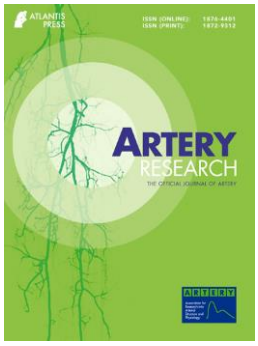

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P1.10: INTERLEUKIN GENETIC POLYMORPHISM IN RELATION TO ATHEROSCLEROSIS IN A FLEMISH POPULATION

Y.-P. Liu, L. Thijs, T. Kuznetsova, K. Asayama, Y.-M. Gu, P. Verhamme, H. Struijker-Boudier, H. Schmidt, J.A. Staessen

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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

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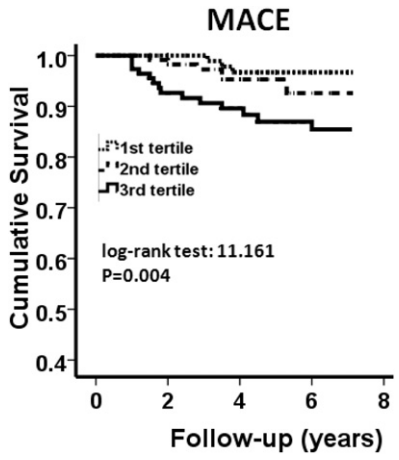
Background: Erectile dysfunction (ED) confers an independent risk for cardiovascular events and total mortality. Aortic pulse wave velocity (PWV) is an important predictor of cardiovascular events and all-cause mortality. We investigated whether PWV predicts major adverse cardiovascular events (MACE) 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

Y.-P. Liu [1], L. Thijs [1], T. Kuznetsova [1], K. Asayama [1,2], Y.-M Gu [1], P. Verhamme [3], H. Struijker-Boudier [4], H. Schmidt [4], J. A. Staessen [1,5]
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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 ± 0.016 *vs* 0.549 ± 0.038, $P=0.045$) and in *IL-4Rα GG homozygotes* (0.655 ± 0.022 *vs* 0.603 ± 0.016, $P=0.027$). *IL-5 GG* homozygotes had lower femoral IMT than their *A* allele counterparts did (0.665 ± 0.022 *vs* 0.728 ± 0.027, $P=0.020$). Carotid and brachial IMT were lower in *IL-9 CC* homozygotes than in T allele carriers (0.610 ± 0.016 *vs* 0.671 ± 0.029, $P=0.020$; 0.313 ± 0.008 *vs* 0.348 ± 0.016, $P=0.027$).

Conclusions: In line with experimental studies in animals and high heritability of carotid IMT, we demonstrated that IMT was associated with genetic variations in several interleukins components.

P1.11
CENTRAL SYSTOLIC AUGMENTATION INDEXES AND URINARY SODIUM IN A WHITE POPULATION

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Background: The association between cardiovascular health and salt intake remains controversial.
Methods: In 630 participants (mean age 40.6 years; 51% women), randomly recruited from F. alemish population, we measured sodium and creatinine in 24 hour urine samples at baseline and follow-up (median, 9.7 years) and the carotid and aortic augmentation indexes (AI) standardized to heart rate at follow-up only.
Results: The carotid AI (130.2% vs 113.7%) and aortic AI (145.7 vs 127.4) were higher ($P<0.0001$) in women than men and increased with age (10.1% and 8.5% per 10 years). From baseline to follow-up, the urinary sodium concentration decreased (117.1 vs 105.2 mmol/L; $P<0.0001$), whereas 24 hour urinary sodium did not change (166.5 vs 171.5 mmol; $P=0.12$). In multivariable-adjusted longitudinal analyses, a 40 mmol/L ($\sim$1 SD) increase in the urinary sodium concentration at baseline was independently and inversely associated with the carotid AI (effect size, 1.38±0.66%; $P=0.038$) and aortic AI (1.54±0.72%; $P=0.019$). In cross-sectional analyses of follow-up data, these estimates were 1.26±0.70% ($P=0.07$) and 1.52±0.76% ($P=0.045$), respectively. In the longitudinal and cross-sectional analyses, the carotid and aortic AIs were unrelated to the 24 hour urinary excretion of sodium ($P\geq0.43$).
Conclusions: Our study showed an inverse association between the AIs in the central arteries and the urinary sodium concentration, but not sodium excretion. Vasodilatation of the afferent renal arterioles in response to higher sodium concentration is mediated via the connecting tubule glomerular feedback mechanism; this might move reflection sites in the renal arteries more distally and thereby explain our observations.

P1.12
ETHNIC DIFFERENCES IN LEFT VENTRICLE MYOCARDIAL OXYGEN DEMAND

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Background: There are marked inter-ethnic differences in coronary heart disease (CHD). Indian Asians (IA) have 50% greater and African Caribbeans (AC) 50% less CHD than white Europeans (E) in the UK. Reasons for this are unclear. We compared ventricular structure and function, specifically myocardial oxygen demand, by ethnicity.
Methods and Results: 3D echocardiography (Philips iE33) and radial applanation tonometry (SphygmoCor) were performed on 800 men and women (age 55-85) from the Southall And Brent REvisited (SABRE) tri-ethnic population-based cohort. Left ventricular mass index (LVMI) was measured, and 3D LV remodelling index (LVRI) was calculated as LV mass/LV end diastolic volume. 3D cardiac output (CO) and total peripheral resistance (TPR) were calculated and 3D LV end systolic active fibre stress (AFS) and wasted effort (E_w) were derived as markers of myocardial oxygen demand.
LVMI did not differ between E and AC but was significantly lower in IA. LVRI was greatest in AC and smallest in IA. IA and AC had lower CO and higher TPR compared to E. AFS and E_w were significantly higher in IA. These ethnic differences persisted after multivariate adjustment for age, sex, heart rate, systolic blood pressure, fasting blood glucose and insulin concentrations and medication.
Conclusions: AC have comparable LVMI and myocardial oxygen demand to E. In contrast IA generate significantly more AFS and E_w despite having less myocardial muscle. This implies that IA have increased myocardial oxygen demand which may increase susceptibility to myocardial ischemia, and which could contribute to their excess risk of CHD.

Table 1 Data are mean±SE by ethnicity (adjusted for age). * = $p<0.05$ ** = $p<0.01$ compared with Europeans by post hoc test following ANOVA.

	European	Indian Asian	African Caribbean	ANOVA P value
n	372	294	134	
LVMI (g/m $^{2.7}$)	29.7±0.3	28.2±0.4*	29.6±0.6	0.02
LVRI	1.52±0.02	1.48±0.02	1.60±0.03*	0.005
CO (L)	3.5±0.04	3.1±0.05**	3.01±0.07**	<0.0001
TPR(mmHg/L)	29.5±0.5	33.4±0.5**	36.1±0.8**	<0.0001
AFS(kPa)	22.6±0.5	24.3±0.6*	22.2±0.8	0.04
E_w(dyne/s/cm^2 10^2)	45±1	52±2*	49±3	<0.0001

P1.13
ETHNIC DIFFERENCES IN WAVE INTENSITY AND ARTERIAL STIFFNESS IN THE CAROTID ARTERY

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Background: In comparison with Europeans (E) in the UK, Indian Asian (IA) people have a 1.5 to 2-fold elevated risk of cardiovascular disease (CVD), and the risk of stroke is more than 2-fold higher in African Caribbean (AC) people. Arterial stiffness and wave reflections influence the development of CVD. We therefore investigated whether there are ethnic differences in wave intensity and arterial stiffness that might play a role in the increased risk of CVD.
Methods and Results: 260 participants, aged 59-82years in the Southall And Brent REvisited (SABRE) population-based study had wave intensity analysis and measurement of stiffness index (β) performed in the left common carotid artery using an Aloka SSD 5500 ultrasound system (ALOKA, Japan) equipped with a 7.5MHz linear array vascular probe and a combined colour Doppler and echo-tracking system. The intensity of the forward compression wave (FCW) due to left ventricular ejection was significantly increased in IA. The peak intensity of the reflected (backward) compression wave (BCW) was significantly larger in AC. β was significantly higher in both IA and AC. The ethnic differences in the FCW and β persisted after adjustment for key CVD risk factors (Model 2).
Conclusion: Both IA and AC have adverse wave intensity and arterial stiffness patterns, independent of conventional CVD risk factors, that may contribute to the increased risk of CVD in IA and AC.

	European n=112	**Indian Asian** n=97	**African Caribbean** n=51	**ANOVA P**
FCW (W/m^2)				
Model 1	9.06±0.05	9.27±0.05**	9.05±0.07	0.009
Model 2	9.06±0.05	9.23±0.05**	9.04±0.07	<0.0001
BCW (W/m^2)				
Model 1	3.48±0.05	3.58±0.06	3.66±0.08*	0.1
Model 2	3.49±0.06	3.56±0.06	3.68±0.08	0.4
β				
Model 1	2.21±0.04	2.34±0.04*	2.50±0.06**	<0.0001
Model 2	2.22±0.04	2.33±0.04	2.47±0.06**	<0.0001

Data are presented as mean±SE and ANCOVA was performed to examine differences between ethnic groups; * = $p<0.05$, ** = $p<0.01$. Model 1: adjusted for age. Model 2: adjusted for age, sex, heart rate, height, smoking status, diabetes, hypertension and CVD.