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P9.07: CAROTID STIFFNESS AND WAVE REFLECTION DURING ANTIHYPERTENSIVE THERAPY WITH CALCIUM ANTAGONISTS: INSIGHT FROM A WAVE INTENSITY APPROACH

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have an additional positive effect on wave reflection, possibly linked to a effect on the peripheral microcirculation.

P9.04

EFFECT OF ANTIHYPERTENSIVE TREATMENT ON PULSE WAVE VELOCITY AFTER ONE YEAR IN NEVER TREATED, NEWLY DIAGNOSED HYPERTENSIVE PATIENTS AND ITS DETERMINANTS

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Background: Aorto-femoral pulse wave velocity (PWV) is a well established method to stratify hypertensive patients, but information about the influence of treatment on this variable is scarce.

Methods: Longitudinal study that included 212 (122 men, 56 %) non-diabetic, never treated hypertensive patients. We measured at the initial visit standard clinical variables, as well as PWV (Sphygmocor-System), left ventricular mass index (echocardiography) and microalbuminuria to asses target organ damage. At a median of 1,07 (SD±0,34) years, a second visit was performed, measures were repeated.

Results: The mean age was 50±13 years with initial systolic and diastolic BP of 148/88 mmHg (SD±16/10). The initial prevalence of left ventricular hypertrophy (LVH), pathological urinary albumin excretion rate (UAER) and PWV > 12 m/sec were 30,7, 15,0 and 9,2 %, respectively. Considering a decrease of 1 m/sec as a significant change in PWV, 43 % of patients showed an improvement in PWV. In a logistic multivariate regression analysis, age (OR: -0,9, p<0,0001), systolic BP reduction > 15 mmHg (OR: 2,9, p<0,005), initial Cholesterol-LDL (OR: 1,1, p<0,006), use of angiotension-receptor-blockers (ARB) (OR: 2,5, p<0,022) and waist diameter (OR: -0,95, p<0,04) were independently associated with a decrease of PWV.

Conclusions: In untreated hypertensive patients, age and abdominal obesity are negative predictors of changes in PWV, whereas BP treatment, high cholesterol-LDL and use of ARB seem to favour a decrease of PWV during the first year of treatment.

Key Words: arterial stiffness, pulse wave velocity, applanation tonometry.

P9.05

EFFECT OF ANTIHYPERTENSIVE TREATMENT ON PULSE WAVE VELOCITY AFTER ONE YEAR IN PATIENTS WITH REFRACTORY HYPERTENSION AND ITS DETERMINANTS

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Background: Aorto-femoral pulse wave velocity (PWV) has been shown to be modifiable by antihypertensive treatment in newly diagnosed hypertension (HT), but little is known about the effect of treatment on longer standing, refractory HT.

Methods: Longitudinal study that included 79 (49 men, 62 %) patients with refractory hypertension, treated with at least three drugs in standard dosis. We measured at the initial visit standard clinical variables, as well as PWV (Sphygmocor-System), ECG-left ventricular mass (CORNELL-product and SOKOLOV) and microalbuminuria to asses target organ damage. At a median of 1,15 (SD±0,34) years, a second visit was performed, measures were repeated.

Results: The mean age was 64±11 years with initial systolic and diastolic BP of 155/79 mmHg (SD±25/11). The initial prevalence of left ventricular hypertrophy (LVH), pathological urinary albumin excretion rate (UAER) and PWV > 12 m/sec were 42, 16 and 27 %, respectively. Considering a decrease of 1 m/sec as a significant change in PWV, 36 % of patients showed an improvement in PWV. In a logistic multivariate regression analysis, systolic BP reduction > 9 mmHg (OR: 4,1, p<0,01), initial PWV (OR: 1,5, p<0,009) and glucemic control (HbA1c > 6,5 %, OR: - 0,2, p<0,049) were independently associated with a decrease of PWV.

Conclusions: In hypertensive patients with refractory HT, BP treatment is able to decrease PWV, correcting for age, gender and initial PWV-values, whereas a poor glucemic control appears to hinder the positive effect of antihypertensive treatment.

Key Words: arterial stiffness, pulse wave velocity, applanation tonometry.

P9.06

CORRELATES OF AUGMENTATION INDEX IN PATIENTS WITH NEVER TREATED UNCOMPLICATED NON-DIABETIC PATIENTS WITH ESSENTIAL HYPERTENSION

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Objective: Assessment of the association between augmentation index (AI75) and hemodynamic factors and target organ damage in 98 patients with:

1) prehypertension (N=56, BP=120-139 / 80-89 mmHg)- GI

2) grade 1 hypertension (N=42, BP=140-160 / 90-100mmHg)- GII

Methods: Evaluated parameters: biochemical profile, sphygmocardiography (Augmentation Index-AI75 and central BP), echocardiography (Left Ventricular Mass/Height^{2.7}- LVM/Ht^{2.7}) and renal functional indices (Creatinine Clearance-Ccr and Urinary Albumin Excretion-UAE).

Results: (table)

	GI	GII
Age (Years)	45.5 ± 2	67.5 ± 1.9*
BMI (kg/m ²)	27.9 ± 0.6	27.7 ± 0.6
SBPb (mmHg)	122 ± 1.9	143 ± 3.2*
DBPb (mmHg)	81 ± 1.4	78.5 ± 2.1
SBPc (mmHg)	114 ± 1.6	134 ± 3*
DBPc (mmHg)	82 ± 1.5	79 ± 2.2
PPb (mmHg)	41 ± 1.4	65 ± 3.1*
PPc (mmHg)	32 ± 0.8	55 ± 2.7*
LVM/Ht ^{2.7} (g/m ^{2.7})	60 ± 2	76 ± 4.9*
AI75 (%)	10.2 ± 5.6	39 ± 1*
Ccr (ml/min)	109.2 ± 5.6	71.9 ± 5.1*
UAE (mg/24hrs)	32 ± 8.2	56 ± 24.6

* p< 0.05, SBP=systolic blood pressure, DBP=diastolic blood pressure, b=brachial, c=central, PP=pulse pressure, BMI=Body Mass Index

In middle age and elderly hypertensive subjects, increased AI75 is:

1) associated with increased central/brachial SBP and PP, increased LVM/Ht^{2.7}, reduced Ccr and high UAE 2) independent of changes in biochemical profile.

Conclusion: Increased AI75 in never treated uncomplicated essential hypertension is: 1) associated with target organ damage; 2) probably a cardiovascular risk factor; 3) a sign of vascular disease which should be included in the evaluation of hypertensive patients.

P9.07

CAROTID STIFFNESS AND WAVE REFLECTION DURING ANTIHYPERTENSIVE THERAPY WITH CALCIUM ANTAGONISTS: INSIGHT FROM A WAVE INTENSITY APPROACH

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Background: Increasing evidence emphasizes the role of central pressure augmentation in the development of hypertension-related complications, and highlights the importance of targeting arterial stiffness and wave reflection with treatment.

Objective: Of this study was to evaluate the effects of the calcium antagonist barnidipine on large artery stiffness and wave reflection by means of separated wave analysis.

Methods: In twenty-one naïf-treatment hypertensive patients, carotid artery mechanics was investigated at baseline and after 3 and 6 months of barnidipine therapy by a double-beam carotid ultrasound technique (Aloka SSD 5500) which provides simultaneous recording of diameter-derived pressure and flow velocity signals and allows wave intensity (WI) analysis. Indices of local arterial stiffness and wave reflection, and separated forward and backward pressures were estimated. Twenty normotensive subjects were also .

Results: Compared to controls, hypertensive patients had higher forward and backward pressures (137±17 vs 108±7 and 21±6 vs 17±5 mmHg,

$p < 0.05$), augmentation index (Alx, 22.0 ± 7.0 vs $13.1 \pm 5.2\%$, $p < 0.01$) and pressure-dependent elastic modulus. After barnidipine, in hypertensive patients, office BP fell from $159 \pm 14/95 \pm 11$ to $138 \pm 16/81 \pm 9$ mmHg ($p < 0.001$), due to a significant reduction in forward and backward pressures, and Alx decreased to $17.0 \pm 8.0\%$ ($p < 0.01$), without changes in arterial stiffness indices. A significant direct relationship between Alx and pulse pressure observed in hypertensive patients at baseline disappeared after therapy ($r = 0.45$ before and 0.25 after therapy).

Conclusions. These data suggest that a reduced wave reflection during therapy with the calcium antagonist barnidipine is depending on its effects on muscular artery tone rather than on large artery stiffness.

P9.08

THE L-ARGININE/ASYMMETRIC DIMETHYLARGININE (ADMA) RATIO IS IMPROVED DURING ANTI-TUMOR NECROSIS FACTOR- α THERAPY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES: ASSOCIATION WITH AORTIC STIFFNESS

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Background: Anti-Tumor Necrosis Factor (TNF)- α therapy seems to improve cardiovascular risk in patients with inflammatory arthropathies such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of nitric oxide synthase (NOS). ADMA competes with L-arginine as a substrate for NOS, and the L-arginine/ADMA ratio is suggested to be important for modulation of NOS activity. **Objective:** To examine the effect of anti-TNF- α therapy on ADMA and L-arginine/ADMA, and the associations between ADMA, L-arginine/ADMA and aortic stiffness in patients with inflammatory arthropathies.

Methods: Fifty-five patients with RA, AS or PsA and a clinical indication for anti-TNF- α therapy were included. 36 patients started with a TNF- α antagonist and were compared with a non-treated group of 19 patients. Plasma ADMA, L-arginine and aortic stiffness (aortic pulse wave velocity, aPWV) were assessed at baseline and after 3 and 12 months.

Results: Baseline aPWV was associated with ADMA ($P = 0.02$) and L-arginine/ADMA ($P = 0.02$) in multiple linear regression analyses. One-year anti-TNF- α therapy improved the L-arginine/ADMA ratio (median [interquartile range]) in the treatment group compared to the control group (5 [-4, 16] vs. -10 [-20, 2], respectively; $P = 0.04$), but did not affect ADMA (0.01 [-0.03, 0.04] $\mu\text{mol/L}$ vs. 0.00 [-0.05, 0.06] $\mu\text{mol/L}$, respectively; $P = 0.78$). The L-arginine/ADMA ratio was longitudinally associated with aPWV in a multivariable mixed analysis ($P = 0.03$).

Conclusion: Plasma ADMA levels were associated with aortic stiffness in patients with inflammatory arthropathies. Anti-TNF- α therapy improved the L-arginine/ADMA ratio. The L-arginine/ADMA ratio was associated with aortic stiffness over time.

P9.10

COMPARATIVE EVALUATION OF VASCULAR AND METABOLIC EFFECTS OF PERINDOPRIL COMBINATION WITH INDAPAMIDE-RETARD OR HYDROCHLOROTHIAZIDE IN HYPERTENSIVE PATIENTS

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Our aim was to compare the changes of arterial stiffness (AS), endothelial function (EF) and metabolic parameters in patients with essential hypertension on treatment with combination of perindopril with either indapamide-retard or hydrochlorothiazide. The study involved 40 patients (mean age 52.4 ± 7.1 years) who were randomly assigned to perindopril 5-10 mg o.d. in combination with indapamide-retard (P+IR) 1.5 mg o.d. ($n = 20$) or with hydrochlorothiazide (P+HT) 25 mg o.d. ($n = 20$). EF determined as the change of resistance index after inhalation of 400 mcg of salbutamol, AS measured as mean stiffness index after 500 mcg of sublingual trinitroglycerin (SI_{tng}), blood lipids and glucose were evaluated at baseline and 6 months thereafter. Vascular responses were calculated from digital pulse waves registered using photoplethysmography. Dynamics of BP after 6 months did not differ significantly between groups (-19.3% versus -19.2% and -16.2% versus -14.1% for systolic and diastolic BP on P+IR and P+HT, respectively, $p < 0.001$ for all). Changes of vascular and metabolic parameters are depicted in the table.

	P+IR	P+HT
EF	+2.0% ($p = 0.64$)	-24.3% ($p < 0.01$)
SI_{tng}	-13.4% ($p < 0.001$)	-9.8% ($p < 0.01$)
Total cholesterol	-2.7% ($p = 0.54$)	-6.4% ($p = 0.19$)
LDL cholesterol	-4.9% ($p = 0.36$)	-7.3% ($p = 0.22$)
HDL cholesterol	-1.0% ($p = 0.83$)	-4.6% ($p = 0.36$)
Triglycerides	+3.8% ($p = 0.58$)	+12.1% ($p < 0.05$)
Glucose	+1.8% ($p = 0.63$)	+9.4% ($p < 0.05$)

Arterial stiffness significantly decreases on both regimens of treatment with the trend in favor of P+IR. Treatment with combination of P+HT resulted in significant decrease of EF accompanied by negative changes of triglycerides and glucose levels, whereas combination of P+IR did not affect endothelial function and was metabolically neutral.

Thus, despite the similar BP reduction the combinations of ACE-inhibitor – perindopril with two different diuretics significantly differ in vascular and metabolic effects. Worsening of endothelial function on P+HT combination may be attributed to negative metabolic effects of hydrochlorothiazide.

P9.11

STABILIZATION OR REGRESSION OF ATHEROSCLEROSIS BY LIFESTYLE MODIFICATION USING MOTIVATIONAL INTERVIEWING AND CAROTID ULTRASOUND

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Purpose: The preventive use of noninvasive measurement of carotid intima media thickness and plaque visualization (CIMT+P) is in the Netherlands a relatively new method to detect subclinical atherosclerosis of employees. The aim of the use of CIMT+P is to archive enduring lifestyle modification in employees without cardiovascular disease.

Methods: In one and the same Dutch company (a Steel Mill) we did CIMT+P measurements in 2008, 2009 and 2011 to follow the progression of atherosclerosis of the employees. With motivational interviewing and health advice by a dedicated occupational health physician we have been stimulating the employees to modify their lifestyle (quit smoking, eat a healthy life style, increase exercise, relaxation techniques in addition to treat hypertension). With a longitudinal analysis we investigate the effects of our intervention using both CIMT and plaque formation images as end-points and as additional substitute modifiers

Results: The mean thickness of the common carotid arteries right and left in 169 cases average age 49 years range 39-64 y. were combined plaque formation was measured in the bulb when these were present. A distinction was made between soft plaques and calcified plaques.

The results were the following: 2008 2009 2011

Mean value of CIMT (mm) was 0.7104 0.7023 0.7001

Number of cases with soft plaques 26 13 11

Number of cases with all plaques 46 43 36

Conclusions: CIMT+P can be used as a preventive method for lifestyle modification in healthy Dutch employees. In a longitudinal follow up of 3 years a stabilization or even regression of subclinical atherosclerosis can be archived as an effect of lifestyle modification. It is noteworthy that cases that were smoking and quit smoking were the ones where the soft plaque disappeared or calcified. Hypertension treatment was another significant risk factor that correlated well with plaque formation whereas LDL-cholesterol control and a HDL-c increase was significant correlated to the change on the average CIMT. Motivational interviewing may have played an important role.

P10 – Basic Science and Modelling 2

P10.01

EFFECTS OF VEGFR-1 (FLT-1) INHIBITION DURING PREGNANCY ON THE UTERINE CIRCULATION OF THE MOUSE

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Recent attention has focused on the role of soluble VEGFR-1 (sFlt-1) in the genesis of preeclampsia; less is known about the role of the non-soluble form