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P.030: ARTERIAL STIFFNESS IS PREDICTOR CARDIOVASCULAR EVENTS IN MEN WITH CORONARY ARTERY DISEASE

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Aim: Evaluating efficiency of antianginal therapy with β -adrenoblockers (BAB) in patients with stable angina during the switch to nebivolol; evaluating the dynamics of vasculature functional state and concentration of NO metabolites during the nebivolol treatment.

Materials and Methods: Open-label observational study was conducted on 30 patients with II-III FC angina. Prior to the nebivolol administration and also after 12 weeks of treatment, in addition to the evaluation of clinical state and nebivolol tolerance. The assessment of arterial stiffness was done by way of measuring brachial-ankle pulse wave velocity (baPWV). A new parameter presenting stiffness of the vascular wall independent on the BP dynamics. Endothelial function was calculated based on flow-mediated dilatation (FMD) parameters. Serum nitrate and nitrite as NO metabolic products were measured.

Results: After 12 weeks of the nebivolol therapy, the rate of anginal attacks significantly decreased by 60%, and nitroglycerin (NG) intake reduced by 75% as compared to the previous treatment. Switching the patients to nebivolol was associated with a significant decrease in baPWV by 6.1% while FDV increased by 27%. Serum level of NO metabolites increased by 47%.

Conclusion: The nebivolol treatment was generally well tolerated and lead to significant patient condition improvement. This effect of nebivolol of should be attributed to baPWV lowering and endothelial function bettering.

P.027

ARTERIAL STIFFNESS IN RELATION TO URINARY ALDOSTERONE EXCRETION AND COLLAGEN METABOLISM IN ESSENTIAL HYPERTENSION

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Background: In animal experiments, aldosterone has been shown to substantially contribute to the accumulation of collagen fibres in the arterial wall, which can increase arterial stiffness. The aim of the study was to examine the above relationships in human hypertension.

Methods: The study group included 50 hypertensive patients (mean age = 56.8 years, 16/34 M/F) and 29 normotensive controls (mean age = 54.6 years, 15/14 M/F). A Sphygmocor device was used to measure the carotid, radial and aortic augmentation index (Alx) of systolic blood pressure, as well as the aortic pulse wave velocity (PWV). 24-hour urinary aldosterone excretion was assessed. The plasma levels of collagen synthesis marker - procollagen type III amino-terminal peptide (PIIINP) were evaluated.

Results: Hypertensive patients as compared to normotensive controls had higher carotid Alx (142.8 ± 25.2 vs $124.2 \pm 24.7\%$; $p = 0.004$), higher aortic Alx (39.4 ± 10.1 vs $30.8 \pm 13.5\%$; $p = 0.005$), and higher PWV (9.57 ± 2.86 vs 8.58 ± 1.51 m/sec; $p = 0.05$). With adjustments applied for age, gender, body height, mean arterial pressure and current smoking, 24-hour urinary aldosterone excretion correlated positively with carotid Alx ($r = +0.22$; $p = 0.05$) and aortic Alx ($r = +0.19$; $p = 0.09$). We observed also positive correlations between plasma level of PIIINP and carotid Alx ($r = +0.20$; $p = 0.06$) and aortic Alx ($r = +0.24$; $p = 0.05$).

Conclusion: In our study group, aldosterone excretion tended to correlate to carotid and aortic, but not radial, augmentation index. The increased arterial stiffness in hypertensive patients could be caused by the deleterious effects of aldosterone excess on the fibrosis and remodeling of the arterial wall, as assessed by circulating PIIINP.

P.028

EPIGENETIC INTERACTION BETWEEN α -ADDUCIN AND RENIN-ANGIOTENSIN-SYSTEM GENES IN RELATION TO THE ELASTIC PROPERTIES OF THE FEMORAL ARTERY

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Background: We previously demonstrated that epigenetic interaction between the α -adducin (ADD1) Gly460Trp and the ACE I/D polymorphism modulates the properties of the femoral artery. Here, we investigated multiple-gene interactions between ADD1, ACE and other genes of the renin-angiotensin system: angiotensinogen (AGT) C-532T, G-6A, and angiotensin II receptor type 1 (AGTR1) A1166C.

Methods and results: We assessed the properties of the femoral artery with a wall-track system in a family-based random sample of 1064 subjects (participation rate 64.3%, mean age 43.6 years, 50.4% women). In population-based analyses, we computed phenotype-genotype associations, while adjusting for confounders, life style, and family clusters. In family-based analyses, we used a multivariate-adjusted quantitative transmission disequilibrium test (QTDT).

Results: In ADD1 Trp allele carriers, but not in ADD1 GlyGly homozygotes, AGTR1 AA subjects had lower femoral cross-sectional compliance (0.649 ± 0.030 vs 0.742 ± 0.029 mm²/kPa, $P = 0.027$) and a lower distensibility coefficient (10.18 ± 0.43 vs 11.27 ± 0.41 10⁻³/kPa, $P = 0.067$) than AGTR1 C allele carriers. QTDT confirmed these associations. The between-family component of phenotypic variability was not significant, suggesting that there was not population stratification. None of the gene-gene interactions involving AGT was statistically significant ($P \geq 0.088$).

Conclusions: The ADD1 Gly460Trp, AGTR1 A1166C and ACE I/D jointly influence the functional properties of the femoral artery.

P.029

MECHANICAL CHARACTERISTICS OF CAROTID ARTERY WALLS IN RELATION WITH PREVALENT CARDIOVASCULAR DISEASES

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Background: Cardiovascular diseases (CVD) modify the mechanical characteristics of arteries. A better understanding of the corresponding changes will improve diagnostic possibilities.

Methods: With a 7.5 MHz linear array ultrasound system, the left and right common carotid artery of 97 subjects (54m; age 36-95y, average 65y) were assessed. The displacement of the arterial walls was calculated for half-overlapping windows of 20 ms by 0.3 mm, at maximum wall deformation rate, together with their standard deviations across the echo lines. The ultrasound images were separately processed to measure manually intima media thickness (IMT) and IMT-inhomogeneity.

Results: 82% of the patients were hypertensive, 37% of the patients were diagnosed with CVD, all patients had high cholesterol and LDL with low HDL levels. 64% of the patients presented an inhomogeneous posterior wall structure. The maximum strain rate varied between 0.5%/ms and 4.3%/ms with an average of 2%/ms. Distension at peak acceleration varied between 0.04 and 0.5 mm (average 0.24 mm). Patients with a high standard deviation of strain rate and distension had an increased IMT (560 mm vs 475 ± 10 mm), with an inhomogeneity between 2 and 19%.

Conclusions: The present investigation shows that the standard deviations of distension and strain rate are indicative for an irregular wall-lumen transition. The results underline the necessity of detailed analysis of arterial wall characteristics in patients with increased CVD risk.

P.030

ARTERIAL STIFFNESS IS PREDICTOR CARDIOVASCULAR EVENTS IN MEN WITH CORONARY ARTERY DISEASE

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Measuring of brachial-ankle pulse wave velocity (baPWV) is a valid and viable method by which to assess arterial stiffness, a potential surrogate marker of atherosclerosis. The AIM of the study was to for the first time ever establish whether baPWV is a predictor of major adverse cardiovascular events (MACE) in patients already diagnosed with Coronary Artery Disease (CAD) while all previous studies dealt solely with those having the risk factors.

Methods and Results: baPWV measurement was performed on 178 men with CAD aged 39-72 years (mean age 54.5 ± 7.7). The examination comprised body mass index, blood pressure, blood glucose, total cholesterol. During

the 3-year follow-up period 38 patients experienced MACE (acute myocardial infarction, coronary intervention, or cardiac death). A receiver operating characteristic curve demonstrated that the best cut-off point of a baPWV for predicting a MACE was 13.35 m/s. A univariate binary logistic regression model demonstrated that only the baPWV had a significant odds ratio for MACE: 2.30 (1.10-4.81), $p=0.024$. Other risk factors including BP and age (with the cut-off point at the lowest tercile - 49.0 years) were not significantly associated with prognosis.

Conclusions: baPWV is the only significant predictor of MACE for middle aged men with CAD.

P.031

CHRONIC COFFEE CONSUMPTION HAS A LESS POTENT EFFECT ON AORTIC STIFFNESS THAN CAFFEINE

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Purpose: Aortic stiffness is an independent marker of cardiovascular risk. Caffeine, which is the strongest compound of coffee, has been associated with an acute, unfavorable effect on aortic elastic properties. Whether there is a differential chronic effect of coffee and caffeine on aortic stiffness has not been defined.

Methods: The chronic effect of coffee and caffeine were studied in 9 healthy volunteers. The study was carried out on four separate arms: a) triple espresso, b) decaffeinated triple espresso, c) 240mg of caffeine alone (amount contained in a triple espresso) and d) placebo. Each treatment period of two weeks was separated by wash-out periods of one week. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness.

Results: The effect of daily caffeine and coffee intake on PWV is described as response of each variable, where response is defined as net caffeine or coffee minus placebo and decaffeinated coffee respectively values at each time point. PWV was significantly increased with caffeine compared to placebo ($P<0.05$, responses of 0.40 m/sec at 14 days). Furthermore PWV was significantly increased with coffee compared to decaffeinated coffee ($P<0.05$, responses of 0.43 m/s at 7 days and 0.57 m/s at 14 days). Both caffeine and coffee increased PWV, however, the effect of caffeine was more pronounced ($P=0.07$, response of 0.31 m/sec at 14 days).

Conclusions: Both coffee and caffeine increase PWV, however caffeine intake leads to a more potent chronic response. These findings indicate that substances other caffeine may partially counterbalance the chronic unfavorable effects of caffeine on the cardiovascular system.

P.032

GRADED ASSOCIATION BETWEEN LARGE ARTERY STIFFNESS AND ERECTILE DYSFUNCTION SEVERITY AND DURATION IN ESSENTIAL HYPERTENSIVE MEN

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Purpose: Erectile dysfunction (ED) is very common in men with hypertension. Increased arterial stiffness and clinical evidence of ED are both associated with atherosclerosis process. We examined the possible correlations between large artery stiffening and ED severity in essential hypertensive patients.

Methods: Our population of 140 non-diabetic patients with vasculogenic ED and stage I to II essential hypertension was divided into three groups according to carotid-femoral pulse wave velocity (PWV) values, by means of an automated non-invasive device. Group A (PWV < 8.1 m/sec), group B (PWV = 8.2-9.4 m/sec) and group C (PWV > 9.5 m/sec). Pharmacologically stimulated peak systolic velocity (PSV) of cavernous arteries was used to assess penile vascular damage.

Results: Patients in group C ($n=42$) compared to subjects in group A ($n=55$) and B ($n=43$) had higher systolic BP ($P<0.01$ for all) and longer duration of essential hypertension ($P<0.05$ for all). Moreover, patients in group C had longer duration of ED (3.3 ± 1.7 vs 2.8 ± 1.5 vs 1.7 ± 1.2 years, respectively; $P<0.05$ for all) and lower PSV (29 ± 8 vs 32 ± 10 vs 36 ± 10 cm/s, respectively; $P<0.05$ for all). In the total population, PWV was correlated with PSV ($r=-0.29$, $P<0.01$), while PSV was associated with systolic BP ($r=-0.18$, $P<0.05$) and pulse pressure ($r=-0.23$, $P<0.05$). Analysis of covariance revealed that PSV and ED duration remained significantly different between groups after adjustment for confounding factors ($P<0.05$).

Conclusions: In men with ED and essential hypertension, there is an augmentation in penile inflow insufficiency and longer duration of ED throughout increasing PWV tertiles. These findings suggest that arterial stiffening is closely related to ED processes, in this setting.

P.033

ASSOCIATION BETWEEN ARTERIAL WAVE REFLECTIONS AND PENILE DOPPLER FINDINGS IN HYPERTENSIVE MEN WITH VASCULOGENIC ERECTILE DYSFUNCTION

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Purpose: Hypertension is the most common comorbidity in patients with erectile dysfunction (ED). Wave reflections (WR) are an important predictor of cardiovascular risk. The association of ED with WR in hypertensive patients has not been investigated.

Methods: 88 consecutive non diabetic treated hypertensive patients (61 ± 8 yrs) affected by non-psychogenic and non-hormonal ED for more than 6 months were evaluated for penile vascular disease severity by penile Doppler ultrasound. Augmentation index (Alx) and augmented pressure (AP) were measured as an estimate of WR. Subendocardial-viability ratio (SVR) which is the ratio of diastolic pressure time interval/systolic pressure time interval was evaluated as a sensitive measurement of the adequacy of subendocardial muscle perfusion in response to myocardial oxygen demand.

Results: In univariate analysis, a negative correlation between Alx, AP and mean peak systolic velocity (PSV) of cavernous arteries ($r=-0.33$, $P<0.01$ and $r=-0.24$, $P<0.05$, respectively) and a positive correlation between SVR and PSV ($r=0.28$, $P<0.05$) was observed. Furthermore, in a multiple regression model, Alx was significantly associated with penile vascular disease severity ($P<0.01$) after controlling for age, heart rate, height, body-mass index, mean pressure, lipid profile, C-reactive protein, intensity of smoking (pack-years), antihypertensive agents and statines, (adjusted R2 of model: 0.42).

Conclusions: Our study shows that in hypertensive patients with ED, WR correlate significantly with increasing severity of penile vascular disease as measured by penile Doppler. This finding provides further insights into the pathophysiology of ED and may have implications for the cardiovascular risk in these patients.

P.034

THE INFLUENCE OF GENDER, CYCLOOXYGENASE-2 INHIBITION, AND HYPERGLYCEMIA ON VASCULAR FUNCTION IN UNCOMPLICATED TYPE 1 DIABETES MELLITUS

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Purpose: We have previously shown that young women vs. men with uncomplicated type 1 diabetes mellitus (DM-1) exhibit a deleterious renal vasoconstrictive response to clamped hyperglycemia. Since the cyclooxygenase-2 (COX2) system has important systemic hemodynamic effects in DM-1 and is activated by hyperglycemia, we hypothesized we would find a similar gender-based systemic vascular response to selective COX2 inhibition and accentuation during clamped hyperglycemia.

Methods: Outpatient ambulatory blood pressure monitoring and inpatient vascular function assessment (applanation tonometry and brachial artery reactivity) during clamped euglycemia and hyperglycemia were assessed before and after COX2 inhibition (celecoxib 200mg daily for 14 days).

Results: Before COX2 inhibition, women [$n=9$] vs. men [$n=12$] with DM-1 exhibited a lower ambulatory systolic BP (114 ± 3 vs. 124 ± 3 mmHg, $p=0.029$), which was no longer present after COX2 inhibition. Radial augmentation index was higher before (euglycemia 11.5 ± 4.2 vs. $0.8 \pm 3.1\%$, $p=0.048$; hyperglycemia 10.8 ± 4.5 vs. $-3.1 \pm 3.6\%$, $p=0.024$) and after COX2 inhibition (euglycemia 13.1 ± 2.3 vs. $-1.3 \pm 3.5\%$, $p=0.005$; hyperglycemia 9.1 ± 2.7 vs. $1.1 \pm 4.0\%$, $p=0.045$). No differences in pulse wave velocity were detected. Endothelial-dependent FMD responses were also not different, but endothelial-independent GTN response was higher before (euglycemia 14.0 ± 0.2 vs. $10.8 \pm 1.0\%$, $p=0.045$; hyperglycemia 16.6 ± 2.3 vs. $11.5 \pm 1.1\%$, $p=0.045$) and then no different after COX2 inhibition.

Conclusions: COX2 inhibition in women with DM-1 results in a loss of gender-based systolic BP protection. Increased augmentation index in women with