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P8.09: 25-HYDROXYVITAMIN D MAY CONTRIBUTE TO DIFFERENCES IN ARTERIAL STIFFNESS AND ENDOTHELIAL FUNCTION IN HEALTHY AFRICAN AMERICANS COMPARED TO EUROPEAN AMERICANS

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isoform in vascular smooth muscle is PMCA4 however its effect on arterial constriction is unclear. Here, PMCA4 ablated mice (KO^{-/-}) and a novel specific PMCA4 inhibitor, AP2 were used to study effects of PMCA4 on arterial contractility. Vascular constrictor responses to 100mM potassium & noradrenaline (1x10⁻⁶M-3x10⁻⁵M) of isolated, pressurised mesenteric arteries from male PMCA4 KO^{-/-} and wild type, (WT^{+/+}) mice were determined by myography. Effects of acute PMCA4 inhibition with AP2, nitric oxide synthase (NOS) inhibition with N_ω-Nitro-L-arginine (LNNA) & neuronal NOS inhibition (nNOS) with Vinyl-L-Nio were also investigated. PMCA4 ablation had no effect on the magnitude of constrictions to 00mM K⁺ (KO^{-/-} 53.2% ± 3.5 n=11; WT^{+/+} 56.3% ± 3.6 n=14) or noradrenaline (KO^{-/-} 59.5% ± 4.7 n=11; WT^{+/+} 58.2% ± 2.5 n=14). PMCA4 inhibition with AP2, significantly attenuated constriction to noradrenaline in arteries from WT^{+/+} mice (70.6% ± 3.4 n=8 and 63.8% ± 2.6 n=10 in the absence and presence of AP2 respectively) but had no effect on KO^{-/-} mice arteries. Inhibitory effects of AP2 were reversed in arteries by NOS inhibition with LNNA (AP2 treated 61.8% ± 4 n=8; AP2+LNNA treated 69.2% ± 1.7 n=10) and also by nNOS inhibition with Vinyl-L-Nio (AP2 61.8% ± 4 n=8; AP2+Vinyl-L-Nio 75.2% ± 1.3 n=5). Therefore, PMCA4 inhibition with AP2 reduces vascular constriction by a nNOS-dependent mechanism. Ablation and acute inhibition of PMCA4 have different effects on mouse mesenteric arterial contractility.

P8.05 REACTIVE HYPEREMIA INDEX AND DETECTION OF ENDOTHELIAL DYSFUNCTION IN PAEDIATRIC HEMATO/ONCOLOGY PATIENTS

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Objective: The aim of our study was to evaluate endothelial dysfunction (ED) in children following treatment for acute lymphoblastic leukemia (ALL) in comparison with healthy controls (HC) and to correlate Reactive Hyperemia Index (RHI) with anthropometric and biochemical parameters.

Research design and methods: As part of new non-invasive plethysmographic technique, an EndoPAT 2000[®] recorder was used for the determination of RHI by measuring postocclusive endothelium-dependent changes in vascular tone (PAT) in subjects fingertips. There were also assessed plasma levels of selectin, ADMA, hsCRP, sVCAM as biochemical markers of ED in ALL children and reference controls. Meeting the including criteria 40 eligible study participants were enrolled in the study. A group of 28 ALL patients were matched with control group of 12 healthy children (HC).

Results: Significantly lower RHI were revealed in ALL patients in comparison with HC (1.57±0.50, 1.96±0.63; p<0.05) respectively, implying impaired endothelial-dependent dilation. Furthermore, significantly elevated plasma levels of selectin and hsCRP were found in ALL patients when compared to HC supporting the theory of premature endothelial dysfunction in high risk group of children. There were discovered no correlations between RHI and biochemical parameters of ED.

Conclusion: Our study demonstrated that ALL patients might have impaired endothelial dysfunction, which is associated with high risk of premature atherosclerosis manifestation. RHI is a promising non-invasive method for the assessment of ED in children with high risk of premature atherosclerosis. This work was supported by the Charles University Student Research Project SVV-2010- 260805.

P8.07 ASSESSMENT OF ENDOTHELIAL FUNCTION AND ARTERIAL STIFFNESS IN PATIENTS WITH GENETICALLY CONFIRMED FAMILIAL HYPERCHOLESTEROLEMIA WITHOUT PREVIOUS CARDIOVASCULAR EVENTS

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Purpose: The purpose of this study was assessment of endothelial function and arterial stiffness parameters in subjects with familial and non-familial hypercholesterolemia.

Methods: We studied endothelial function and arterial stiffness in 60 subjects (mean age 41.9±7.7 years): 20 patients with elevated LDL and genetically confirmed familial hypercholesterolemia; 20 patients with elevated LDL without mutations causing FH; 20 healthy controls with normal LDL. All study subjects were without previous cardiovascular events and had no symptoms of cardiovascular diseases. High-resolution ultrasound was

used to determine flow-mediated dilation in the brachial artery. Echo-tracking and photoplethysmography technique were used for assessment of the arterial stiffness parameters.

Results: FMD was significantly lower in patients with FH and in all patients with elevated LDL compared with controls (10.5±9.6% vs 21±14.3%, p<0.05; 12.5±10 vs 21±14.3%, p<0.05). There were no differences in arterial stiffness parameters in all groups. Significant correlation between FMD and arterial stiffness parameters measured with used echo-tracking methods were noted. There were no significant correlations between echo-tracking and photoplethysmographically assessed arterial stiffness parameters.

Conclusions: Reduced FMD in FH patients may be due to endothelial dysfunction. No significant differences in arterial stiffness parameters show that atherosclerosis is not advanced in patients with hypercholesterolemia. Significant correlations between ultrasonographically assessed arterial stiffness parameters and endothelial dysfunction show that echo-tracking methods can be used for early detection of arterial remodeling in patients with hypercholesterolemia. FMD can be used for early detection of endothelial dysfunction preceding atherosclerotic process in patients with FH without significant cardiovascular disease.

P8.08 THE RELATIONSHIP BETWEEN BRACHIAL ARTERY FLOW-MEDIATED DILATION AND SHEAR RATE IN INDIVIDUALS WITH INCREASED CARDIOVASCULAR RISK

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Brachial artery flow-mediated dilation (baFMD) is a frequently-used technique to assess endothelial function. Although shear rate (SR) is currently considered as a determinant of baFMD, a previous study in healthy humans found that the relationship between baFMD and SR was not evident in older adults. Furthermore, the relationship has not been studied in individuals with increased cardiovascular (CV) risk. The purpose of this study was to examine the relationship between FMD and estimated SR stimulus in middle-aged and older adults with increased CV risk. Data from 2 groups [37 individuals with increased CV risk (history of recent stroke or transient ischemic attack, presence of hypertension and type2 diabetes, 68.9±9.1 yrs, 6F), and 17 apparently healthy individuals (64.2±4.6 yrs, 12F)] were compared. baFMD was assessed using a 5-min forearm occlusion method. Diameter and blood velocity data obtained by a Doppler ultrasound machine were used for the calculation of baFMD and SR using semi-automated edge detection software. In the increased CV risk group, baFMD was significantly correlated with baseline SR (r=0.52), peak SR (r=0.62), and SR area under the curve until time to peak dilation (r=0.62, all p<0.05), whereas no SR indices were associated with baFMD in the healthy group. Multivariate analysis revealed that age and baseline diameter were independent determinants of baFMD in the pooled data set (R²=0.322). These findings suggest that in individuals with increased CV risk baFMD is correlated well with SR stimulus. The significance of the association between SR stimulus and baFMD in this population requires further investigation.

P8.09 25-HYDROXYVITAMIN D MAY CONTRIBUTE TO DIFFERENCES IN ARTERIAL STIFFNESS AND ENDOTHELIAL FUNCTION IN HEALTHY AFRICAN AMERICANS COMPARED TO EUROPEAN AMERICANS

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Vascular function is reportedly influenced by vitamin D and is worse in African Americans (AAs) relative to European Americans (EAs). Reasons remain unclear especially if ethnic differences in 25-hydroxyvitamin D [25(OH)D] levels mediate differences in vascular function. This prospective study investigated the relationships of serum 25(OH)D with indices of vascular function among 45 healthy, 18-50 yo AA and EA adults. The main outcomes were augmentation index (AIx75), central aortic pressure, pulse wave velocity (PWV), flow-mediated dilation (FMD), and seated and supine blood pressures. Results showed that 25(OH)D was inversely associated with AIx75, supine systolic blood pressure (SBP), central aortic SBP and central aortic diastolic blood pressure (DBP), independent of age, sex, and percent body fat (P<0.05 for all). 25(OH)D was associated with AIx75, PWV and FMD (P=0.05 to 0.08) among AAs, but not EAs (P=0.44 to 0.96). AAs had greater

Aix75 ($P=0.04$) and PWV ($P=0.07$) and lower FMD ($P=0.02$). The relationship between age and PWV was significant in low 25(OH)D versus normal 25(OH)D status. In conclusion, 25(OH)D may have favorable effects on vascular function, particularly AAs, and lower 25(OH)D among AAs may contribute to their greater arterial stiffness and endothelial dysfunction. Furthermore, adequate vitamin D levels may attenuate age-related increases in arterial stiffness.

P8.10

THE PATIENTS WITH ISCHEMIC STROKE IN THE POSTERIOR CIRCULATION TERRITORY HAVE IMPAIRED ENDOTHELIAL FUNCTION AND CEREBROVASCULAR REACTIVITY

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²the Russian Medical Academy of the Postgraduate Education, Moscow, Russian Federation Impaired endothelial function (EF), cerebrovascular reactivity (CVR) and atherosclerosis can all play a role in the ischemic stroke (IS) pathogenesis

The aim was to assess EF, CVR and intima-media thickness (IMT) in patients with IS in the posterior circulation territory (PCT).

Methods: The study population consisted of 13 patients with IS (without atrial fibrillation) in PCT (72 hours after stroke onset). For these subjects, EF and CVR were compared against an age and gender-matched group consisting of 10 healthy individuals (control group, CG). EF was assessed using the brachial flow-mediated vasodilatation (FMD). Breath-holding test (CVR_{BHT}=test/baseline mean velocity) and hyperventilation (CVR_{HV}=baseline/test mean velocity) were used for CVR evaluation in basilar artery (using transcranial Doppler).

Results: We observed a significant difference in FMD between IS patients and CG ($5.45\pm 0.9\%$ and $8.97\pm 1.37\%$ respectively, $p=0.04$). IS patients and CG differed in CVR_{BHT} (1.25 ± 0.49 and 1.44 ± 0.6 respectively, $p=0.04$), no difference was detected in CVR_{HV} (1.5 ± 0.33 and 1.36 ± 0.8 respectively, $p>0.05$). IMT was similar for IS patients and CG ($0.95\text{mm}\pm 0.12$ and $0.91\text{mm}\pm 0.1$ respectively, $p>0.05$). Correlation analysis revealed significant interrelationships between FMD and CVR_{BHT} ($r=0.38$); no significant correlations were found between FMD and CVR_{HV}.

Conclusion: Patients with IS in PST showed impaired EF and CVR (vasodilatation reaction), both being strong indicators of stroke development. The significant correlation between these parameters is a sign that vasodilatation of brain arterioles can be at least partially mediated by the endothelium. The absence of any significant differences in IMT is an evidence of equal prevalence of atherosclerosis among general population.

P8.11

ENDOTHELIAL FUNCTION IS DECREASED IN PATIENTS WITH LACUNAR ISCHEMIC STROKE AND INTACT IN PATIENTS WITH ATHEROTHROMBOTIC STROKE

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²Federal State Clinical Hospital #86, Moscow, Russian Federation Impaired endothelial function (EF) plays a role in pathogenesis of a small vessel disease and lacunar stroke (LS)

The aim of this study was to compare EF and cerebrovascular reactivity (CVR) in patients with LS and patients with atherothrombotic stroke (AS).

Methods: The study population consisted of 10 patients with LS (21 days after stroke onset). For these subjects, EF and CVR were compared against an age and gender-matched group consisting of 10 patients with AS. The stroke subtype was classified according to TOAST criteria. EF was assessed using the brachial flow-mediated vasodilatation (FMD). Peak shear stress was used for FMD normalization. Breath-holding test (CVR_{BHT}=test/baseline mean velocity), hyperventilation (CVR_{HV}=baseline/test mean velocity) and test with nitroglycerine (CVR_{NG}=baseline/test mean velocity) were used for CVR evaluation in middle cerebral and basilar artery (using transcranial Doppler).

Results: We observed a significant difference in FMD between LS and AS patients ($6.65\pm 0.8\%$ and $10.03\pm 1.1\%$ respectively, $p=0.03$). The difference in FMD remained after normalization ($0.011\pm 0.005\text{s}^{-1}$ and $0.018\pm 0.007\text{s}^{-1}$ respectively, $p=0.02$). However, no difference in CVR was detected between IS and AS groups (CVR_{BHT}= 1.25 ± 0.17 and 1.24 ± 0.1 , CVR_{HV}= 1.34 ± 0.24 and 1.16 ± 0.1 , CVR_{NG}= 1.08 ± 0.05 and 1.09 ± 0.1 for LS and AS patients respectively).

Conclusion: Patients with LS demonstrated impaired EF in comparison with patients with AS, however, no difference between these groups was observed in CVR. The impairment of EF in LS patients may reflect a role of endothelial dysfunction in the pathogenesis of LS.

P8.12

GENETIC INFLUENCES ON THE RELATION BETWEEN EXHALED NITRIC OXIDE AND ARTERIAL STIFFNESS: A TWIN STUDY

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Objectives: Fractional exhaled nitric oxide (FE_{NO}) has an important physiological role in the airways and vessel walls.

Methods: 117 adult twin pairs were recruited in Hungary, Italy and in the United States (83 monozygotic and 34 dizygotic pairs; age 48 ± 16 years). FE_{NO} was measured by an electrochemical sensor-based device and markers of arterial stiffness (augmentation index on brachial artery, Aix_{bra} and on aorta, Aix_{ao}; Pulse Wave Velocity on aorta, PWV_{ao}) by oscillometric method (TensioMed Arteriograph, TensioMed Ltd., Budapest). Bivariate Cholesky decomposition models were applied.

Results: Genetic effects accounted for 59% (95% confidence interval [CI]: 43, 71%) of the variation in FE_{NO} with the remaining 41% (95%CI: 29, 57%) due to non-shared environmental influences. Significant correlation was observed between FE_{NO} and Aix_{bra} ($r=-0.20$, 95% CI:-0.34,-0.05), or Aix_{ao} ($r=-0.19$, 95%CI:-0.33,-0.05). No significant correlation was found between FE_{NO} and PWV_{ao}. Genetic factors explained the entire phenotypic correlation between FE_{NO} and Aix_{bra} or FE_{NO} and Aix_{ao}. FE_{NO} showed a significant negative genetic correlation with Aix_{bra} and Aix_{ao} ($r_g=-0.29$, 95%CI:-0.49,-0.07).

Conclusions: Variations in FE_{NO} are explained by genetic and non-shared environmental effects. Covariances between FE_{NO} and Aix_{bra} or Aix_{ao} are explained entirely by genetic factors suggesting a remarkable overlap among the sets of genes involved in the expression of these phenotypes and providing a basis for further studies on cardiovascular and respiratory diseases.

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P8.13

INCREASED AORTIC PULSE WAVE VELOCITY IS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS BUT NOT WITH ENDOTHELIAL DYSFUNCTION IN HYPERTENSIVE PATIENTS

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Background: Increased vascular stiffness has been recently considered a marker of cardiovascular risk and a predictor of cardiac events

Objective: To compare parameters of endothelial dysfunction and carotid atherosclerosis in hypertensive patients presenting increased vascular stiffness.

Methods: A cross-sectional study was carried out to evaluate hypertensive patients, both genders, aged 30-65 years. Macro- and microcirculation parameters were evaluated with measurement of blood pressure (BP), carotid intima-media thickness (IMT), brachial flow-mediated dilation (FMD), peripheral arterial tonometry (EndoPAT), determination of aortic (carotid-femoral) pulse wave velocity (cfPWV) by Complior SP.