND ARTERIAL STIFFNESS: A CROSS-SECTIONAL ANALYSIS

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**Introduction:** The radiofrequency (RF) matrix conveys information on texture and composition of atherosclerotic plaques. Few studies have analyzed the "normal" carotid wall out of plaques. We tested a novel method to measure echoes from the media layer and analyzed their correlation with clinical variables and arterial stiffness in a large population sample.

**Methods:** We analyzed RF matrices from ultrasound scans of the common carotid in 1,827 untreated subjects recruited from the general population, aged 50 to 75, for the Etude Prospective Parisienne 3. The first strong echo from the blood-intima interface was excluded; media power (MP) was defined as the ratio of amplitude of RF echoes from the media and that from the lumen. Intima-media thickness (IMT) was also measured.

**Results:** IMT was correlated with carotid diameter, age, pressure, and body size. MP was inversely correlated with body size and serum lipids, but not with age or pressure. IMT was higher, and MP lower, in obesity and metabolic syndrome (MS); obese with MS had higher IMT, and lower MP, than non-obese

non-MS; the difference in MP was significant also for these latter vs. non-obese with MS. MP was positively correlated with distensibility ( $r=0.097$ ,  $p<0.001$ ) and inversely with Young's modulus ( $r=-0.121$ ,  $p<0.001$ ); IMT had a negative correlation with both.

**Conclusion:** Obesity and MS decrease echogenicity of the carotid media. MP is influenced by different parameters than IMT, and conveys different information; it is inversely correlated with intrinsic and total vessel stiffness. Its histological and clinical meaning are to be investigated.

#### P1.08

##### PREDICTION OF CARDIOVASCULAR EVENTS WITH AORTIC STIFFNESS IN PATIENTS WITH ERECTILE DYSFUNCTION

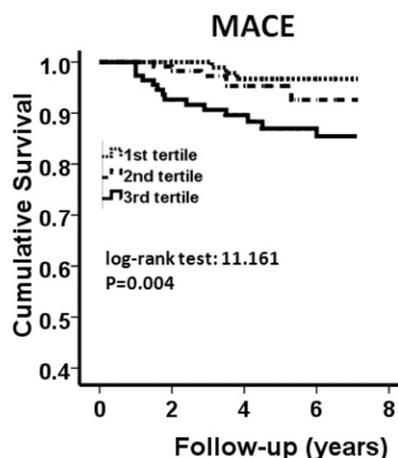
C. Vlachopoulos, N. Ioakeimidis, K. Aznaouridis, A. Aggelis, D. Terentes-Printzios, A. Aggelakos, M. Abdelrasoul, A. Synodinos, G. Lazaros, C. Stefanadis  
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**Background:** Erectile dysfunction (ED) confers an independent risk for cardiovascular events and total mortality. Aortic pulse wave velocity (PWV) is an important predictor of cardiovascular events and all-cause mortality. We investigated whether PWV predicts major adverse cardiovascular events (MACE) in patients with ED beyond traditional risk factors.

**Methods:** MACE in relation to PWV were analyzed with proportional hazards models in 344 patients (mean age 56 years) without established cardiovascular disease.

**Results:** During a mean follow-up of 4.7 years (range 1-8.5), 24/344 participants experienced a MACE. ED population was divided into tertiles according to the PWV values (low tertile  $<7.6$  m/s; middle tertile 7.6-8.8 m/s; high tertile  $>8.8$  m/s). Kaplan-Meier survival analysis showed that PWV was associated with MACE and the difference between the tertiles was significant (Mantel log-rank test: 11.161;  $P=0.004$ , figure). Subjects in the highest PWV tertile had a 4-fold higher risk of MACE compared to those in the lowest PWV tertile (adjusted HR 3.97,  $P=0.035$ ). A PWV value of 7.81 m/sec was associated with a negative predictive value (ability to "rule out" MACE) of 98.1%. Addition of PWV to standard risk factors model yielded correct patient reclassification to higher or lower risk category by 27.6% ( $P=0.0332$ ) in the whole cohort.

**Conclusions:** Higher aortic stiffness is associated with increased risk for a MACE in ED patients without known cardiovascular disease. Aortic PWV improves risk prediction when added to standard risk factors and may represent a valuable biomarker of prediction of cardiovascular disease risk in these patients.



#### P1.09

##### HERITABILITY OF RETINAL MICROCIRCULATION IN FLEMISH FAMILIES

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**Aims:** The aim of this study was to describe the heritability of retinal vessel diameter in complex pedigrees of a Flemish population. We also investigated genetic and environmental correlations of retinal microvascular phenotypes.

**Methods:** In 413 participants from 70 families (mean age 51.5 years; 50.1% women), randomly recruited from a Flemish population, we post-processed retinal images using IVAN software to generate the central retinal arteriole and venule equivalents (CRAE and CRVE) and the arteriole-to-venule-ratio (AVR). We used S.A.G.E. Statistical Analysis to estimate heritability and to calculate the genetic and environmental correlations.

**Results:** In multivariable-adjusted analyses, CRAE decreased with age and mean arterial pressure, and was higher in women than in men. CRVE decreased with mean arterial pressure. Current smokers had higher CRAE and CRVE. These common cardiovascular risk factors only explained 12.7% and 7.3% of the total variance of CRAE and CRVE, respectively. With adjustments applied for these covariables, the heritability estimates of CRAE, CRVE, and AVR were 0.213 ( $P=0.044$ ), 0.339 ( $P=0.010$ ) and 0.272 ( $P=0.004$ ), respectively. The genetic correlation was 0.360 ( $P<0.0001$ ) between CRAE and CRVE.

**Conclusions:** Retinal microvascular phenotypes play an important role in prediction of cardiovascular disease. However, traditional cardiovascular risk factors explained only a little of the variance of retinal microcirculation. Our study showed moderate heritability for CRAE, CRVE and AVR, and significant genetic correlation between CRAE and CRVE in a Flemish population. This suggested that genetic variants might play an important role in the association between retinal diameter and cardiovascular disease.

#### P1.10

##### INTERLEUKIN GENETIC POLYMORPHISM IN RELATION TO ATHEROSCLEROSIS IN A FLEMISH POPULATION

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**Aims:** Atherosclerosis, a chronic inflammatory disease, is the most important cause of cardiovascular morbidity and mortality. Interleukins (ILs) play a crucial role in balancing anti- and pro-inflammatory stimuli. The aim of our study was to investigate the association between intima-media thickness (IMT) and genetic variation in ILs.

**Methods:** In 360 participants (mean age 41.7 years; 52.8% women), randomly recruited from a Flemish population, we measured carotid ( $n=348$ ), femoral ( $n=355$ ) and brachial ( $n=355$ ) IMT using ultrasound. After amplifying DNA fragments, we genotyped for IL-1a 549C/T, IL-1b 4336C/T, IL-4 582C/T, IL-4 receptor (IL-4R) 398A/G, IL-4R 1682T/C, IL-5R 482G/A, IL-6 589G/C, IL-6 987G/C, IL-9 4244C/T, IL-10 8700C/A polymorphisms and IL-13 4045C/T. We applied a mixed model to assess phenotype-genotype associations while accounting for relatedness and covariables.

**Results:** In multiple regression analyses, IMT in all arteries increased with age, and brachial IMT increased with systolic blood pressure. Women had higher femoral IMT than men. With adjustments applied for these covariables, carotid IMT was higher in IL-1a C allele carriers ( $0.624\pm 0.016$  vs  $0.549\pm 0.038$ ,  $P=0.045$ ) and in IL-4R GG homozygotes ( $0.655\pm 0.022$  vs  $0.603\pm 0.016$ ,  $P=0.027$ ). IL-5 GG homozygotes had lower femoral IMT than their A allele counterparts did ( $0.665\pm 0.022$  vs  $0.728\pm 0.027$ ,  $P=0.020$ ). Carotid and brachial IMT were lower in IL-9 CC homozygotes than in T allele carriers ( $0.610\pm 0.016$  vs  $0.671\pm 0.029$ ,  $P=0.020$ ;  $0.313\pm 0.008$  vs  $0.348\pm 0.016$ ,  $P=0.027$ ).