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Final Programme and Abstracts of the 4th International Symposium on Arterial Stiffness and the 2nd Congress of the Hungarian Society of Arterial Stiffness

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Final Programme and Abstracts of the 4th International Symposium on Arterial Stiffness and the 2nd Congress of the Hungarian Society of Arterial Stiffness

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Session 1: Physiology, pathophysiology

1./1 ENDOTHEL DYSFUNCTION AS THE EARLIEST PHASE OF THE ATHEROSCLEROSIS

Jens Nürnbergger. *Department of Nephrology and Hypertension, University of Essen, Essen, Germany*

1./2 FROM MICROVASCULAR DISEASE TO MACROVASCULAR ATHEROSCLEROSIS

Miklós Illyés. *Heart Institute, University of Pécs, Faculty of Medicine, Pécs, Hungary*

Session 2: The value of the classical CV risk factors for revealing pre-clinical atherosclerosis

2./1 LIMITATION OF CLASSICAL RISK FACTORS AND SCORES IN PREDICTION OF CARDIOVASCULAR DISEASES

Alain Simon. *Hôpital Broussais, Faculté de Médecine René Descartes, Paris, France*

Detection of more people asymptomatic and clinically free of coronary heart disease but sufficiently at high cardiovascular risk to justify intensive risk reduction treatment is needed. It is based on measurement of traditional risk factors (*age, sex, high blood pressure, smoking, dyslipidemia, and diabetes*) and multivariable risk prediction algorithms incorporating these factors (*e.g. Framingham risk score, FRS*). However, traditional risk factor individually and score of risk factors cluster have a relatively limited predictive accuracy. When traditional risk factor prediction may have a poor accuracy, especially in the category of intermediate risk (10-20% FRS), optional use of new tools to refine risk prediction may be considered. These prediction tools include emerging circulating biomarkers of arterial disease (*e.g. hs-CRP, lipoprotein(a), homocysteine*) and subclinical atherosclerosis markers (*e.g. ultrasound-assessed carotid plaque or EBCT-assessed coronary calcium*). Extreme levels of these circulating and arterial biomarkers may allow the reclassification of subjects with intermediate traditional risk in higher risk category and justify to treat them more aggressively.

References: 1. Simon A, Chironi G, Levenson J. Comparative performance of subclinical atherosclerosis tests in predicting coronary heart disease in asymptomatic individuals. *Eur Heart J* (2007) 28, 2967–71.

2. Simon A, Chironi G, Levenson J. The performance of subclinical arterial disease detection as screening test for coronary heart disease. *Hypertension* 2006;48(3):392–6.

2./2 LARGE ARTERY FUNCTIONAL PROPERTIES IN THE CLINICAL ASSESSMENT OF THE HYPERTENSIVE PATIENT

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Arterial stiffness, defined as the pressure required to obtain a given dilatation in an arterial segment or in the whole arterial tree, has been used increasingly in the last few years in the clinical assessment of hypertensive patients, mainly due to the availability of noninvasive, indirect measures of stiffness. Large-artery stiffness is more and more recognized as a major index of target-organ damage in hypertension, and an important harbinger of future cardiovascular morbidity and mortality in different clinical settings, including essential hypertension. The 2007 European guidelines for the management of arterial hypertension have included for the first time arterial stiffness among the indexes of subclinical organ damage able to influence prognosis of hypertensive patients. Indeed, evidence is accumulating that noninvasive measures of arterial stiffness, from the simplest ones (pulse pressure) to those requiring dedicated equipment and observers (among which aortic pulse wave velocity and aortic augmentation index), have strong relationships with other measures of subclinical cardiovascular damage and with adverse cardiovascular prognosis. Major methodological problems are still unresolved in the measurement of arterial stiffness. A number of surrogate measures of large-artery stiffness have been proposed, but each has important limitations, and any proposed index of arterial stiffness necessarily represents a surrogate of "true" stiffness, and a trade-off between simplicity and accuracy. For the time being, a wider implementation of arterial stiffness measurement in the management of hypertension and at the population level is limited by the need of dedicated and rather expensive instrumentation and trained observers. The development of better and easy-to-use techniques is of paramount importance for increasing the availability of arterial stiffness measurement in the clinical practice.

2./3 CONSECUTIVE OFFICE RECORDINGS: CHANGES IN BLOOD PRESSURE AND AIX IN HYPERTENSIVE PATIENTS

Dieter Magometschnigg. *Institut für Hypertoniker, Wien, Austria*

2./4 AORTIC STIFFNESS AND PULSE WAVE CHARACTERISTICS IN PATIENTS WITH OPERATED AORTIC ANEURYSM

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Background: Endovascular aneurysm repair (EVAR) of aortic aneurysm has been suggested as an alternative to open repair (OR). The large trial EVAR-1 comparing these two methods resulted in lower aneurysm-related 4-year mortality with EVAR as against 7% with OR ($p=0.04$), but all-cause mortality

was similar in both groups, 28%. We wished to explore in a pilot study whether pulse wave (PW) characteristics were different with these two methods.

Methods: Seventeen patients, 9 EVAR and 8 OR operated, mean age 73 years, were investigated >2 months after operation. Augmentation of the systolic pulse in relation to pulse pressure (augmentation index, Alx) and pulse wave velocity (PWV) were measured using Arteriograph™ (AG) and SphygmoCor™ (SC). Elasticity modulus of graft and non-grafted parts of the aorta was measured with abdominal ultrasound.

Results: Graft elasticity modulus and graft stiffness did not differ between the two groups. Average blood pressure was 135/87. MAP tended to be higher in the EVAR group (107 mmHg vs. 95, $p < 0.10$). Brachial Alx was 13.2% units and aortic PWV 13.6 m/s with no difference between groups. Mean aortic Alx was 31.1 with AG and 31.7 with SC. Wave return time (Tr) obtained by SC 138.4 ms. A 'pulsatility index' equal to pulse pressure divide by MAP was greater with OR (= .57) than with EVAR (0.45, $p = 0.03$). In a comparative group of patients with established coronary heart disease (mean age 79 years), mean BP was 137/72, aortic Alx by SC 31.7% units and Tr time 139.6 ms.

Conclusion: Pulse wave characteristics were similar for aortic stenosis patients operated with OR or EVAR, and also similar for CHD patients of the same age-group. Mean systolic BP was similar in both these groups but diastolic BP was lower in the CHD control group. EVAR operated patients had a lower pulsatility index than OR patients, but otherwise, pulse wave and stiffness characteristics did not differ between operating methods.

2./5

COULD MEASUREMENT OF ARTERIAL STIFFNESS PROVIDE BETTER APPROACH IN RISK ASSESSMENT THAN THE CONVENTIONAL RISK FACTOR-BASED STRATIFICATION (SCORE)?

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Background: Although traditional risk factors may account for 90% of the attributable cardiovascular risk their prediction of CVD is weak based on SCORE Chart. For this reason there is urgent need to find new established risk factors and to detect subclinical arterial disease to predict future coronary events. Stiffening of the aorta is one of the earliest surrogate marker of vascular damage and measurement of arterial stiffness has a growing interest in risk assessment.

Aim: Authors investigated the correlation between the high risk state characterized by SCORE $\geq 5\%$ and elevated aortic pulse wave velocity (PWVao, increased arterial stiffness) measured by a new validated oscillometric device (arteriograph).

Subject and methods: From our whole database of 14701 patients examined by arteriograph 2243 adults were included to the analysis in which SCORE could be calculated. A subgroup of 1697 patients between 35-65 ys was also created as they are the main target of CV screening (mean age: 52 ys). Sensitivity, specificity and predictive values of SCORE to detect increased PWVao were calculated by SPSS software.

Results: Elevated PWVao ($>9,62$ m/s) was detected in 38% of our patients but sensitivity of SCORE high risk category ($\geq 5\%$) to detect elevated PWV was poor (33%) despite its high specificity (88%) while false negative cases were in 26%. The predictive value of SCORE was much less when the age group of 35-65 ys was examined (sensitivity was 17%). Sensitivity of SCORE was a little bit better in males (65%) but much poorer in females (17%). 10% of males and 36% of females are underestimated by SCORE assessment. The ROC curve of SCORE at the cut-off value of 5% has shown 33% sensitivity but 89% specificity. If cut-off value was decreased to 3% sensitivity markedly improved (53%) while specificity slightly decreased (75%). According to ROC curve in female SCORE cut-off value couldn't be so decreased (eg. 1%) than sensitivity wouldn't improve.

Conclusions: If PWVao is a good surrogate of preclinical atherosclerosis (which was proved in our other work examining the predictive value of PWVao to detect carotid atherosclerosis) SCORE risk assessment seems to be quiet acceptable in men but not in women because it markedly underestimates females' CV risk. SCORE is relatively sensitive to predict high PWVao in males but inappropriate to assess females' risk which is more pronounced in target age range of screening.

Session 3/A: Methods for assessing pre-clinical atherosclerosis among asymptomatic subjects

3.A/1

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Objective: Patients with autoimmune diseases may have increased vascular risk leading to higher mortality rates. Novel imaging techniques are necessary for the early assessment and management of patients with accelerated atherosclerosis. In this study, we compared augmentation index (Alx) and pulse wave velocity (PWV), indicators of arterial stiffness, to brachial arterial flow-mediated vasodilation (FMD) and common carotid artery intima-media thickness (ccIMT), standard indicators of endothelial dysfunction and atherosclerosis, respectively. The aim of this study to assess the vascular status of autoimmune patients by using a novel, cheap and reproducible technique, the arteriograph, and to compare this method to other standard techniques.

Patients and Methods: Altogether 101 patients with systemic autoimmune diseases including primary antiphospholipid syndrome, systemic sclerosis, rheumatoid arthritis and polymyositis, all having various types of vasculopathies, as well as 36 healthy individuals were investigated. Arterial stiffness was assessed by a TensioClinic arteriograph, a recently validated technique. Brachial arterial FMD and ccIMT were determined using high-resolution ultrasonography.

Results: Autoimmune patients exerted impaired FMD ($3.7 \pm 3.8\%$), as well as increased ccIMT (0.7 ± 0.2 mm), Alx ($1.2 \pm 32.2\%$) and PWV (9.7 ± 2.4 m/s) in comparison to control subjects (FMD: $8.4 \pm 4.0\%$; ccIMT: 0.6 ± 0.1 mm; Alx: $-41.1 \pm 22.5\%$; PWV: 8.0 ± 1.5 m/s) ($p < 0.05$). We found a significant negative correlation of FMD with Alx ($R = -0.64$; $p < 0.0001$) and PWV ($R = -0.37$; $p = 0.00014$). There were significant positive correlations between ccIMT and Alx ($R = 0.34$; $p = 0.0009$), ccIMT and PWV ($R = 0.44$; $p < 0.0001$) as well as Alx and PWV ($R = 0.47$; $p < 0.0001$). Alx, PWV and ccIMT positively, FMD negatively correlated with the age of the autoimmune patients.

Conclusions: Arterial stiffness indicated by increased Alx and PWV may be strongly associated with endothelial dysfunction and overt atherosclerosis in patients with autoimmune diseases. Assessment of arterial stiffness by arteriograph, as well as that of FMD and ccIMT are fast, reproducible and reliable non-invasive techniques for the complex assessment of vascular abnormalities in patients at high risk.

3.A/2

CAROTID INTIMA-MEDIA THICKNESS – A RELIABLE MARKER OF ATHEROSCLEROSIS/

István Madarász. *Nemocnica s poliklinikou Levice, Levice, Slovakia*

Atherosclerosis is diagnosed only if murmur can be heard over the arteries or symptoms of ischaemic injuries manifested in most cases. Unfortunately this stage means advanced atherosclerotic disease in which severe stenosis occurs.

Different manifestations of atherosclerosis (MI, stroke, peripheral arterial disease) are the leading cause of death in industrialized countries. For this reason much more emphasis was put on the prevention of CVD. There are a lot of method to reveal preclinical atherosclerosis to diagnose earlier and earlier phase of the disease. These vascular tests should be fulfill the next criteria: 1. Non-invasive method 2. Simple and fast 3. Repeatable several times as needed 4. Not inconvenient for the patients. These needs are met by carotid IMT measurement.

It is well known that CIMT is an established marker of atherosclerosis and easily performed by B-mode ultrasonography. CIMT-measurements are well reproducible so appropriate method for follow-up of progression or regression of atherosclerosis.

Author reviews the anatomy of carotid intima-media, emphasises the clinical implications of B-mode ultrasonography in measuring CIMT in the follow-up of progression of atherosclerosis. Large-scale trials proved that improving risk factors can slow the progression of CIMT which probably decrease the likelihood of occurrence of vascular events.

3.A/3

THE CARDIO-CT

Gábor Kerecsen. *PET Pozitron Ltd., Budapest, Hungary*

3.A/4

IS ANKLE-BRACHIAL INDEX AN APPROPRIATE SCREENING METHOD FOR PRE-CLINICAL ATHEROSCLEROSIS?

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Ankle-brachial index (ABI) is widely recommended by guidelines to screen asymptomatic atherosclerosis. Decreased ABI is associated with high prevalence of coexisting CAD or stroke and CV mortality. ABI is an inexpensive simple method to reveal PAD characterized by more than 50% stenosis of lower arm arteries. However diagnosis of PAD doesn't equal to diagnosis of early (asymptomatic) phase of atherosclerosis. The evidences which prove that ABI is a good predictor of forthcoming CV events are originated from trials recruiting elderly populations above 70 years of age (eg. getABI trial). In a recently published study including 493 middle-aged asymptomatic patients decreased ABI was confirmed only in one case while presence of carotid plaques was revealed more than 50%. In another metaanalysis consisted in 7 population-based and 2 high-risk cohort using ABI as a predictor of future CV events including more than 30.000 pts proved that ABI has a poor sensitivity in general middle aged population and normal ABI doesn't rule out high risk patient. Its sensitivity is much more better in high-risk cohorts (elderly smoking and/or diabetic patients) to predict CV outcome.

Conclusion: Despite recommendations ABI alone is not suitable for screening of early asymptomatic stage of atherosclerosis due to its low sensitivity in middle-aged asymptomatic population.

Session 3/B: Methods and devices for assessing arterial stiffness parameters

3.B/1 WAVE REFLECTIONS IN THE ARTERIAL TREE: FROM CLINICAL RESEARCH TO THE HYDRAULIC BENCH

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Pressure wave reflection is, more and more, being recognized as an important factor that contributes to the increase in blood pressure in hypertension. When the heart ejects, a forward running (from the heart to the periphery) pressure wave is generated, which reflects in the periphery and returns as a backward running wave from the periphery towards the heart. The pressure as measured will therefore consist of the superposition of this forward and backward pressure wave. The morphology of the measured pressure wave, as well as its amplitude (the pulse pressure), will depend on the magnitude and relative timing of the forward and backward wave. We measured wave reflection parameters in the Asklepios study, where central pressure and flow have been acquired in >2500 healthy middle-aged (35-55 years) men and women. We have used wave separation analysis to obtain reference values for wave reflection as well as waveform analysis to derive augmentation index. Over the age range, the reflection magnitude increased from 0.449 ± 0.080 to 0.506 ± 0.097 ($P < 0.001$), with no difference between men and women. The augmentation index also increased with age, but in contrast to the reflection magnitude, it was higher in women than in men ($p < 0.001$) even after correction for confounding factors. It was found that the augmentation index only moderately correlates with the true wave reflection magnitude ($r < 0.6$). As a second application, we used experimental and numerical methods to study wave reflections in presence of an abdominal aortic aneurysm (AAA), relying on a realistic AAA-geometry constructed from patient CT-images. Pressure and flow waves were measured and simulated before and after AAA-repair, and wave reflections were analyzed using linear wave separation and wave intensity analysis. With AAA pronounced reflections were present in the pressure and flow waveforms. The reflection coefficient measured experimentally in the upper aorta was negative with AAA (-0.10) versus 0.47 without. Wave intensity analysis confirmed the presence of a backward expansion wave caused by sudden expansion of the aorta; this was absent without AAA. These results were confirmed using a 1D numerical model. A preliminary non-invasive study in 3 patients before and after AAA-repair demonstrated that AAA-repair increased the reflection coefficient. We conclude that wave reflection is ideally analysed using both the pressure and flow waveforms. In normal subjects, reflected waves add to the forward wave, increasing the load on the heart. However, arterial pathologies such as a severe abdominal aneurysms might have such a drastic impact on central hemodynamics that they reverse this normal reflection pattern.

3.B/2 SCREENING FOR ATHEROSCLEROSIS AND ARTERIAL STIFFNESS IN GENERAL POPULATION; THE ASKLEPIOS EXPERIENCE

Ernst Rietzschel. *Department of Cardiovascular Diseases, Gent University, Gent, Belgium*

3.B/3 MEASURING PULSE WAVE VELOCITY WITH ECG GATED PULSATILE DOPPLER ULTRASOUND

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Arterial stiffness is characterized by angiological parameters (such as pulse wave velocity (PWV), augmentation index (Aix), distensibility modulus) as new cardiovascular risk factors currently getting into application in clinical practice. We can measure arterial stiffness by invasive and noninvasive mode, and there is an opportunity to detect systemic, regional or local stiffness. Carotid-femoral PWV is the 'gold standard' measurement of arterial stiffness and it has several noninvasive methods to detect.

To determine carotid-femoral PWV we applied ECG gated pulsed wave Doppler ultrasound, which theoretical background is the "foot-to-foot velocity measurement". This method is based on a newly published article, which demonstrate, that frequently used arterial tonometry is fungible with pulsed wave Doppler ultrasound in the determination of pulse waveforms. In this way, knowing the distance between carotid and femoral arterial sites, we can define PWV by using electrocardiogram (ECG) as a timing reference to determine the time delay between the upstroke of carotid and femoral pulse waveforms.

PWV measurements were performed on 31 asymptomatic individuals. Results were correlated with PWV values detected by Arteriograph ($p < 0.0001$, $R = 0.86$).

These results suggest that PWV determination by ECG gated pulsed wave Doppler ultrasound is a proper noninvasive method, which has a good clinical applicability, because it is easy, noninvasive, results are reproducible, and parallelly, complex angiological parameters can be obtained (intima-media thickness, sclerotic plaque analysis of carotid and femoral artery).

3.B/4 METHODOLOGICAL REVIEW ON DIFFERENT APPROACHES FOR ASSESSING ARTERIAL STIFFNESS

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In clinical practice, a myriad of methods exist to measure arterial stiffness. An overview of the most commonly applied methods is given, classification according to whether the method targets local, regional or global arterial mechanical properties.

Local indices of arterial stiffness: distensibility (DC) and compliance (CC) coefficient

DC and CC are based on local measurements of arterial pressure and vessel diameter, and are defined as

$$DC = (DA/A) / DP \text{ (in mmHg}^{-1} \text{ or Pa}^{-1}\text{)}$$

$$CC = DA/DP \text{ (in mm}^2 \cdot \text{mmHg}^{-1} \text{ or mm}^2 \cdot \text{Pa}^{-1}\text{)}$$

with A the cross-sectional area of the artery in diastole, DA the systolic-diastolic difference in cross-sectional area, and DP the locally assessed pulse pressure. DC describes the intrinsic stiffness of the vessel that is studied, while CC reflects the local buffer capacity.

Regional measurements: Pulse Wave Velocity (PWV)

PWV is the velocity by which a "perturbation" propagates over an arterial segment. This perturbation can be a pressure wave, but also a diameter distension or flow velocity wave. Because of the elasticity of the vessel, it will take an instant (DT) before the perturbation has propagated from location 1 to location 2, a distance Dx away. PWV is calculated as Dx/DT . For a uniform, straight cylindrical tube, PWV is directly related to the aforementioned DC:

$$PMV = \sqrt{\frac{1}{\rho DC}}$$

with ρ the density of blood. A problem is the measurement of Dx, especially when PWV is calculated from measurements on the carotid and femoral artery. In older people, and in patients with aortic pathologies, the aorta may be tortuous, complicating the reliable measurement of Dx.

Global measures of the complete (systemic) circulation: Total Arterial Compliance (TAC)

As it is possible to measure central pressure (applanation tonometry) and flow (ultrasound) using non-invasive technology, arterial input impedance can be assessed and, probably more useful, the total arterial compliance. A disadvantage of this global index is that it is strongly determined by height and weight of the individual, introducing considerable variability in the measurements. The necessity of measurement of pressure and flow also impedes the clinical use of these measures.

The assessment of TAC is generally based on an approximation of the arterial tree by a simple, lumped parameter "windkessel" model. A model well known in clinical practice is a windkessel model containing 4 elements, including a proximal (C_1) and a second, smaller "distal", "oscillatory" compliance (C_2). The model generally provides excellent fittings to measured data (radial artery pressure waveforms) but the physical/physiological meaning of the model parameters, especially C_2 , is unclear and the method is still subject of controversy.

3.B/5

OSCILLOMETRIC METHOD FOR ASSESSING ARTERIAL STIFFNESS

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3.B/6

MEASURING ARTERIAL STIFFNESS: TONOMETRICALLY, PIEZZO-ELECTRONICALLY OR OSCILLOMETRICALLY?

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Introduction: Pulse wave velocity (PWV) and augmentation index (Alx) are parameters of arterial stiffness and wave reflection. PWV and Alx are strong indicators for cardiovascular risk and are used increasingly in clinical practice. Previous systems for assessment of PWV and Alx are investigator dependent and time consuming. The aim of this study was to validate the new oscillometric method (Arteriograph) for determining PWV and Alx by comparing it to two clinically validated, broadly accepted tonometric and piezo-electronic systems (SphygmoCor and Complior).

Design and method: PWV and Alx were measured up to five times in 51 patients with the SphygmoCor, Complior and Arteriograph. In 35 patients, the measurements were repeated after 1 week in a second session using the same protocol.

Results: The correlations of the PWV as assessed with the Arteriograph with the values obtained using the SphygmoCor ($r=0.67$, $P < 0.001$) and the Complior ($r=0.69$, $P < 0.001$) were highly significant. Variability and reproducibility for PWV were best for the Arteriograph, followed by Complior and SphygmoCor. Alx (SphygmoCor versus Arteriograph) were very closely correlated ($r=0.92$, $P < 0.001$).

Perspectives: The Arteriograph is a new, easy-to-use and time-effective method for assessing arterial stiffness and wave reflection.

3.B/7

THE DAILY USE OF THE ARTERIOGRAPH IN THE MEDICAL PRACTICE – THE CHANCE FOR AN EARLIER DETECTION AND PREVENTION OF CARDIOVASCULAR DISEASES

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3.B/8

ARTERIAL STIFFNESS (aPWV) OR IS IT CENTRAL BLOOD PRESSURE? FROM CRADLE TO GRAVE

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Session 3/C: Which method/device is appropriate for population screening (according to WHO criteria) in order to reveal asymptomatic atherosclerosis?

3.C/1

CORRELATION BETWEEN AORTIC PULSE WAVE VELOCITY AND ASYMPTOMATIC CAROTID ATHEROSCLEROSIS

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Background: It seems that the traditional risk factors in many ways are not sufficient predictors of the atherosclerosis and cardiovascular disease (CVD). Aortic pulse wave velocity has been associated with the carotid ultrasonography in asymptomatic patients, because the carotid ultrasonography is a gold standard of the detection of asymptomatic atherosclerosis.

Methods: The present prospective study included 498 asymptomatic subjects (204 men and 294 women) without known heart- and vascular diseases. They visited our clinic for preventive cardiological screening. We measured the arterial stiffness (PWVao) with non-invasive oscillometric method (TensioMed Arteriograph) and we performed in a "blinded" way carotid ultrasonography for every subjects as well. During the carotid ultrasonography we measured the whole carotid system, the measurements were done by the same examiner. The patients before the PWVao measurements had to have 10 minutes rest time in supine position, drank liquid in a separated room, in room temperature.

Results: We have found 249 carotid negative and 249 carotid positive subjects. The carotid ultrasonography was considered to be positive when the IMT > 1.3 mm or calcificated plaque ≥ 1 mm was detected. The mean values were: age 57, BP 135/82Hgmm, HR 72/min, Aix -9%, PWVao 10,1m/s. In data analysis we used the SPSS software and the ROC (Receiving Operating Characteristic) curve to determine the best cut-off value of PWVao. It was found 9.62 m/s for the whole population. The sensitivity of the increased PWVao value was 78.7%, the specificity 66.3%, the positive predictive value (PPV) 70%, and the negative predictive value (NPV) was 75.7%. We made a calculation for male and female as well. For male the sensitivity was 67.6%, specificity 80.8%, PPV 78.9%, NPV 71.2%, the cut off value of PWVao was 9.62m/s; for female sensitivity was 86.8% that was extremely good, specificity 56.7%, PPV 66.1%, NPV 81.9%, PWVao cut off value was 9.7 m/s. The significance between these values was very good. We created a subgroup (age 35-65, 366 subjects) and calculated these values, too. Sensitivity was 77.2%, specificity 65.2%, PPV 63.8%, NPV 78.2%. The values for male and female in the same subgroup were. Male: sensitivity 62.9%, specificity 82.5%, PPV 75.9%, NPV 71.7%, for female: sensitivity 88.1%, specificity 54.1%, PPV 58.7%, NPV 85.9%.

Conclusion: The increased (>9.62 m/s) PWVao shows a strong association with the asymptomatic carotid plaques. Therefore the PWVao measured with Arteriograph is a suitable method and a surrogate marker to detect the preclinical atherosclerosis, because it has a high sensitivity and high predictive value for male and female as well.

3.C/2

COMPARING CAROTID INTIMA-MEDIA THICKNESS WITH RESULTS OBTAINED BY ARTERIOGRAPH MEASUREMENTS

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Aim: The investigators searched the answer to determine the association level between the PWVao which is the specificity of the stiffness of the aortic wall, the carotid intima-media thickness and the traditional risk factors.

Subjects and methods: We have investigated 53 asymptomatic subjects without known cardiovascular disease, where we measured the carotid intima-media thickness (CIMT). Two groups of patients were created according to CIMT (normal and abnormal). These groups didn't show any difference in the regards of age and gender. The subjects with CIMT > 0.9 mm were classified into the abnormal group. Pulse wave velocity (PWV) was measured in both groups with Arteriograph. After that we made an association in individuals between the results with Arteriograph, the CIMT and the traditional risk factors.

Results: In the normal group the CIMT results were normal in 62% to the PWV values. In the abnormal group the occurrence of the abnormal CIMT results were in every case abnormal with the Arteriograph, too. In this study the sensitivity of the Arteriograph was 100%, the specificity 62%, the positive predictive value 68% and the negative predictive value 100%. Between the two parameter we found a linear correlation. In subjects with increased CIMT the LDL cholesterol level was significantly higher (4.3mmol/l vs. 2.8mmol/l). We have not found association between the blood pressure (151/88Hgmm vs. 148/86Hgmm), smoking habits (8 vs. 7 subjects) and obesity (BMI: 28.8 vs. 28.1). In the occurrence of diabetes we can not make an association, because we had a small number of it. In patients with high cardiovascular risk factors the PWV was abnormal in 70%.

Summary: According to our study we can say that the abnormal PWV is a preclinical, surrogate marker of the atherosclerosis. With the Arteriograph

the atherosclerosis can be revealed and the consequent cardiovascular events could be prevented in early stage.

Poster session

P1

POSTER SESSION: EFFECTS LACIDIPIN VS FELODIPINE ON BLOOD PRESSURE CONTROL AND ON PULSE WAVE VELOCITY IN MILD AND MODERATE ARTERIAL HYPERTENSION PATIENTS

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Objective: to compare the antihypertensive effects and influence on arterial stiffness of two dihydropyridines- lacidipine and felodipine and patients with mild to moderate arterial hypertension.

Patients and Methods: 42 patients (52,2 ± 1,86 years) with office SBP 140-179 mm Hg and DBP 90-109 mm Hg were included in study. All patients were done the ambulatory BP monitoring and measurement of pulse wave velocity (PWV) (Complior SP) on elastic (a. carotis-femoralis) and muscular (a. carotis-radialis) arteries. All patients were randomized to take lacidipine (L, n=21) or felodipine (F, n=21) in increasing dose (every month) from 4 to 8 mg and 5 to 10 mg respectively. In case of ineffective monotherapy for achieving target BP hydrochlorothiazide (12,5 mg). Follow-up period was 6 months.

Results: baseline groups did not differ in office and 24-th BP, heart rate, age, gender. The target BP was achieved in 66,6 % patients in L group and 71,4 % in F group (P=NS). Dynamic of BP, heart rate (HR) and PWV are present in table (*- P<0,05 in comparison baseline). In our study we observed less rate of adverse reaction in L group (4,8 % VS 23 % P=NS).

Conclusion: in our observation L did not have any benefits in BP reduction or in influence on elastic or muscular arteries stiffness in comparison with F. Only less rate of adverse events was noted in L group.

P2

CAROTID INTIMA-MEDIA THICKNESS IS ASSOCIATED WITH FLOW-MEDIATED DILATATION IN INDIVIDUALS WITHOUT CARDIOVASCULAR DISEASE

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Introduction: Carotid intima-media thickness and brachial artery flow-mediated dilatation are used as surrogate markers of subclinical atherosclerosis. The relationship between carotid intima-media thickness and brachial flow-mediated dilatation has not been well established.

Objectives: The purpose of the study was to determine the relationship of carotid intima-media thickness with brachial artery flow-mediated dilatation in individuals without cardiovascular disease.

Methods: We assessed traditional risk factors, carotid intima-media thickness and brachial artery flow-mediated dilatation in 209 individuals (97 males, aged 50,98 ± 7,32 years) without clinical evidence of atherosclerotic cardiovascular disease and analyzed relationship of carotid intima-media thickness with brachial artery flow-mediated dilatation. Flow mediated dilatation of the brachial artery as the measurement of endothelial function and carotid intima-media thickness were determined using high resolution B-mode ultrasonography.

Results: Carotid intima-media thickness correlated with age (p=0.001), diabetes mellitus (p<0.001), low density lipoprotein cholesterol (p=0.015) and with ten-year total fatal CV risk, estimated by SCORE (p=0.0037). Brachial artery flow-mediated dilatation inversely correlated with age (p<0.001), diabetes mellitus (p=0.01), body mass index (p=0.016) and with SCORE risk (p=0.019). Multivariate analysis revealed that after adjustment for brachial artery diameter carotid intima-media thickness remains significant predictor of flow-mediated dilatation (p<0.001 for both).

Conclusion: Carotid intima-media thickness and brachial flow-mediated dilatation correlated with ten-year total fatal CV risk, estimated by SCORE. The carotid intima-media thickness was associated with flow-mediated dilatation in patients without cardiovascular disease.

P3

A METHODOLOGICAL COMPARISON BETWEEN ARTERIOGRAPH AND SPHYGMOCOR MEASURES OF ARTERIAL STIFFNESS

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Background: Arteriosclerotic disease is associated with high morbidity and mortality. Non-invasive Augmentation Index (AI %) and Pulse Wave Velocity

(PWV) are suggested to indicate degree of arterial stiffness or even extent of arteriosclerosis. Early detection of stiffer arteries by a simple technique might allow preventive measures. To evaluate possible methodological differences, we compared two approaches to determine AI% and PWV.

Methods: Augmentation Index (AI%), aortic Pulse Wave Velocity (PWV), systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were measured by Arteriograph (TensioMed Ltd., Hungary) and SphygmoCor (Atcor Medical Pty Ltd, West Ryde, Sydney, Australia). Arteriograph and SphygmoCor recordings were performed within 20-30 minutes of each other. We evaluated forty middle age subjects without known cardiac disease, 13 men and 27 women, mean±SD (min-max) age of 53±10 (34-70) years and BMI 23±3 (18-31).

Results: Mean ±SE and Pearson's correlation coefficients were for Arteriograph vs SphygmoCor; AI% 31.2±2.3 vs. 27.4±2.4 (r=0.91, p<0.0001), calculated aortic blood pressure 118±3 vs. 112±3 mmHg (r=0.85, p<0.0001); PWV 8.59 ±0.38 vs. 7.27±0.22 m/s (r=0.43, p<0.01); HR 55±1 vs. 56±1 bpm (r=0.92, p<0.0001); SBP 120±3 vs. 119±2 mmHg (r=0.79, p<0.0001); DBP 76±2 vs. 75±1 mmHg (r=0.82, p<0.0001). Women had a higher AI% than men by Arteriograph 36.24 vs. 20.76; and SphygmoCor 32.08 vs. 17.61. AI% correlated with age, similarly with both methods; r=0.72, p<0.0001 while Arteriographic PWV was closer related to age, r=0.63, p<0.0001 vs. r=0.35, p<0.05.

Conclusion: Our study shows a good correlation for AI% between Arteriograph and SphygmoCor. Women have higher AI%, which has also been shown in other studies, and AI% correlated to age as expected. PWV showed less agreement between techniques than AI%, and PWV by Arteriograph was closer related to age. This does not mean that one method is superior, but implies that the techniques cannot be used interchangeably and that more methodological studies are warranted.

P4

ARTERIAL PULSE WAVE VELOCITY AND ASYMPTOMATIC LEFT VENTRICULAR DYSFUNCTION IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME OR DIABETES MELLITUS

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Background: The aim of this study was to evaluate myocardial function and vascular wall elasticity using pulse wave velocity (PWV) between aorta and femoral artery in patients with hypertension and metabolic syndrome (MS) or type 2 diabetes mellitus (HT+DM).

Methods: In our study group we examined 53 patients (pts) with MS (mean age: 45,6 years, mean body mass index (BMI): 31,75, mean blood pressure (BP) 150/94 mmHg, and 57 pts with HT and DM type 2 (HT + DM) (mean age: 62,9 years, mean BMI:30,34, mean BP 156/101 mmHg) and normal renal function. LV function was assessed by brain natriuretic peptide plasma levels (BNP and NTproBNP), echocardiographically detected ejection fraction (EF), pulsed doppler assessment of transmitral blood flow velocities (E, A, E/A ratio) and pulsed doppler tissue imaging (TDI) of velocities of mitral annular movements (Svm, Evm, Avm).

Results: Pts in both groups revealed normal LV systolic function (EF 65 % vs. 61%), pts with HT+DM had higher values of the LV mass than the group with MS (44,9 vs. 54,0 g/height 2,7, p=0.005) Average values of PWV were lower in the group with MS than in HT+DM group (11,38m/s vs. 12,79 m/s, p=0.002) as well as BNP (54,7 vs. 141,12 pg/l, p=0.005) and NTproBNP(66,5 vs. 279,6 pg/l). In both groups increased PWV value was significantly correlated with TDI measurement, indicating reduced diastolic function (PWV and E/Evm r = 0,698, p<0,001) and also with level of natriuretic peptides (PWV vs. NTproBNP r = 0,776, p<0,001).

Conclusions: Arterial stiffness in hypertensive patients revealed some relation to the LV dysfunction. The measurement of the PWV may contribute to the prediction of LV diastolic dysfunction in hypertensive patients with metabolic syndrome or diabetes mellitus.

P5

ANKLE-BRACHIAL PRESSURE INDEX IN THE EVALUATION OF CARDIOVASCULAR RISK IN HYPERTENSIVE DIABETICS

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Introduction: Aim of our study was to follow the incidence of cardiovascular (CV) events and estimate the prognosis in hypertensive patients with diabetes mellitus (DM) - group A compared to hypertensive patients without DM - group B.

Methods: We examined and followed up 174 patients (140 men, 34 women, average age 65,6 years) with hypertension and asymptomatic or

symptomatic atherosclerotic disease of lower limbs with ankle-brachial pressure index (ABI) below 0,9. In group A there were 75 diabetic patients (63 men, 12 women, average age 65 years), group B consisted of 99 non diabetic patients (77 men, 22 women, average age 65 years). Mean ABI value was 0,64 in group A and 0,78 in group B. There were only small differences between both groups in the use of antihypertensive drugs, statins and antiplatelet therapy.

Results: During 32 months follow-up we monitored in both groups the incidence of CV events. Significant difference was observed in the incidence of unstable angina pectoris (A 13,3% vs. B 7,1%), revascularization surgery (A 17,7% vs. B 10%), the necessity of coronary intervention (A 6,5% vs. B 2,2%). The most remarkable difference was found in the occurrence of cerebrovascular events, which were almost doubled in group A (9,3% vs. B 5,1%).

Conclusion: Mortality of diabetic patients during follow-up period was 20% in comparison with 9,1% in non-diabetic patients. The hypertensive diabetics with decreased ABI represent the most risky group of patients with highly increased incidence of CV complications even though they are under contemporary intensive treatment.

P6

HOMOCYSTEIN AND PULSE WAVE VELOCITY IN PATIENTS WITH HYPERTENSION AND METABOLIC SYNDROME

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Aim: The metabolic syndrome (MS) is associated with increased cardiovascular risk. Elevated plasma homocysteine may cause or result from insulin resistance, and may indicate vascular risk or be actively involved in atherogenesis. Studies investigating the association between MS and homocysteine levels have shown conflicting results. The aim of the study was to investigate the relationship between homocysteine, the MS and the velocity of the carotid-femoral pulse wave (PWV) in patients with hypertension (HT) and MS.

Methods: Plasma homocysteine was measured in a group of 128 patients (91 men, 37 women, age 55 years \pm -13,0), with HT and MS with normal renal function. Metabolic syndrome was defined by NCEP criteria. The properties of peripheral arteries were evaluated by measurement of pulse wave velocity (PWV) between carotid and femoral artery.

Results: Mild hyperhomocysteinemia was found in 44 patients (34%) and levels increased with the presence of components of MS (from 0 to 5) (11.9 to 15.9 mmol/l; $p < 0.001$). We observed a significant positive association ($r = -0.575$, $p < 0.001$) between serum homocystein and PWV. Serum homocystein concentrations continued to be independently associated ($b = 0.187$, $p = 0.043$) with PWV in a multiple linear regression model ($R^2 = 0.929$, $p = 0.011$) after adjusting for all the variables that could have acted as cofounders on homocystein levels or on PWV measurements. (age, gender, lipids level – LDL, HDL, hsCRP, blood pressure)

Conclusions: The present study shows that homocystein level is positively associated with PWV in patients with metabolic syndrome and hypertension suggesting in the clinical setting that homocystein has an effect on arterial elastic properties.

P7

PULSE WAVE VELOCITY AND CARDIOVASCULAR RISK PROFILE IN ESSENTIAL ARTERIAL HYPERTENSION

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Objective: To determine the relationship between pulse wave velocity (PWV) as marker of subclinical organ damage in arterial hypertension and cardiovascular risk factors.

Material and methods: We studied 92 hypertensive patients (mean age 60.72 \pm 6.4, 57.6% females, without diabetes) before and after 6, 12 months of treatment. Carotid-femoral PWV was assessed by Complior method, also PWV variation under pharmacodynamic study defined as central endothelial dysfunction (ED). NO-dependent/independent vasodilatation were studied using 400 mg Ventolin spray (DPWVC-F % = BRC-F) and 0.4 mg sublingual NTG (DPWVC-F % = NRC-F), respectively. The relationship with risk factors (age, gender, genetic factor, blood pressure and pulse pressure (PP) values, lipidic profile, smoking, body mass index – BMI) were evaluated in untreated subjects and after antihypertensive treatment.

Results: 1. PWV is related with hemodynamic parameters – systolic but not diastolic blood pressure (SBP/DBP), peripheral and aortic PP ($p < 0.05$). Heart

rate has no influence before or after treatment. 2. In contrast, BRC-F is related only after 12 months of treatment with normal values of SBP ($r = 0.23$, $p = 0.02$), with aortic PP ($r = 0.45$, $p < 0.03$) and heart rate ($p = 0.04$). 3. Our study confirm the relation between PWV and decades of age ($r = 0.46$, $p < 0.001$) and suggests the influence of male gender irrespective the age ($p < 0.02$) and BMI ($r = 0.32$, $p < 0.05$). There are no correlations with smoker status, family history of premature cardiovascular disease or lipidic profile. 4. Gender is independent related with central ED before treatment (ANCOVA). BMI as index of obesity is related with NRC-F ($r = -0.35$, $p = 0.001$), also cholesterol fractions – both components of central ED for HDL ($p < 0.03$) and BRC-F for LDL ($p = 0.04$). 5. PWV and central ED are both influenced by number of risk factors.

Conclusions: 1. PWV is closely related with profile of risk in essential arterial hypertension. 2. Complior method might be useful for assessing the influence of cardiovascular risk factors, even in treated hypertensive patients. 3. NO and arterial stiffness should be taken into consideration as a surrogate end point. 4. The results suggest that the combination of these parameters will be of stronger clinical relevance.

Session 4: The significance of measuring arterial stiffness in pediatrics

4/1

EVALUATING VASCULAR (DYS)FUNCTION IN CHILDREN

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Atherosclerotic vascular disease begins in childhood, progresses through a long preclinical stage, and eventually manifests clinically, usually from middle age. It has become clear that the initiation and the progression of disease, and its later activation to increase the risk of morbid events, depends on profound dynamic changes in vascular biology. The endothelium has emerged as the key regulator of vascular homeostasis, having a barrier function but also an active signal transducer function for influences that modify the vessel wall (1). These vascular changes already appearing in childhood and adolescence can be reinforced by atherogenic risk factors such as diabetes, dyslipidemia, hypertension, chronic kidney disease, inflammation, obesity, family history of accelerated coronary heart disease, physical inactivity, smoking, ... (2, 3). These risk factors are also associated with increased elastic artery stiffness, which is itself an important predictor of outcome in a number of patient groups. Observations in animal models but also in humans support the hypothesis of a relationship between endothelial function and measures of arterial stiffness. An improved understanding of the vascular biology has permitted the development of clinical tests that evaluate vascular function. Ideally, such tests should be cheap, reproducible, repeatable, standardized, and certainly for the use in children safe and noninvasive; these tests should in fact not only provide information on subclinical disease processes but also provide prognostic information for the later clinical phase. NO-dependent flow mediated dilatation is the most widely used technique to assess pure endothelial function, also in children and adolescents. High resolution ultrasound is used to measure intima-medial thickness, an early manifestation of atherosclerosis. Increased arterial stiffness, by estimating pulse wave velocity and augmentation index, a measure of arterial wave reflections, has also already been described in children with different pathological conditions, mostly using piezo-electronic or applanation tonometry (4).

Most of these tests however need complete cooperation, not always evident in (young) children, and are observer/user dependent. Oscillometric assessment of arterial stiffness could be a valuable alternative for children, as it is easy to use, and observer independent.

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4/2

FIRST HUNGARIAN DATABASE OF PARAMETERS MEASURED BY ARTERIOGRAPH AMONG HEALTHY CHILDREN AND ADOLESCENTS

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Introduction: There is a great need for assessing the actual state of the arterial system non-invasively among several childhood diseases (e.g. chr. renal diseases, type 1 diabetes mellitus, dyslipidemia, obesity, coarctatio a...). The methods (Sphygmocor, Complior) available so far are too difficult and time consuming to use them extensively among children. The Tensio-Clinic Arteriograph measures PWV and Aix non-invasively and can be used as an easy and fast measurement from the age of 2-3.

The goal of our study was to measure arterial stiffness parameters with Arteriograph among healthy children under the age of 18 and to create a database of these records.

Methods: Measurements were carried out with Arteriograph among healthy children in medical offices, in primary and secondary schools by three different workgroups (in Dabas, Szolnok and Tapolca). Children with chronic diseases were excluded. Before the measurement the patients had 3-4 minutes rest in supine position. Obese children were excluded from the joint database based on body mass index in every age and sex group. Children with actual systolic blood pressure (SBP) above the 95 percentile value in each age and sex group were also excluded. For statistical analysis the independent samples T-test was used.

Results: Data of 1549 children (Tapolca: 709 patients, Dabas: 67 pts, Szolnok: 773 pts; age: 2–18 years) were analyzed. In the first step 83 obese children were excluded, while an additional 548 patients were excluded due to high SBP. Consequently the database contained recordings of 917 healthy children (454 boy and 463 girl). No significant change in PWV could be observed with age, although it shows a slightly increasing trend (at age of 5: 5.5 m/s, at age of 18: 6.1 m/s; $R = 0.31$). Aix decreases significantly with age (age of 5: -30%, age of 18: -70%; $R = 0.44$) especially between the age of 2 and 5.

Conclusions: 1. Arteriograph allows us to measure 2-18 years old patients non-invasively quickly and easily. 2. The first Hungarian database of arterial stiffness parameters of 2-18 years old patients. 3. The PWV shows a slightly increasing trend with age, whereas Aix decreases significantly. 4. Due to small number of cases further measurements are needed among 2-6 years old children. 5. Extensive use of Arteriograph can open up new dimensions in scientific research and in pediatric diagnostics.

4/3

WHAT IS THE REASON FOR THE SIGNIFICANT DECREASE OF AIX FROM EARLY CHILDHOOD TO ADOLESCENT AGE?

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Introduction: Analyzing the formerly completed first Hungarian database of arterial stiffness parameters of 2-18 years old healthy children it turned out that significant changes in Aix could be observed among 2-6 years old patients. However due to the small number of cases the data could not be evaluated correctly.

The goal of this study was to gather data among patients aged between 2 and 6 and to analyze the changes in Aix in this age group.

Methods: 263 children (143 boy and 120 girl) in the above mentioned age range were investigated in 2 kindergartens in Szolnok. Measurements were carried out after 3-4 minutes of rest. There were no obese or actually hypertensive patients among the measured children. These recordings were joint to our former database. Statistical analysis was carried out with use of the independent samples T-test.

Results: Recordings of 1180 children (597 boy and 583 girl) were analyzed. The results of the new completed database do not differ from our previous findings – Aix shows decreasing trend with age, with a more expressed decrease in the age group of 2-6. The Aix correlates inversely with height and consequently with Jugulum–Symphysis distance. The explanation can be that the pressure wave has to travel a shorter distance which means smaller damping.

Conclusions: 1. Joining the data of 263 children between the age of 2-6 to the first Hungarian database of arterial stiffness parameters of children the trends in PWV vs. age and Aix vs. age remained unchanged. 2. Aix decreases significantly with age between the age of 2-6. There is strong correlation between Aix and height and so Aix and Jugulum–Symphysis distance. 3. This finding has physiological explanation, clearly not a consequence of

methodological error. 4. This phenomenon should be taken into account when evaluating results.

4/4

DOES THE ACTUAL BLOOD PRESSURE INFLUENCE THE PARAMETERS OBTAINED BY ARTERIOGRAPH IN CHILDHOOD?

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4/5

COMPARISONS OF RESULTS MEASURED BY ARTERIOGRAPH BETWEEN HEALTHY AND OBESE CHILDREN/

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Session 5: Free communications

5/1

ARTERIAL FUNCTION AND CORRELATES IN LEAN AND OBESE GRADE I NEVER MEDICATED NON DIABETIC UNCOMPLICATED ESSENTIAL HYPERTENSION (GI UEH)

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Introduction: It is well established that obesity, an increasing epidemic, is a major predictor of cardiorenal complications. The aim of this study is to examine the effect of central obesity on arterial function and its correlates in never medicated non diabetic GI UEH.

Methods: This study includes 72 lean ($Gr1-BMI = 22.7 \pm 0.2 \text{ g/m}^2$) and 84 obese ($Gr2-BMI = 32.6 \pm 0.4 \text{ g/m}^2$) middle aged (47.3 ± 1.9 vs 46.6 ± 1.3 years) GI UEH male patients. In all patients, evaluation included a biochemical profile, left ventricular mass by echocardiography (LVM/Ht2.7), arterial dynamics by sphygmocardiography (augmentation index – AI and time to reflection – Tr) and CR2000 cardiovascular profile (capacitive - C1 and reflective - C2 arterial compliances), and estimation of GFR (eGFR) by MDRD (Modification of Diet in Renal Disease) formula.

Results: Compared to Gr1, Gr2 had: 1) a greater waist circumference (104.8 ± 1.5 vs 80.4 ± 1.2 cm), SBP (143.4 ± 2.2 vs 133.5 ± 2.5 mmHg), DBP (91.2 ± 1.3 vs 81.9 ± 1.5 mmHg), MAP (108.8 ± 1.4 vs 99.1 ± 1.7 mmHg), serum triglycerides (158.0 ± 8.8 vs 124.7 ± 10.8 mg/dl), serum glucose (101.8 ± 2.5 vs 97.8 ± 4.5 mg/dl), insulin (26.4 ± 2.7 vs 18.4 ± 2.2 $\mu\text{U/ml}$) and left ventricular mass (67.7 ± 2.3 vs 50.9 ± 2.3 g/m2.7), 2) normal C1 (15.5 ± 0.8 vs 14.0 ± 0.5 ml/mmHg x 10), time to reflection (139.6 ± 2.5 vs 133.6 ± 2.0 ms), augmentation index (20.4 ± 1.6 vs 19.3 ± 1.9 %), and GFR (84.8 ± 1.9 vs 84.8 ± 3.0 ml/min/1.73m²), and 3) lower HDL-C (44.0 ± 1.0 vs 54.7 ± 1.9 mg/dl). Reflective arterial compliance (C2) was equally reduced in Gr1 and Gr2 (5.4 ± 0.5 vs 5.8 ± 0.5 ml/mmHg x 100).

By multiple regression analysis, there was no relation between BMI, waist circumference, and large arterial dynamics.

Conclusion: In middle aged GI UEH male patients, increased abdominal adiposity confers: 1) an increased risk of hypertension, 2) disturbed biochemical profile, and 3) increased left ventricular mass, but 4) may preserve arterial function.

5/2

CONTRIBUTION OF VASCULAR AND NEURAL SEGMENTS TO BAROREFLEX SENSITIVITY IN RESPONSE TO POSTURAL STRESS

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Background: The baroreflex pathway is composed of a vascular and a neural segment, both modulated by variations in peripheral blood pressure. Besides the assessment of overall baroreceptor sensitivity (BRS), defined as the spectral relationship between changes in peripheral blood pressure and R-R interval within the frequency band of 0.05-0.15Hz, it has become possible to distinguish the contributions of the vascular and neural segments to this overall BRS.

Objective: We test the hypothesis that the observed changes in overall BRS, as a result of a postural maneuver, are mainly originating from the vascular (peripheral pressure to carotid artery diameter) rather than the neural segment (carotid artery diameter to R-R interval).

Methods: Recordings were made of the peripheral pressure waveform (Finapres system), the diameter variations of the common carotid artery (CCA) during the cardiac cycle (ultrasound system in B/M-mode) and R-R

interval of 20 young subjects in supine and upright-seated postures. Transfer gains were computed to reveal the segmental and overall responses.

Results: Postural change significantly increases peripheral blood pressure and carotid artery diameter. The vascular segment has a uniform spectral distribution. Statistical analyses revealed that the postural change decreased the overall ($p < 0.004$) and vascular ($p < 0.000$) transfer gains, but did not modify the neural gain.

Conclusions: Unlike the neural segment, the vascular segment is frequency non-specific. The observed decrease in overall BRS due to a postural change is explained by the reduced transfer gain of the vascular segment.

Session 6: What to do when pre-clinical atherosclerosis has been revealed?

6/1

NON PHARMACOLOGICAL AND PHARMACOLOGICAL INTERVENTIONS TO PROTECT ARTERIAL VESSELS IN HYPERTENSION

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Session 7: Which are the most effective drugs in different stages of asymptomatic atherosclerosis?

7/1

ANTIHYPERTENSIVES ARE NOT ALL EQUAL – LESSONS FROM ARTERIAL STIFFNESS

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A major development in our understanding of hypertension has been an appreciation of the important role of arterial stiffness in both the pathogenesis and prognosis of hypertensive patients. Evidence showing that arterial stiffness is an independent determinant of outcome has stimulated research for agents that preferentially reduce stiffness in addition to reducing blood pressure. In general most antihypertensive agents will lower aortic pulse wave velocity in parallel with a reduction in blood pressure although evidence that this occurs in thiazide diuretics remains to be established. Other agents through ancillary properties including vasodilatation, vascular remodelling and change in heart rate may also significantly alter wave reflection and augmentation index. That a number of non-antihypertensive agents including statins, thiazolidinediones and non-pharmacological measures reduce stiffness further encourages our search for agents that consistently reduce blood pressure and both pulse wave velocity and augmentation index. To date this has been seen repeatedly with drugs affecting the renal angiotensin system particularly ACE inhibitors, angiotensin receptor antagonists and aldosterone antagonists. A number of such studies suggest the reduction in arterial stiffness is in part independent of the extent of blood pressure reduction. Individual calcium channel blockers have been shown to reduce the pulse wave velocity or augmentation index.

Reduction in augmentation index is particularly associated with an effect on aortic systolic blood pressure. In the CAFÉ Study both arms had a similar reduction in brachial blood pressure, the Amlodipine/Perindopril arm reduced aortic blood pressure to a greater extent than the beta-blocker atenolol/thiazide regimen and this was associated with an outcome advantage. This, the LIFE Study and a recent meta-analysis suggest that atenolol should not be used routinely as an antihypertensive. Whether this extends to other beta blockers is a subject of intense investigation. Recent studies comparing nebivolol, a vasodilating beta blocker through increased nitric oxide availability, and atenolol suggest that while both agents produce a similar reduction in brachial blood pressure and aortic pulse wave velocity atenolol has a greater effect on reducing heart rate, increasing augmentation index, an effect that was less with nebivolol. Nebivolol consequently produced a greater reduction in aortic systolic blood pressure than atenolol. It is clear that not all antihypertensives are the same in relation to their effect on arterial stiffness. Increasingly this measurement will be included in the routine assessment of hypertensive patients both to assist in the choice of therapy and in follow up to ensure there is a reduction both in blood pressure and arterial stiffness.

7/2

THE EFFECT OF DRUGS AND LIFE-STYLE FACTORS ON ARTERIAL STIFFNESS – THE ARTERIOGRAPH EXPERIENCE

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7/3

EFFECTS OF COMBINED ANTIHYPERTENSIVE THERAPY ON BLOOD PRESSURE AND ARTERIAL STIFFNESS PARAMETERS IN DIFFERENT AGE GROUPS OF HYPERTENSIVE PATIENTS

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7/4

DO THE STIFFNESS PARAMETERS INFLUENCE THE THERAPEUTIC DECISION AMONG HYPERTENSIVE PATIENTS?

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Objective: For the purpose of the optimization of the individualised antihypertensive therapy it is necessary to carry out an entire assessment of the risk situation of patients. On the basis of the recommendation of ESH the examination of stiffness parameters should also be an integral part of such assessment! An optimal antihypertensive therapy should not only mean to achieve the optimal blood pressure value, it also requires to achieve the optimal haemodynamic and angiological situation.

Our objective was to determine which type of medication and/or changes of lifestyle should be used in clinical practice to influence most efficiently the vascular dysfunction detected during a period showing no symptoms.

Methods: We have determined stiffness parameters in patients on a random basis. In one of the groups of patients we have used CardioVision device, which, working on oscillometric principle, measures the stiffness values of the artery in the upper arm (ASI) simultaneously with measuring the blood pressure and the pulse. In the other group of patients we have carried out the examinations utilising a TensioClinic make arteriograph device, which also operates on the basis of oscillometry. In this case, in addition to the blood pressure and the pulse values, also Alx and PWV values have been evaluated. The stiffness parameters, measured by the two devices, are not convertible!

Following the identification of the basic and associated diseases, having no contraindication, we have commenced treatment using nebivolol. In addition to medication therapy, in each case we have provided counselling on lifestyle changes, too. Patients have been ordered for control 3 months following the commencement of the therapy.

Achievements: In the course of the examinations with CardioVision device 38 patients from 57 have appeared for control: 20 women and 18 men. The average nebivolol dosage was: 4.5mg/day. Following the treatment over three months, in female patients the initial tension value of 162/83Hgmm has dropped to 147/81Hgmm, and the pulse from 77/min to 71/min value, accompanied by the decrease of the ASI value from 115 to 50. In practice the values from 0 to 70 have been considered the normal range of values, on the basis of the bibliographic reference of the manufacturer of the device. In case of male patients the tension has dropped from 166/86Hgmm to 144/78, the pulse from 76/min to 72/min, and ASI from 131 to 69.

In the group, where examination has been performed by arteriograph, 48 patients from 69 have appeared for control. In case of female patients the initial blood pressure of 142/87Hgmm has dropped to 124/78Hgmm, the pulse from 79/min to 73/min, the Alx value from 23.7% to 10.9%. The value of PWV has not changed on the merit. In case of male patients the initial blood pressure has dropped from 148/91Hgmm to 138/86Hgmm, the pulse from 76/min to 74/min. The Alx value has changed from 22.4% to -6.4%, while the PWV value has not changed on the merit in this group of patients, either. The average dosage of a nebivolol in this group was 3,6mg.

Conclusion: On the basis of the examinations performed as a result of the applied treatment with nebivolol (utilise either as mono or combined treatment) we could achieve significant decrease of blood pressure, and moderate decrease of pulse number. The unique NO donor capability has remarkably improved the stiffness parameters in both sexes, which parameters could be detected in a perfect manner with both the arteriograph, and the CardioVision device, in this type of self-controlled manner. From bibliographic data it is known that the increase of Alx by 10% increases the number of cardiovascular events by 28%. This examination points out that in addition to the normalization of blood pressure also the considerable decrease of CV risk can be achieved by the improvement of stiffness parameters!