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P.069: EFFECTS OF ACUTE MENTAL STRESS ON PERIPHERAL VASCULAR ACTIVITY IN YOUNG HEALTHY ADULTS WITH AND WITHOUT FAMILY PREDISPOSITION OF HYPERTENSION

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P.065

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IS ASSOCIATED WITH ARTERIAL STIFFNESS IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Background: Left ventricular (LV) diastolic dysfunction with preserved systolic function is an echocardiographic finding in the early stage of arterial hypertension. Arterial stiffness is increased in hypertensives enhancing LV afterload. The aim of the study was to evaluate the relationship between LV diastolic dysfunction and arterial stiffness both in patients with essential hypertension (EH) and white coat hypertension (WCH).

Methods: We studied 200 consecutive patients with uncomplicated, newly diagnosed and never treated EH and 120 age-matched patients with WCH. All subjects underwent a transthoracic echocardiogram (TTE) in which the peak early diastolic to peak early systolic velocity ratio (E/A) was estimated using pulse wave doppler imaging of transmitral diastolic flow. Arterial stiffness was assessed by the measurement of carotid-femoral pulse wave velocity (PWVc-f) using the Complior SP device.

Results: PWVc-f values were higher in patients with ES compared to patients with WCH (7.81 ± 1.38 vs 7.40 ± 1.37 m/s, $p=0.01$). In univariate analysis, PWVc-f was correlated with E/A ratio in both groups ($r=-0.25$, $p=0.0003$ for patients with ES and $r=-0.23$, $p=0.01$ for patients with WCH). After adjustment for age, PWVc-f sustained the independent association with E/A in the ES group ($p=0.04$) but not in the WCH group as well ($p=NS$). In both groups, PWVc-f values were not related to LV systolic function indices ($p=NS$).

Conclusion: In patients with newly diagnosed essential hypertension, impaired LV diastolic filling is related to arterial stiffness independently of LV systolic function, while this association is weaker in patients with WCH.

P.066

BENEFICIAL EFFECT OF ANGIOTENSIN-II TYPE I RECEPTOR BLOCKER ANTIHYPERTENSIVE TREATMENT ON ARTERIAL STIFFNESS: A DRUG-COMPARISON STUDY

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Background: Arterial stiffness has been recognized as a significant predictor of cardiovascular risk, while experimental data indicate that angiotensin II receptor blocker (ARB) treatment reduces arterial stiffness. The purpose of the present study was to assess ARB treatment on arterial stiffness in hypertensive patients.

Methods: We studied 81 consecutive, untreated, nondiabetic patients (mean age 52 years, 47 males) with uncomplicated essential hypertension who were administered to 6-month monotherapy with either irbesartan ($n=47$) or candesartan ($n=34$). Large-artery stiffness and arterial wave reflections indices [carotid-femoral pulse wave velocity (PWVc-f), carotid-radial pulse wave velocity (PWVc-r) and augmentation index (Alx)] were measured before and after ARB antihypertensive treatment.

Results: ARB antihypertensive treatment reduced all elastic properties indices (Alx: from 26.3 to 21.2%, PWVc-f: from 7.7 to 7.3 m/s and PWVc-r: from 8.9 to 8.3 m/s, $p < 0.001$). After adjusting for systolic blood pressure, PWVc-f change remained significant ($p < 0.001$), but that was not seen for PWVc-r and Alx change ($p=NS$). No differences between the two agents were detected ($p=NS$).

Conclusion: Chronic ARB treatment may affect favorably arterial stiffness and wave reflections in hypertensive patients, while lowering of PWVc-f may account for the therapeutic benefit conferred by irbesartan and candesartan independently of their blood pressure lowering effect.

P.067

NO DIFFERENCES IN AUGMENTATION INDEX OR ENDOTHELIAL FUNCTION IN ESSENTIAL HYPERTENSIVE PATIENTS WITH OR WITHOUT THE METABOLIC SYNDROME

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We recruited 229 untreated essential hypertensive patients (HT) (age: 22-73 years) to evaluate augmentation index (Alx) and endothelial function in the presence (MS+) or absence (MS-) of the metabolic syndrome (MS). Alx was measured by applanation tonometry (Sphygmocor). Endothelium-dependent (FMD) and -independent dilation (25 μ g sublingual glyceryl trinitrate, GTN) were evaluated by ultrasound and automatic computerized analysis of

brachial artery diameter (BAD) changes. MS was defined using the ATP III criteria (2001).

No significant ($p < 0.05$) differences between MS+ ($N=71$) or MS- ($N=162$) were found for Alx (23.9 ± 8.0 vs 25.9 ± 10.4), FMD (4.8 ± 2.6 vs $5.2 \pm 2.6\%$) or response to GTN (8.0 ± 3.8 vs $7.7 \pm 3.3\%$). Age, systolic (SBP), diastolic blood pressure (DBP) and total cholesterol did not differ significantly ($p < 0.05$, or less). Body mass index (BMI) (29.0 ± 3.3 vs 25.5 ± 3.1 kg/m²), waist circumference (WC) (102.6 ± 8.6 vs 90.8 ± 9.2 cm), plasma glucose (103.4 ± 23.0 vs 90.5 ± 9.6 mg/dl) and BAD (4.9 ± 0.8 vs 4.4 ± 0.9 mm) were significantly ($p < 0.05$, or less) higher in MS+ as compared to MS-, while HDL cholesterol was lower (41.9 ± 11.5 vs 54.5 ± 13.3 mg/dl, respectively). In the whole group, Alx correlated ($p < 0.05$ or less) with age ($r=0.37$), SBP ($r=0.20$), DBP ($r=0.17$), BAD ($r=-0.24$), total cholesterol ($r=0.20$), BMI ($r=-0.17$) and WC ($r=-0.17$). FMD correlated negatively with BAD ($r=-0.43$), age ($r=-0.31$), SBP ($r=-0.16$) and BMI ($r=-0.13$). In multivariate analysis, age, BAD and DBP resulted significant predictors of Alx ($R^2=0.42$), while age and BAD resulted as significant predictors for FMD ($R^2=0.14$). In hypertensive patients the presence of the metabolic syndrome does not account for a further deterioration of vascular function and structure.

P.068

ENDOTHELIAL FUNCTION AND ARTERIAL STIFFNESS IN PATIENTS WITH SCLERODERMIA

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In 40 patients (36 females, mean age 56 ± 13 years) with capillaroscopic pattern of sclerodermia (SSc) and 30 matched healthy subjects (27 females), we assessed endothelium-dependent (flow-mediated dilation, FMD), and -independent vasodilation (sublingual administration of glycerol trinitrate, GTN, 25 μ g), by ultrasounds and computerized analysis. Augmentation index (Alx) and brachial pulse wave velocity (PWV) were assessed by applanation tonometry (Sphygmocor®). Disease activity and severity scores and inflammatory parameters (erythrocyte sedimentation rate, ESR; C reactive protein, CRP; interleukin-6, IL-6) were evaluated.

FMD was significantly ($p < 0.001$) lower in SSc ($4.3 \pm 2.3\%$) than in controls ($6.9 \pm 3.3\%$), while response to GTN was similar. FMD was not related to disease's activity and severity score or CRP and IL-6 levels. Alx (26.0 ± 13.1 vs $24.8 \pm 7.5\%$) and PWV (8.8 ± 1.4 vs 8.3 ± 1.4 m/s) were not significantly different in SSc as compared to controls. However, Alx was significantly ($p < 0.05$ or less) related to activity ($r=0.30$) and severity score ($r=0.30$), ESR ($r=0.32$), but not with CRP and IL-6 levels. Alx was related to age ($r=0.65$), total cholesterol ($r=0.49$) and systolic blood pressure (PAS, $r=0.33$). PWV was significantly ($p < 0.05$ or less) related to severity score ($r=0.49$), CRP ($r=0.47$) and total cholesterol ($r=0.49$) levels, but not to activity score, ESR or IL-6 levels.

In conclusion, SSc patients show marked endothelial dysfunction in the peripheral macrocirculation, which is not related with disease's grade. Upper limb arterial stiffness seems not to be affected by SSc, but increased indexes of arterial stiffening are related to greater disease activity and severity, inflammatory markers and cardiovascular risk factors.

P.069

EFFECTS OF ACUTE MENTAL STRESS ON PERIPHERAL VASCULAR ACTIVITY IN YOUNG HEALTHY ADULTS WITH AND WITHOUT FAMILY PREDISPOSITION OF HYPERTENSION

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A predominance of sympathetic activity has been described in patients with developed essential hypertension. We were interested to know whether the peripheral vascular activity and its changes provoked by mental stress were different in young healthy adults with family predisposition of hypertension (group A) and those without (group B). Peripheral vascular activity was assessed by measuring the finger artery compliance.

Experiments were performed on 38 healthy adults 19-24 years old (17 in group A, 21 in group B). We measured ECG, arterial blood pressure and finger artery compliance at rest, 3 minutes during standard arithmetic challenge and 3 minutes immediately after it. A noninvasive method was used to measure finger artery compliance, compliance index (CI) was calculated. There were no differences in systolic and diastolic blood pressure or in RR interval between the two groups.

Our results revealed the reduced CI in group A compared to group B (0.52 ± 0.05 and 1.33 ± 0.16 , $p < 0.05$, t-test) at rest. CI decreased during mental stress in both groups, but only in group B the change was statistically different ($p < 0.05$, paired t-test). During mental stress the CI between both groups did not differ, but immediately after performing arithmetic challenge CI increased in both groups ($p < 0.05$, paired t-test) nearly to the control

values ($CI = 0.57 \pm 0.07$ for group A and $CI = 1.23 \pm 0.19$ for group B) and differed statistically significant as at rest ($p < 0.05$, t-test).

These differences suggests that young healthy adults of group A could have increased sympathetic tonus compared to group B or there are changes in other peripheral mechanisms governing the small vascular behavior between both groups.

P.070

NON-INVASIVE QUANTITATIVE EVALUATION OF SYSTOLIC CARDIOVASCULAR INTERACTION BY CAROTID ARTERY ULTRASONOGRAPHY

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Introduction: We investigated non-invasive quantification of the systolic interaction between left ventricle and central arterial system by carotid artery distension waveform analysis.

Methods: ECG, finger-cuff pressure, and common carotid artery distension waveforms (M-mode ultrasound) were obtained in 14 young healthy volunteers in supine and sitting position.

Results: Distension waveform analysis enabled determination of isovolumic contraction period (ICP), ejection period (EP), aorta-carotid (TTa-c) and aorta-femoral (TTa-f) transit times with a precision of 3.2, 4.5, 3.1, and 7.9 ms, respectively. From supine to sitting position, diastolic arterial pressure (DAP) increased by 7 ± 4 mmHg ($p < 0.001$, paired t-test) and the R-R interval decreased by 70 ± 87 ms ($p < 0.05$) due to the baroreflex response. The decrease in carotid transmural pressure in sitting position was reflected by an increase in TTa-c of 15 ± 9 ms ($p < 0.001$). ICP increased from 42 ± 7 to 49 ± 5 ms ($p < 0.001$) while DAP/ICP, a load-independent measure of left ventricular contractility, decreased by 7% ($p = 0.058$). This implies that the cardiac response to the postural intervention is predominantly based on an increase in heart rate. EP decreased from 303 ± 18 to 267 ± 19 ms ($p < 0.001$) as a result of the earlier arrival of the lower body reflection wave (TTa-f decreased by 57 ± 25 ms, $p < 0.001$). The ejection period and the peripheral transit time exhibited a clear correlation ($R^2 = 0.66$).

Conclusions: Modest postural changes affect systolic cardiovascular interaction through changes in arterial transmural pressure and the baroreflex but leave left ventricular contractility unaltered. Carotid artery ultrasonography enables precise quantitative evaluation of systolic cardiovascular interaction. The application of this non-invasive method in patients appears promising.

P.071

ANGIOTENSIN RECEPTOR ANTAGONISM WITH VALSARTAN DECREASES ARTERIAL STIFFNESS IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME

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Background: Angiotensin II (AT II) plays a key role in the development of vascular disease. Arterial stiffness is an important, independent predictor of cardiovascular risk. We investigated the long-term effects of selective AT₁ receptor blockade with valsartan on arterial stiffness in patients with hypertension and metabolic syndrome (MS).

Study design and Methods: We have examined 30 patients (16 males and 14 females, aged 47 ± 1 years, BMI $29-46$ kg/m²) with the MS and mild essential hypertension in the double blind, placebo controlled study. We measured brachial blood pressure (BD, mmHg), brachial-ankle pulse wave velocity (baPWV, cm/s) and the augmentation index (Aix, %) by using tonometry, volume-plethysmography and Doppler ultrasonography before and after 20 weeks of treatment with valsartan (40 to 160 mg/day). Statistical significance was assessed by t-test or two-way ANOVA of the dose responses curves.

Results: After 20 weeks of treatment with valsartan, baPWV and Aix were reduced: mean delta systolic BP 12 ± 1.6 mmHg ($P = 0.02$ vs. baseline), diastolic BP 5.1 ± 1.8 mmHg ($P < 0.0001$ vs. baseline), mean BP 7.5 ± 2.7 mmHg ($P = 0.003$ vs. baseline), baPWV 2.4 ± 0.03 cm/s ($P = 0.02$ vs. baseline), Aix $23 \pm 8\%$ ($P = 0.002$ vs. baseline). Delta baPWV was significantly higher in the group of female patients with the MS (F/M: 2.9 ± 0.02 cm/s vs. 2.1 ± 0.05 cm/s, $P = 0.003$).

Conclusion: AT₁ receptor antagonism reduced the arterial stiffness in hypertensive patients with MS, and may provide new therapeutic strategies for cardiovascular risk reduction.

P.072

THE DIFFERENTIATION IN THE CONTRIBUTION OF VASCULAR AND CEREBRAL SEGMENTS TO BRS

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Background: The baroreflex pathway is composed of vascular and cerebral segments, which are individually affected by variations in blood pressure. Baroreceptor sensitivity (BRS) is conventionally derived from spectral relationship between changes in peripheral blood pressure and heart-rate (R-R), and recently from carotid artery (CA) diameter and R-R, within the spectral frequency band of 0.05-0.15 Hz.

Objective: To discriminate the contribution of distinct segments to the overall BRS value calculated, in response to blood pressure variations induced by posture changes.

Methods: The common CA was visualised in B/M-mode with an ultrasound system. Processing of received signal resulted in beat to beat changes in diameter characteristics as a function of time, over 10min. To reveal the segmental response to local changes in transmural pressure, the BRS mean amplitudes were computed for 20 young subjects in supine and upright-seated postures.

Results: Correlation analysis revealed variation in the transfer function of the cerebral segment, has a dominant contribution to the overall BRS value. Paired t-test revealed that the pressure-based BRS value is significantly lower in sitting than supine position ($p < 0.01$), while the strain-based BRS value did not change.

Conclusions: Shifting to an upright posture results in a lower CA transmural pressure, causing a larger change in diameter for a given blood pressure stimulus, thus enhancing the pressure-based BRS. The arterial pressure to CA diameter transfer function has the largest contribution to the change in the pressure-based BRS value, in response to the variation in pressure by posture.

P.073

INTEGRATED ARTERIAL SYSTEM ANALYSIS IN A POPULATION OF HEALTHY MIDDLE-AGED MEN AND WOMEN: AUGMENTATION INDEX VERSUS WAVE REFLECTION INDICES

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Background: Age-induced alterations in arterial impedance and wave reflection contribute to elevated systolic and pulse pressure. Surrogate indices such as the augmentation index (Aix), suggest increased susceptibility for wave reflection in women.

Methods and Results: Carotid pressure and central flow waveforms were acquired non-invasively in 2132 apparently healthy subjects (1093 F/1039 M), aged between 35 and 55 at inclusion (a subgroup of the 'Asklepios' population). Input impedance, reflection coefficient $|r_1|$ and the ratio of backward-to-forward pressure amplitude, P_b/P_f , both direct measures of wave reflection, were derived. Aix was assessed using (automated) identification of characteristic points on the pressure waveform, and the effective length of the arterial tree, L_{eff} , was calculated from the timing of the reflected wave and pulse wave velocity. In addition, we calculated Aix^* and L_{eff}^* where information from pressure and flow was used to obtain the timing of the reflected wave (through wave separation analysis). Both $|r_1|$ (from 0.4143 ± 0.0033 at age 38 to 0.4618 ± 0.0048 at 54; mean \pm SEM) and P_b/P_f (0.4491 ± 0.0033 to 0.5038 ± 0.0044) increased with age ($P < 0.001$) without gender differences. Aix also increased with age, but was persistently higher in women ($P < 0.001$), while L_{eff} spuriously increased with age. Interestingly, while still increasing with age, there was virtually no gender difference in Aix^* and L_{eff}^* demonstrated the anticipated shift of reflection sites towards the heart.

Conclusion: With ageing, wave reflection increases to a similar degree in middle-aged healthy men and women. Analysis of wave reflection, using a modified Aix^* , appears to yield more consistent results than conventional Aix.

P.074

VASCULAR STRUCTURAL AND FUNCTIONAL CHANGES IN PATIENTS WITH HEART FAILURE

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Purpose: Heart failure (HF) is increasing in prevalence and a common cause of morbidity and mortality. We evaluated vascular structure and function in patients with HF.