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P37: REFERENCE VALUES OF CARDIO-ANKLE VASCULAR INDEX IN A RANDOM SAMPLE OF A CAUCASIAN POPULATION

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ARRHGEF1/RhoA SIGNALING PARTICIPATE IN AGEING-INDUCED ARTERIAL STIFFNESS AND HYPERCOAGULABILITY

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The RhoA signaling pathway is a master regulator of mechanotransduction and plasticity of vascular smooth muscle cells (VSMCs) that controls arterial stiffening. The RhoA exchange factor Arhgef1 is causally involved in the development of angiotensin II-dependent hypertension.

Our aim was to determine whether Arhgef1 plays a key role in age-associated arterial stiffness and the coupling with modifications of the procoagulant properties of blood and VSMCs. We used 65 week-old transgenic mice invalidated for Arhgef1 (Arhgef1^{-/-}) and age-matched controls (Arhgef1^{+/+}). In vivo arterial diameter pressure, distensibility/arterial pressure and elastic modulus/circumferential stress curves at the level of carotid artery were recorded using an echotracking system (VEVO 770 Visualsonics Imaging) in anesthetized animals.

Systolic blood pressure, pulse pressure and heart rate were not different between mutant and control mice. Isobaric carotid distensibility was increased in Arhgef1^{-/-} mice compared to Arhgef1^{+/+} mice. The elastic modulus/circumferential stress curves were shifted significantly rightwards in Arhgef1^{-/-} mice compared to Arhgef1^{+/+} mice. Thrombin generation in blood and at the surface of VSMCs cultured from aorta was reduced in Arhgef1^{-/-} mice. Anticoagulant markers secreted by the vascular wall (tissue factor pathway inhibitor and thrombomodulin) were increased in plasma of Arhgef1^{-/-} mice.

The time of formation of an occlusive thrombus induced by FeCl₃ in the carotid artery was prolonged in Arhgef1^{-/-} mice.

In conclusion, the Arhgef1/RhoA contractile pathway contributes to arterial stiffening and VSMC procoagulant properties in aging. Whether this reduced procoagulant properties of the vascular wall is a cause or consequence of arterial stiffness remains to be elucidated.

Poster Session I – Epidemiology

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SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS AND AGE-DEPENDENT ARTERIAL STIFFENING IN GENERAL POPULATION BASED PROSPECTIVE STUDY

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Background: Accumulation of advanced glycation end-products (AGEs) is one of pathophysiological processes, responsible for progressive stiffening of vessel wall. In contrast, soluble isoform of receptor for AGEs (sRAGE) act as "decoy" and physiological defense against circulating AGEs. We hypothesized that low levels of sRAGE might be associated with accelerated age-dependent arterial stiffening.

Methods: We followed 429 population-based subjects (mean age 50.8 (±11.7) years, 41.5% males) in prospective study. Aortic pulse wave velocity (aPWV) was measured using a Sphygmocor device. sRAGE concentrations were assessed in frozen samples by ELISA methods (R&D Systems). Baseline examination was done in 2008/9, while follow-up visit in 2016/17 (median time of follow-up was 7.6 years)

Results: Mean intra-individual increase of aPWV during follow-up was 1.37 (±1.88) m/sec and was inversely associated with baseline sRAGE concentration – the aPWV difference [follow-up minus baseline] across its quintiles was 2.08(±1.89), 1.51(±2.16), 1.20(±2.10), 0.99(±1.70), 1.13(±1.21) in 1st–5th quintiles of sRAGE, resp.; p = 0.003 (adjusted for age, gender and baseline mean arterial pressure) Baseline concentration of sRAGE <917 pg/mL (1st quintile) was associated with about two-fold higher risk, that aPWV increased by more than 0.8 m/sec (expectable "secular" age-dependent increase) even if adjusted for baseline risk profile and pharmacotherapy [fully adjusted odds ratio was 1.95 (95%CI: 1.12–3.39, p = 0.018)].

Conclusions: Low concentration of circulating sRAGE was in our sample of generally healthy subjects associated with markedly accelerated age-dependent arterial stiffening, probably as a consequence of higher deposition of

AGEs in vessel wall (supported by SVV 02684, PROGRES Q39 and AZV 15-27109 grants).

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PULSE PRESSURE AMPLIFICATION AND ITS RELATIONSHIP WITH AGE IN YOUNG, APPARENTLY HEALTHY BLACK AND WHITE ADULTS: THE AFRICAN-PREDICT STUDY

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Background: Pulse pressure amplification (PPA), i.e. the amplification from central arteries to the periphery, is inversely related to arterial stiffness, organ damage and mortality. It is known that arterial stiffness is higher in black than white populations, but it is unclear if this is due to early vascular aging. We therefore investigated whether PPA declines earlier in young normotensive black South Africans, when compared to their white counterparts.

Methods: We included 875 black and white men and women from the African-PREDICT study (55% black, 41% men), aged 20–30 years, with no prior diagnosis of chronic disease, screened for normotensive clinic blood pressure (BP). We determined supine central PP (cPP), and supine brachial systolic – and diastolic BP, from which brachial PP (bPP) was calculated. PPA was defined as the ratio of the amplitude of the PP between these distal and proximal locations (bPP/cPP).

Results: We found the mean PPA to be lower in black compared to white participants (1.43 vs. 1.46; P = 0.013). In black adults PPA declined earlier with increasing age (P-trend < 0.001), with a weak trend in whites (P = 0.063) after adjustment for sex, socio-economic status, height and mean arterial pressure. In multivariable-adjusted regression, we found an independent inverse association between PPA and age only in the black group (β = -0.22, P < 0.001).

Conclusion: PPA declines earlier with age in normotensive black adults younger than 30 years, exemplifying early vascular aging which may predispose black individuals to future cardiovascular outcomes.

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REFERENCE VALUES OF CARDIO-ANKLE VASCULAR INDEX IN A RANDOM SAMPLE OF A CAUCASIAN POPULATION

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Objectives: Cardio-ankle vascular index (CAVI), a parameter of arterial stiffness, has been increasingly used for cardiovascular risk estimation. Currently used CAVI reference values are derived from the Japanese population. It is not clear whether the same reference values can be used in the Caucasian population. The aim of the present study was to describe cardiovascular risk factors influencing CAVI and to establish CAVI reference values.

Methods: 2160 individuals randomly selected from the Brno city population aged 25–65 years were examined. Of these, 1347 subjects were free from cardiovascular disease, non-diabetic and untreated by antihypertensive or lipid-lowering drugs, forming the reference value population. CAVI was measured using the VaSera VS-1000 device.

Results: At each blood pressure (BP) level, there was a quadratic association between CAVI and age, except for a linear association in the optimal BP group. While there was no association between BP and CAVI in younger subjects, there was a linear association between CAVI and BP after 40 years of age. Reference values by age and gender were established. In each age group, except for the male 60–65 group, reference values in our population were lower than in the Japanese one with the difference ranging from –0.29 to 0.21 for males, and from –0.38 to –0.03 for females.

Conclusion: This is the first study providing CAVI reference values in a random sample of the Caucasian population. Our results suggest that the currently used values slightly overestimate CAVI in younger Caucasian, possibly underestimating cardiovascular risk.

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ASCENDING AORTA DIMENSIONS AND CLINIC AND 24 HOURS BLOOD PRESSURE IN A GENERAL POPULATION IN NORTHERN ITALY: THE VOBARNO STUDY

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Background: Epidemiological studies have suggested that even mild enlargement of the ascending aorta may have independent prognostic significance for cardiovascular events.

Therefore, some Authors have proposed that dilatation of the ascending aorta could be considered as a form of preclinical vascular damage in hypertensive patients.

Aim: To assess the correlation between clinic and 24 hours BP values and the dimensions of the aorta, measured at level of the sinuses of Valsalva (Val), at the left ventricular outflow tract (LVOT), and at the level of the proximal ascending aorta (AscAO) in subjects from a general population.

Methods: 250 subjects (43% males, mean age 56 ± 4 years, 42% hypertensives-HT) underwent laboratory examinations, clinic and 24 hours BP measurement, cardiac and carotid ultrasound, carotid-femoral pulse wave velocity measurement (AoPWV).

Results: aortic diameters were greater HT as compared to NT (Val: 3.41 ± 0.54 vs 3.25 ± 0.41 cm, LVOT 2.10 ± 0.28 vs 2.04 ± 0.26 , AscAo 3.39 ± 0.45 vs 3.18 ± 0.38 , all $p < 0.05$). Aortic diameters were all correlated to clinic and 24 hours BP values. The coefficients of correlation were greater for 24 hours BP (Tab). Val, AscAo, LVOT were also significantly correlated with left ventricular mass ($r = 0.61$, $r = 0.48$, and $r = 0.43$, all $p < 0.001$), mean max intima media thickness ($r = 0.13$, $r = 0.24$, and $r = 0.13$, all $p < 0.05$) and with AoPWV ($r = 0.16$, $p < 0.05$, $r = 0.28$ $p < 0.001$, $r = 0.08$ $p = ns$).

	Ao Valsalva		Asc		LVOT	
	r	p	r	p	r	p
SBP	0.148*	0.019	0.161*	0.016	0.135*	0.037
DBP	0.253**	0.0001	0.223**	0.001	0.189**	0.003
MBP	0.220**	0.0001	0.175**	0.006	0.208**	0.002
PP	–0.046	0.470	0.004	0.948	0.003	0.968
HR	–0.005	0.933	–0.028	0.687	–0.004	0.949
SBP 24 hrs	0.231**	0.0001	0.162*	0.017	0.108	0.097
DBP 24 hrs	0.346**	0.0001	0.264**	0.0001	0.234**	0.0001
MBP 24 hrs	0.267**	0.0001	0.214**	0.002	0.164*	0.011
PP 24 hrs	–0.003	0.962	–0.031	0.645	–0.082	0.209
HR 24 hrs	–0.058	0.370	–0.051	0.454	–0.026	0.687

Conclusions: The dimensions of the proximal ascending aorta are significantly related to BP values in normotensive subjects and in hypertensive patients. Aortic dimension are more strictly related to twenty-four hours BP values than to clinic BP values. In this sample of general population, a significant correlation between aortic dimensions and measures of cardiac and vascular organ damage was also observed, confirming the parallelism between different forms of organ damage.

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LEFT VENTRICULAR STRUCTURE AND FUNCTION IN RELATION TO PERIPHERAL AND CENTRAL BLOOD PRESSURE IN A GENERAL POPULATION

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Background: Central blood pressure (BP) is a predictor of target organ damage. No previous study addressed the question to what extent central compared with peripheral is related to left ventricular (LV) structure and function in a general population.

Methods: In 577 Flemish recruited from the general population (47.8% women; mean age 50.5 years), we assessed the multivariable-adjusted associations of echocardiographic LV structure and systolic and diastolic LV function (Vivid7 Pro device; EchoPac software, version 4.0.4; GE Vingmed, Horten, Norway) with peripheral and central pressure, as recorded by radial applanation tonometry (SphygmoCor software, version 9.0). Association sizes were expressed per 15/10 mmHg increment in peripheral or central systolic/diastolic BP.

Results: Peripheral compared with central systolic BP was 10.2 mm Hg higher ($P < 0.0001$), whereas diastolic BP was similar peripherally and centrally ($P = 0.50$). Associations were closer ($P \leq 0.020$) with central than peripheral systolic BP for LV mass (+0.59 g/m²) and left atrial volume (+0.29 ml/m²) indexed to body surface area, peak A transmitral flow (+0.12 cm/s), peak e' mitral annular movement (–0.18 cm/s) and the E/A ratio (–0.017). Associations were closer ($P \leq 0.038$) with central than peripheral diastolic BP for left atrial volume index (+0.289 ml/m²), e' (–0.123 cm/s) and E/e' (+0.094). Ejection fraction and global longitudinal strain were similarly associated with central and peripheral systolic ($P \geq 0.62$) and diastolic ($P \geq 0.18$) BP.

Conclusions: In asymptomatic people recruited from the general population, LV mass and atrial volume indexes and selected haemodynamic measurements reflecting diastolic LV function are slightly but significantly closer associated with central than peripheral BP.

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DOES ARTERIAL AGEING DIFFER BETWEEN EUROPEANS AND JAPANESE AND KOREAN PATIENT SAMPLES? RESULTS FROM CURRENT UK STUDIES

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Objective: Vascular stiffness has long been linked with the ageing process. However, it is only since the development of accurate methods for measuring arterial compliance that unravelling this relationship has become possible. Arterial stiffening over time appears to differ between ethnic groups and/or geographic areas. We investigated how the cardio-ankle vascular index (CAVI) varied with chronological age to make initial comparisons of its change with age between this European study and published data from Japanese and Korean patient populations.

Method: 312 participants (180 men, 132 women), age 63.7 ± 12.9 (mean \pm SD), range 25–92 years. The following were measured: CAVI using VaSera VS-1500N® (Fukuda Denshi, Japan); brachial BP using OMRON705-IT; baseline characteristics and physical examination of cardiovascular health. These data are from current UK studies of healthy volunteers with approximately 20% having two or more cardiovascular risk factors.

Results: CAVI was significantly correlated with age ($r = 0.63$, $p < 0.001$), more closely in men ($r = 0.71$, $p < 0.001$) than women ($r = 0.54$, $p < 0.001$). These data were used to create a preliminary set of 'usual' average CAVI values for each age category (Table) and compared against data from Japan [1] and Korea [2] (plot 1 & 2). Korean men had lower CAVI values at each age.