P8: PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 LEVELS AND ARTERIAL FUNCTION

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However, stress failed to affect significantly neurogenie contractions of SMA elicited by electrical stimulation of peripheral sympathetic nerves and vasoconstriction induced by exogenous noradrenaline in SMA.

Conclusion: In conclusion, chronic social stress can accelerate the development of hypertension in SHR, which seems to be associated with NO-independent endothelial dysfunction in small resistant arteries. Supported by the grants VEGA No. 2/0190/17 and APVV-16-0263.

P5 ERYTHROCYTE DEFORMABILITY AND NITRIC OXIDE PRODUCTION IN ANIMAL MODEL OF PRIMARY HYPERTENSION AND THEIR AGE-DEPENDENT CHANGES
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Objectives: Reduced deformability of red blood cells (RBC) plays an important role in etiology of various diseases including cardiovascular. The nitric oxide (NO) was identified as one of factors responsible for maintenance of RBC deformability. Reduced bioavailability of NO might be important in the pathogenesis of hypertension. The aim of present study was to determine the effect of hypertension and aging on RBC deformability and NO production of experimental animals.

Methods: Spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto (WKY) rats were divided into 6 groups according to age (7, 20 and 52 weeks) and strain: SHR-7, SHR-20, SHR-52 and WKY-7, WKY-20, WKY-52. Blood was used for determination of RBC deformability using filtration method and NO production in RBCs using fluorescent NO probe DAF-2 DA.

Results: We found reduced deformability at WKY-52 and SHR-52 as compared to strain-matched 20-week-old animals. Strain-related differences in deformability were observed at 7 and 52 weeks of age, where the SHR-7 had reduced deformability and the SHR-52 had increased deformability as compared to age-matched WKY. We have found that at younger age, deformability and NO production in RBCs was able to increase, while in the older age there was a decrease in both parameters.

Conclusions: Changes in the RBC deformability under hypertensive conditions are unlikely to be related to changes in NO production. On the other hand, age-related changes in deformability of both, WKY and SHR are at least partially associated with changes in NO production. Supported by grants VEGA 1/0032/14 and Slovak Society of Cardiology.

P6 ANGIOTENSIN AT2 RECEPTOR AGONIST, COMPOUND 21, MAINTAINS VASCULAR INTEGRITY AND PREVENTS ABDOMINAL AORTIC ANEURYSM PROGRESSION IN THE RAT
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The effects of the selective angiotensin AT2 receptor agonist, compound 21 (C21), on abdominal aortic aneurysm (AAA) formation were investigated in nonobese Wistar rats. AAA was induced by perfusion of isolated aortic segments with elastase (Anidjar/DOBrin model). Treatment with C21 (0.03 and 0.3 mg/kg daily) was started after surgery and continued for 14 days. Sham operated animals and vehicle-treated animals after aneurysm induction (AI) served as controls. Hemodynamic parameters, protein expression of IL1 beta, NF kappa B, MMP9, TGF-beta1 and MLKL in the aorta was significantly (p < 0.05) down-regulated in the C21 group compared with vehicle. In primary rat vascular smooth muscle cells, the release of MMP9, TGF-beta1 and MLKL was significantly diminished after C21 (1μM) treatment. Serum concentration of TGF-beta1 was also decreased by C21 in comparison to vehicle (p < 0.01).

In conclusion, AT2 receptor stimulation with C21 prevented extracellular matrix degradation, maintained vascular integrity of the aorta and prevented AAA progression.

P7 THE URINARY PEPTIDOMIC SIGNATURE OF AORTIC STIFFNESS REVEALS MOLECULAR PATHWAYS AND DRUG TARGETS
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Background: Molecular pathways leading to stiffening of the central arteries are poorly understood. We searched for differentially expressed proteins by urinary peptidomic analysis in patients with arterial stiffness and healthy controls in a case-control study.

Methods: To identify urinary peptides associated with aortic stiffening, we applied capillary electrophoresis coupled to mass spectrometry. We compared 18 cardiovascular disease-free patients with carotid-femoral pulse wave velocity (PWV > 10 m/s standardized to a heart rate of 75/min-1 as measured by the SphygmoCor method) with 18 controls matched for sex, age and mean arterial pressure.

Results: 69 urinary peptides had a different signal amplitude between cases and controls (P < 0.049). Among 33 peptides with known sequence, 26 were members of the extracellular matrix family, including collagen type I, II, V and VIII.

Conclusion: Matrix-related differences in peptide expression were observed between cases and controls. Atherosclerosis signalling pathways and intracellular proinflammatory activation were the top pathways associated with increased PWV. Potential drug targets included collagen type IV (α3 and transforming growth factor β 3. Angiotensin-converting enzyme inhibitors, which are widely used for vascular protection, were among the possible therapeutic agents.

Conclusions: We suggest that stiffening of large elastic arteries involves changes of the extracellular matrix, as reflected by collagen turnover and regulation of myoblast differentiation. Pathway analysis identified potential drug targets, possibly amenable by angiotensin-converting enzyme inhibition.

P8 PROTEIN CONVERTASE SUBLISILIN/KEKIN TYPE 9 LEVELS AND ARTERIAL FUNCTION
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Purpose/Background/Objectives: Proprotein convertase subtilisin/kecin type 9 (PCSK9) levels are modestly but significantly associated with increased risk of total cardiovascular events. Aortic stiffness and wave reflections are also important predictors of cardiovascular events. The aim
of this pilot study was to determine if PCSK9 levels are associated with aortic elastic properties in patients with familial dyslipidemia.

**Methods:** Thirty-three patients with familial dyslipidemia (mean age 45 ± 12 years, 21 men, 14 with heterozygous familial hypercholesterolemia and 19 with familial combined hyperlipidemia) without known cardiovascular disease were enrolled. PCSK9 levels were measured with ELISA. Aortic stiffness was assessed with carotid-femoral pulse wave velocity (cfPWV) and wave reflections were assessed with aortic augmentation index corrected for heart rate (Alx@75). High-sensitivity C-reactive protein (hsCRP) levels were determined as a marker of subclinical inflammation.

**Results:** There was a positive correlation between Alx@75 and PCSK9 levels (r = 0.371, p = 0.034). (Figure) No association was found between levels PCSK9 and cfPWV (r = 0.043, p = 0.813) or hsCRP (r = 0.199, p = 0.274). In multivariate regression analysis, after adjustment for potential confounders such as age and sex, Alx@75 showed a significant positive correlation with PCSK9 levels (Adjusted R² = 0.23, p = 0.007). Even after further adjustment for possible confounders such as the type of familial dyslipidemia, low-density lipoprotein levels, cfPWV and hsCRP this association remained statistically significant (Adjusted R² = 0.16, p = 0.03). Gender was also significantly associated with levels of PCSK9 (p = 0.029).

**Conclusions:** In a group of patients with familial dyslipidemia PCSK9 levels were positively associated with wave reflections but not aortic stiffness.

**P9**

**THE PARTICIPATION OF NITRIC OXIDE AND HYDROGEN SULPHIDE SIGNALISATION IN VASOACTIVE RESPONSES OF RAT THORACIC AORTA IN CONDITION OF DEVELOPED SPONTANEOUS HYPERTENSION**

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**Background:** Nitric oxide (NO) and epoxyeicosatrienoic acids (EETs) regulate arterial wall viscosity (AWV) in young subjects (1). During hypertension, characterised by a decrease in endothelium-derived NO and an early disappearance of EETs, AWV is not modified (2,3). We compared the role of NO and EETs in the regulation of AWV in 18 middle-age untreated hypertensive patients (HT) vs. 14 matched normotensive controls (NT).

**Methods:** Radial artery diameter and pressure were measured before and after infusion of L-NMMA, fluconazole or both. AWV was estimated by the ratio of the area of the hysteresis loop of the pressure-diameter relationship (WV, viscous energy dissipated) to the area under the loading phase, bounded by pulse pressure and diameter (WE, elastic energy stored).

**Results:** At baseline, WV and WE were higher in HT than in NT (WV: 0.71 [0.65–1.19] vs. 0.45 [0.40–0.62] mmHg.mm², p < 0.05; WE: 1.99 [1.45–2.61] vs. 1.09 [0.96–1.54] mmHg.mm², p < 0.01) but WV/WE were similar (40.3 ± 7.1% vs. 40.5 ± 5.9%). In NT, fluconazole and L-NMMA decreased diameter, but did not modify WV, WE and WV/WE. L-NMMA + fluconazole decreased diameter and increased WV/WE (38.9 ± 8.5% to 47.5 ± 8.9%, p < 0.05) due to an increase in WV (+27.1 ± 57.5%) as compared to WE (–1.3 ± 27.8%) (p < 0.05). In HT, whereas fluconazole had no effect on diameter, WV and WE, L-NMMA and L-NMMA + fluconazole decreased these parameters (p < 0.05) without change in WV/WE.

**Conclusion:** In NT, NO and EETs regulate AWV of conduit arteries. Conversely, in HT associated to an increased elastic energy stored, NO regulates elastic work but not AWV that remains stable. Whether this represents an optimal adaptation remains to be investigated.

**References**