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### **P.047: EXAMINATION OF PRESSURE AND VOLUME PULSE WAVES**

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non-invasively by carotid-femoral pulse wave velocity (PWV) and central augmentation index (AI).

**Design:** Twenty two subjects with pheochromocytoma (PHEO), 34 subjects with essential hypertension (EH) and 40 healthy normotensive controls (C) were investigated using an applanation tonometer (Sphygmocor). Twelve patients with pheochromocytoma were studied after tumor removal.

**Results:** The gender, age, body mass index and lipid profiles were comparable among all the groups. Fasting plasma glucose levels in PHEO were higher in comparison to the other groups ( $6.1 \pm 1.7$  vs.  $EH 4.9 \pm 1.1$  vs.  $C 4.8 \pm 0.8$  mmol/l;  $p < 0.001$  for all comparisons). Brachial blood pressure values in PHEO were lower in comparison to EH ( $135 \pm 24/77 \pm 12$  vs.  $153 \pm 6/90 \pm 11$  mmHg;  $p < 0.001/0.001$ ) and higher in comparison to C ( $135 \pm 24/77 \pm 12$  vs.  $121 \pm 11/72 \pm 9$  mmHg;  $p < 0.001/n.s.$ ). The pulse wave velocity in pheochromocytoma did not differ from EH ( $7.1 \pm 1.3$  vs.  $7.3 \pm 1.5$  m.s<sup>-2</sup>, ns.) and was significantly higher than in controls ( $7.1 \pm 1.3$  vs.  $5.9 \pm 0.7$  m.s<sup>-2</sup>;  $p < 0.001$ ). No differences were found in AI among all groups. In multiple regression the only significant variables independently associated with PWV in pheochromocytoma were 24h urine norepinephrine excretion ( $\beta = 0.566$ ,  $p < 0.001$ ) and fasting plasma glucose levels ( $\beta = 0.346$ ,  $p = 0.015$ ). Successful tumor removal led to a significant decrease in PWV ( $6.9 \pm 0.8$  vs.  $5.5 \pm 0.7$  m.s<sup>-2</sup>;  $p < 0.001$ ).

**Conclusion:** Catecholamine excess in pheochromocytoma is accompanied by an increase in pulse wave velocity, which is reversed by the successful tumor removal. Pulse wave velocity in subjects with pheochromocytoma is positively associated with 24h urine norepinephrine levels and fasting plasma glucose levels.

#### Acknowledgements

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#### P.044

##### EFFECT OF MILD INCREASE OF PHYSICAL ACTIVITY ON MICROVASCULAR REACTIVITY IN OBESE SUBJECTS WITH DIABETES MELLITUS TYPE 2

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Microangiopathy, well known in diabetic patients as a cause of late complications, develops mainly due to chronic exposition to elevated glucose and triglyceride level. Physical training acts as a protective factor even if no changes in metabolic parameters are observed. It's supposed, that lifestyle modifications leads to the improvement of endothelial dysfunction and microvascular reactivity, in healthy subjects it has already been proven experimentally.

In 8 patients with type 2 diabetes mellitus was measured microvascular reactivity and perfusion of skin in lower limbs by laser-doppler flowmetry and transcutaneous oximetry. First before the study, second after 3-week's period of habitual physical activity, third after 3-week's period of mild increased physical activity and finally after next 3-week's period of habitual activity. Training intensity was objectified (non sport-practiced subjects) by pedometers. Results were evaluated by Friedman and pair Wilcoxon test.

After mild aerobic activity (walk about 800 [560 - 1400] meters/day) microvascular reactivity was increased in both tests (increase after heating from  $4,9x [4,4-5,4]$  to  $6,1x [5,7-6,8]$ ,  $p < 0.01$ , shorten half time to reach maximum perfusion from  $4,1 [2,7-5,4]$  s to  $3,1 [2,4-4,0]$  s,  $p < 0.05$ . The increased perfusion lasted after following four weeks of habitual activity in smaller extent (microvascular reactivity increase after heating  $5.2 [4.8-6.1]$  s, half time to reach maximum perfusion  $3.8 [2.7-5.0]$ , this increase was not significant in comparison with habitual activity in the first period). Metabolic and anthropometric parameters and transcutaneous oxygen tension didn't change significantly.

#### P.045

##### REVERSIBLE LEFT VENTRICULAR DYSFUNCTION AND BRAIN NATRIURETIC PEPTIDE (BNP) PLASMA LEVELS IN PATIENTS WITH TRAUMATIC BRAIN INJURY

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**Aim:** We investigated the possibility of myocardial dysfunction and pertinent alterations of BNP plasma levels in patients with traumatic brain injury (TBI).

**Patients and Methods:** This study included 30 critically care patients (20 males, mean age  $30 \pm 8$  years old) who were admitted to the intensive care unit with TBI (Glasgow Coma Scale upon admission  $< 8$ ). Patients with a previous history of cardiovascular disease, chest trauma, sepsis and/or other critical illness known to be associated with myocardial dysfunction were excluded. Left ventricular (LV) function was assessed by transoesophageal echocardiography. BNP plasma concentrations were measured in all patients. Echocardiographic and BNP measurements were performed on a weekly basis.

**Results:** Eight patients progressed towards brain death. Five patients presented global reversible LV dysfunction during the first week after the TBI, which normalized over time (within 2 weeks upon presentation). Ten patients exhibited segmental contractility disturbances during the first 2 weeks after the TBI, which normalized over time (within 4 weeks upon presentation). All the above patients presented electrocardiogram changes that normalized in line with the echocardiographic changes. The initial BNP plasma concentrations in the 15 patients with the reversible cardiovascular dysfunction were significantly increased as compared with those without cardiovascular dysfunction ( $105 \pm 53$  pg/ml vs.  $53 \pm 26$  pg/ml,  $p < 0.001$ ). BNP concentrations were positively correlated with diffuse subarachnoid hemorrhage ( $r = 0.85$ ,  $p < 0.001$ ) and poor outcome ( $r = 0.88$ ,  $p < 0.001$ ).

**Conclusion:** Reversible cardiac disturbances developed in almost 50% of patients with TBI. Increased BNP concentrations are associated with a poor outcome in the above patients.

#### P.046

##### IMPAIRED ARTERIAL ELASTIC PROPERTIES IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED NAÏVE PATIENTS. THE ROLE OF SUBCLINICAL INFLAMMATION

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**Introduction:** Subclinical inflammation has been associated with impaired arterial elastic properties. Human immunodeficiency virus (HIV) infection per se represents a model of chronic inflammation, possibly related to progression of atherosclerosis.

**Purpose:** To investigate the impact of HIV infection on arterial elastic properties in HIV naïve patients.

**Methods:** We studied 32 HIV infected naïve patients (aged 32 years, 28 males, 18 smokers) and 26 healthy individuals matched for age, sex and smoking status. Aortic augmentation index (AIx) and augmented pressure (AP) were assessed using assessment applanation tonometry of the radial artery. Carotid femoral pulse wave velocity (PWV) was estimated as an index of aortic stiffness by means of a computerized method (Complior SP).

**Results:** HIV patients compared to controls had increased levels of pulse pressure ( $52$  vs.  $44$  mmHg,  $p = 0.004$ ), while there was no difference regarding body mass index and metabolic profile. AP and AIx were significantly decreased in HIV patients ( $0.3$  vs.  $4$  mmHg,  $p = 0.01$  and  $1\%$  vs.  $12\%$ ,  $p = 0.005$ , respectively) even after correction for heart rate ( $0.6\%$  vs.  $8.3\%$ ,  $p = 0.043$ ). HIV patients and controls exhibited similar values of PWV ( $6$  vs.  $6.1$  m/s, respectively,  $p = 0.83$ ).

**Conclusions:** HIV infected naïve patients compared with controls are characterized by decreased wave reflections and similar values of large artery stiffness. Peripheral vasodilatation is suggested to be the predominant mechanism, induced probably by the chronic subclinical inflammation in this setting.

#### P.047

##### EXAMINATION OF PRESSURE AND VOLUME PULSE WAVES

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Measurements of the arterial pulse were made at the brachial, carotid, and radial artery. The pressure and volume waveforms were obtained using piezoelectric and optical sensors, respectively. The data were digitized using a digital storage oscilloscope interfaced with a personal computer. The time between velocity maxima of the two waveforms was computed after Savitzky-Golay filtering. In the absence of arterial expansion, the derivative

of the volume waveform matched the shape of the pressure waveform. Volume waveforms were found to lag pressure waveforms. Comparisons of the pressure and volume waveforms in two arms were made for different positions of the arms. Control measurements were taken with both hands at heart level. Zero time differential between the pairs of similar sensors was observed. The shapes of the pressure waveforms matched, as did those of the volume waveforms. As one arm was extended vertically, a time differential between the pressure waveforms and the volume waveforms appeared, with the pulse observed later in the extended arm. The time differential between the pressure and volume sensor on the extended arm appeared to lengthen, as did the width of the volume waveform. When the arm was returned to heart level, the shape of the volume pulse returned to normal over a maximum time of 35 seconds. When an arm was lowered, the pressure waveforms remained unchanged, but the volume waveform in the lowered arm was observed prior to the arrival of the volume waveform in the control arm.

#### P.048

##### IDENTIFYING ASSOCIATIONS OF REDUCED ADIPOSITY AND IMPROVED EARLY MARKERS OF ATHEROSCLEROSIS FROM A LIFESTYLE INTERVENTION AIMED AT OVERWEIGHT ADOLESCENTS

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**Purpose:** Overweight adolescents have increased early markers of atherosclerosis (flow-mediated dilation [FMD], carotid intima-media thickening [CIMT], pulse wave velocity [PWV]). We sought to identify associations of reduced adiposity (body mass index z-score [BMIz]) and improvement in these early markers over a 24-week diet-activity-behavior intervention.

**Methods:** N = 32 subjects (BMI >85<sup>th</sup>ile, age 12-16 years) underwent vascular, lipid and glycemic assessments at baseline and 24 weeks. Univariate models evaluated associations of changes in markers with patient characteristics at baseline.

**Results:** After intervention, there was a significant reduction in BMIz ( $-0.09 \pm 0.04$ ,  $p=0.05$ ) and increase in HDL cholesterol ( $0.10 \pm 0.02$  mmol/L,  $p=0.001$ ), but non-significant improvements in CIMT ( $-0.005 \pm 0.004$  mm,  $p=0.16$ ), FMD ( $0.25 \pm 0.68$  %,  $p=0.72$ ) and PWV ( $-0.24 \pm 0.13$  m/sec,  $p=0.08$ ). Greater reduction in adiposity was associated with, at baseline, more episodes/week of vigorous activity ( $-0.05 \pm 0.03$  BMIz per 1 episode/week increase,  $p=0.04$ ), and more hours/day screen time ( $-0.06 \pm 0.03$  BMIz per 1 hour/day increase,  $p=0.03$ ). Improved CIMT was associated with, at baseline, more high-fat or high-sugar food servings/day ( $-0.002 \pm 0.001$  mm per 1 serving/day increase,  $p=0.05$ ). Improved FMD was associated with, at baseline, lower fasting insulin ( $0.03 \pm 0.01$  % per 1 unit insulin decrease,  $p=0.01$ ). Improved PWV was associated with at baseline more hours/day screen time ( $-0.06 \pm 0.03$  m/sec per 1 hour/day increase,  $p=0.05$ ).

**Conclusions:** Reduction in adiposity and cardiovascular risk factors associated with our intervention may be insufficient to cause significant improvements in early atherosclerosis markers. A longer, more intensive intervention may be needed and subjects with more risk factors to target may benefit most.

#### P.049

##### THE P22PHOX -930A/G POLYMORPHISM OF NADPH OXIDASE: AN INDEPENDENT GENETIC DETERMINANT OF WAVE REFLECTIONS

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**Introduction:** Oxidative stress impairs wave reflections, which are independent markers and prognosticators of cardiovascular risk. The NADPH oxidase system maintains the redox state in the vessel wall. Recent studies have reported that the presence of allele G in the -930 polymorphic site of the p22<sup>phox</sup> NADPH subunit is associated with increased enzyme activity, while the presence of allele A accounts for reduced activity. We investigated the relation between the -930<sup>A/G</sup> polymorphism and wave reflections.

**Methods:** The study included 154 healthy individuals (102 males, mean age 40 years). The A-to-G substitution at position -930 in the p22<sup>phox</sup> promoter was typed by BbvI digestion of specific polymerase chain reaction products amplified from genomic DNA. The AA, AG and GG genotypes were determined. Augmentation index (Alx) was measured as index of wave reflections, using a validated device (SphygmoCor).

**Results:** In our population, the prevalence of AA, AG and GG genotypes was 24%, 45.5% and 30.5% respectively. Multiple linear regression analysis revealed that after adjustment for age, systolic blood pressure, heart rate, gender, BMI and HDL cholesterol, subjects with GG genotype had significantly lower values of Alx by 5.89% compared to subjects with AA genotype ( $p<0.01$ ), while subjects with AG genotype had significantly lower values of Alx by 4.77% compared to subjects with AA genotype ( $p<0.01$ ).

**Conclusion:** Our findings suggest that the -930<sup>A/G</sup> polymorphism of the p22<sup>phox</sup> promoter of NADPH oxidase is an independent determinant of wave reflections in healthy individuals. Presence of the G allele is associated with lower values of Alx.

#### P.050

##### PREDICTIVE FACTORS FOR MACRO- AND MICRO-VASCULAR COMPLICATIONS IN TYPE 2 DIABETES

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Patients with type 2 diabetes (DM2) have the extremely elevated cardiovascular risk. The aim of our cross-sectional study was to estimate the prevalence of macro- and micro-angiopathy in DM2 patients and to search out possible predictors of both angiopathies.

The sample of 415 DM2 outpatients - 217 (52%) men and 198 (48%) women, aged  $66 \pm 9$  y, average DM2 duration  $9 \pm 8$  y, was divided into 4 groups: MMC+, n = 112 (with manifest macroangiopathy), MMC-, n = 303 (without it), mmc+, n = 222 (with manifest microangiopathy) and mmc-, n = 193 (without it). All observed parameters were assessed by standard methods and evaluated by the Wilcoxon's test and the multiple logistic regression model.

Patients MMC+ suffered more often from nephropathy (66 vs 39 %,  $p<0,001$ ), neuropathy (24 vs 14%,  $p<0,05$ ) and retinopathy (18 vs 11%,  $p<0,05$ ) than patients MMC-. Independent risk factors for MMC+ development were the age over 60 y. (RR 1,09,  $p<0,001$ ), plasma glucose level  $>5,6$  mmol/L (RR 1,70;  $p<0,05$ ) and hs-CRP  $>1$ mg/L (RR 2,7;  $p<0,05$ ). Protective factors for MMC+ was the female gender (RR 0,42;  $p<0,001$ ), serum HDL-cholesterol  $>1$  mmol/L (RR 0,15;  $p<0,05$ ) and DBP  $>80$  mmHg (RR 0,40;  $p<0,01$ ). Duration of DM2  $\geq 9$  y. (RR 1,16;  $p<0,001$ ), the age  $\geq 60$ y. (RR 1,09;  $p<0,01$ ) and hs-CRP  $>1$ mg/L (RR 2,99;  $p<0,01$ ) were considered as independent predictive factors for mmc+.

Macro- and microvascular complications are associated closely in diabetic patients. Low casual DBP (below 80 mmHg) respectively high pulse pressure, high age (over 60 y.) and high hs-CRP (over 1mg/L) were considered as independent risk factors for the both angiopathies in DM2 patients.

#### P.051

##### ARTERIAL STIFFNESS IS INCREASED IN PATIENTS WITH HEPATITIS C VIRUS SEROPOSITIVITY, BUT NOT IN PATIENTS WITH HEPATITIS B VIRUS SEROPOSITIVITY AND THE ROLE OF LEPTIN

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**Background:** Recent data suggest that chronic systemic inflammation and impaired levels of adipose tissue hormones play a critical role in cardiovascular disease. Aortic stiffness and wave reflections are independent markers of cardiovascular risk. The present study was undertaken to assess whether chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) and the secondary steatosis in HCV patients affect aortic stiffness and wave reflections.

**Methods:** We studied 36 patients (mean age:  $49 \pm 15$  yrs, 16M/20F) positive for HCV chronic infection and 28 patients (mean age:  $56 \pm 11$  yrs, 19M/9F) with HBV chronic infection, who had never been treated with interferon, and 40 control subjects matched for classical risk factors. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV) and wave reflections with augmentation index (Alx) of the aortic pressure waveform. Leptin levels were measured by ELISA kit.

**Results:** Patients with HCV infection had higher PWV than controls ( $7.6 \pm 1.4$  vs.  $6.7 \pm 1.3$  m/s,  $P<0.05$ ), while Alx did not differ ( $27.5 \pm 15$  vs.  $27.1 \pm 14$ %,  $P=NS$ ). Carotid-femoral PWV and Alx in the subjects with HBV infection were similar to those in the control subjects. After adjustment for confounding factors, leptin levels ( $p<0.05$ ,  $t=4.5$ , stand. coefficient = 1) were independently associated with an increase in PWV in patients with HCV.