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P13
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

P35
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).

P36
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 ($\beta = -0.22$, 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.

P37
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.