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P1.15: MODULATING EFFECT OF TARGET PRESSURE ACHIEVEMENT ON PULSE WAVE VELOCITY IN HYPERTENSIVE PATIENTS

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P1.11 ARTERIAL STIFFNESS AND LEFT VENTRICULAR DIASTOLIC FUNCTION IN TREATED AND UNTREATED HYPERTENSIVES

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The study was aimed to compare arterial stiffness and echocardiographically determined parameters in subjects from general population with treated and untreated hypertension.

Methods: We recruited 303 (mean age, 46.9 years). Peripheral and central pulse pressure (pPP; cPP), augmentation index (pAI; cAI) and pulse wave velocity (PWV) were evaluated by means of an oscillometric sphygmomanometer and pulse wave analysis (SphygmoCor). Relative wall thickness (RWT), left atrial (LA) diameter, ascending aorta (AO) diameter, and ratio of early and late diastolic peak of transmitral flow velocities (E/A) as well as ratio of transmitral early filling velocity to tissue doppler early diastolic mitral annular velocity (E/E') were assessed by echocardiography.

Results: In the study group, there were 140 normotensives (NT), 61 untreated hypertensives (UTHT), and 102 treated hypertensives (THT). Parameters of interest significantly differed between these groups ($p < 0.05$). In post-hoc analysis with Bonferroni correction, UTHT had significantly higher blood pressure and evaluated target organ damage parameters in comparison to normotensives participants. Despite higher ($p < 0.05$) office (141.6/95.7 vs 135.1/85.9 (mmHg) and 24-h blood pressure (127.5/79.5 vs 121.2/72.6 mmHg) in UTHT, THT had significantly higher pAI, cAI, cPP, PWV, E/E', lower E/A and larger LA ($p < 0.05$) in comparison to UTHT group.

Conclusions: Antihypertensive treatment was not associated with less pronounced target organ damage. This may reflect inadequate blood pressure control or too late initiation of antihypertensive therapy which result in progression of arterial and left ventricular stiffening. This also emphasizes the need of early diagnosis of elevated BP and early introduction of appropriate therapy.

P1.12 TETRAHYDROBIOPTERIN (BH4) IMPROVES ENDOTHELIAL FUNCTION, BUT NOT AORTIC STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition associated with increased cardiovascular risk. The aetiology is most likely multi-factorial, including endothelial dysfunction, caused by uncoupling of the endothelial nitric oxide synthase (eNOS). We hypothesised that oral tetrahydrobiopterin (BH₄), an essential co-factor for eNOS, would lead to an improvement of endothelial function and subsequently, aortic stiffness.

Methods: This was a randomised, double-blinded crossover study, consisting of two separate regimes, 1: a single dose of BH₄ 400mg vs. placebo and 2: a one-week treatment with BH₄ 400mg OD vs. placebo. In study 1, aortic pulse wave velocity (aPWV), and flow mediated dilatation (FMD) were studied before and 3 hours after BH₄ supplementation and placebo. In study 2, FMD and aPWV were assessed four times, separated by a week.

Results: A single dose of BH₄, but not placebo, improved endothelial dysfunction ($+3.57 \pm 4.14$ vs. $+0.05 \pm 1.17\%$, $P = 0.03$; $n = 18$). There was no change in aPWV following BH₄ or placebo (-0.13 ± 0.58 vs. -0.21 ± 0.43 m/s; $P = 0.6$). One-week treatment with BH₄, improved endothelial function, whereas placebo did not ($+3.69 \pm 4.90$ vs. $+0.19 \pm 2.51\%$, $P = 0.02$; $n = 15$). There was no change in aPWV following BH₄ or placebo (-0.22 ± 1.3 vs. -0.25 ± 0.51 m/s, $P = 0.4$) and no correlation between change in aPWV and FMD in either regime. **Conclusion:** Both acute and chronic BH₄ supplementation lead to an improvement of endothelial function, but did not reduce aortic stiffness. This suggests that there is no causality between endothelial function and aortic stiffness and that these conditions may just exist in parallel, both influenced by common risk factors, such as inflammation.

P1.13 INTRACORONARY AND INTRAVENOUS ADMINISTRATION OF ADENOSINE ACHIEVE COMPARABLE MAXIMAL HYPEREMIA AND STENOSIS PRESSURE GRADIENT-FLOW VELOCITY RELATIONS

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Background: The aim of this study was to compare stenosis hemodynamics resulting from intravenous (iv) and intracoronary (ic) adenosine administration.

Methods: In 12 vessels with 25-57% DS (10 patients, 61 ± 8 years), aortic pressure, distal coronary pressure and flow velocity (v) were simultaneously measured during the hyperemic response to either ic injection (40µg bolus) or iv adenosine infusion (140µg/kg/min). Cycle-averaged stenosis pressure gradient (ΔP) and flow velocity were obtained to derive ΔP-v relations from baseline to maximal velocity. For each lesion, we defined v₁ and v₂ as the lowest and highest common flow velocity for ic and iv-derived ΔP-v relations. The equivalence of both adenosine administrations was assessed by the difference in ΔP at v₁ and v₂.

Results: Maximal flow velocity was 56 ± 19 cm/s for ic and 51 ± 15 cm/s for iv, $p = \text{NS}$. The stenosis ΔP-v relations largely overlapped (95% of the velocity range for ic injections; 85% of the flow velocity range for iv infusions). Common flow velocities ranged from v₁ = 18 ± 5 cm/s to v₂ = 50 ± 15 cm/s. The difference in pressure gradient (ivΔP - icΔP) at v₁ was 0.2 ± 0.7 mmHg and 0.8 ± 3.2 mmHg at v₂ ($p = \text{NS}$), with no trend for differences in ΔP with increasing velocity.

Conclusion: Stenosis ΔP-v relations are not affected by the mode of adenosine administration and comparable hyperemia can be achieved. Ic adenosine injections are preferable, since they are faster and easier to perform and iv infusion tends to induce systemic hemodynamic variability.

P1.14 PWV IMPROVEMENT IN PREVIOUSLY UNTREATED MILD HYPERTENSIVE PATIENTS AFTER 1 YEAR OF MONOTHERAPY

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Objective: Arterial stiffness is a measure of organ damage but procedures to destiffen arteries are still elusive. Our study describes the 1 year change in pulse wave velocity (PWV) in new diagnosed previously untreated, hypertensive patients.

Patients and methods: Longitudinal study including 427 consecutive, never-treated patients with suspected hypertension. After standard clinical assessment, including pulse wave analysis and PWV (Sphygmocor®, AtcorMedical), 231 showed elevated office and ambulatory blood pressure (BP) and received mono-therapy treatment accordingly. Clinical assessment was repeated after a median of 1.1 years in the whole cohort. PWV was adjusted to BP.

Results: 103 patients were female (44,6%), mean age was 48 ± 12 years. The hypertensive diagnosed group tend to be older (50 vs. 46 years, $p < 0.001$) and had higher PWV even after mean BP adjustment (8.6 ± 2.0 vs. 7.9 ± 1.6 m/s, $p < 0.001$), higher baseline office, ambulatory and central BP (145/86, 136/86 and 138/89 mmHg vs. 131/78, 123/79 and 124/83 respectively, $p < 0.001$). After 1 year of treatment, BP was significantly improved in the hypertensive group (follow-up office BP 128 ± 13 / 75 ± 9 mmHg, $p < 0.001$). The reduction of central and peripheral systolic BP was of the same magnitude ($-16 \pm 1,2$ vs. $-17 \pm 1,1$ mmHg, $p = \text{ns}$). PWV was significantly reduced even after BP adjustment ($\Delta = 0,3$ vs. $0,05$ m/s, $p < 0,001$) but remained higher than in the non-hypertensive group. There was no differential effect in PWV reduction depending on antihypertensive class.

Conclusions: Blood pressure reduction in newly diagnosed stage 1 hypertensive patients improves arterial stiffness within a year of treatment confirming that rapid tight controlled of BP is important even mild hypertensive.

P1.15 MODULATING EFFECT OF TARGET PRESSURE ACHIEVEMENT ON PULSE WAVE VELOCITY IN HYPERTENSIVE PATIENTS

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Aim: Carotid-femoral pulse wave velocity (PWV) is a strong independent predictor of cardiovascular morbidity and mortality. The aim of the study was to evaluate treatment-induced changes in PWV in hypertensive subjects treated to target clinic BP (CBP).

Methods: Pts with grade I-II arterial hypertension were treated to target CBP $< 140/90$ mmHg with combination of RAAS-inhibitors and amlodipine for 1 yr. Baseline BP was $163,4 \pm 8,1/100,9 \pm 4,2$ mmHg; achieved BP $123,7 \pm 9,7/76,8 \pm 6,7$ mmHg. Central BP and PWV were measured before treatment and after 8mo of target CBP achievement and maintenance.

Results: 47 pts (20 men, age $58,9 \pm 9,0$ yrs; 4 smokers; 6 diabetics) achieved and maintained target CBP. In 11 (23%) pts PWV decreased by ≥ 1 m/s from baseline (G1), in 15 (32%) pts - unchanged (G2), in 21 (45%) - increased by

≥ 1 m/s from baseline (G3). The groups were similar by age and all risk factors. The baseline (154,8 \pm 7,3/91,7 \pm 10,2, 152,7 \pm 12,1/92,3 \pm 8,3 and 149,3 \pm 8,1/91,7 \pm 6,04 mmHg) and achieved CBP (128,4 \pm 7,26/80,1 \pm 4,55, 125,6 \pm 11,4/79,2 \pm 6,5 and 126,6 \pm 8,4/78,5 \pm 5,97 mmHg) were similar. There was significant difference in baseline PWV (G1 15,9 \pm 2,5 vs G2 13,6 \pm 1,9 vs G3 10,9 \pm 1,7 m/s, $p < 0.05$), but at the end of the study PWV was similar: respectively, 13,0 \pm 2,1, 13,6 \pm 1,9 and 13,4 \pm 1,9 m/s. 72,7% pts in G1 and 66,7% in G2 received the highest recommended doses of RAAS-inhibitors and A10mg vs 28,6% in G3 (Pearson $\chi^2 = 9,0$; $p < 0,05$). Indapamide SR 1,5mg was added in 36,4%, 20% and 9,5%, respectively. Correlation and multiple regression analysis revealed the association between PWV decrease and doses of RAAS-inhibitors and amlodipine ($r = -0,5$, $\beta = -0,45$, $p < 0,05$)

Conclusion: There is modulating effect of target pressure achievement on PWV in hypertensive subjects. PWV reduction is associated with higher doses of RAAS inhibitors and amlodipine.

P2.1

CAROTID PLAQUE MICROVASCULATURE ASSESSED USING DYNAMIC CONTRAST-ENHANCED MRI: COMPARING DIFFERENT REGIONS OF THE VASCULAR WALL

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Background: Pharmacokinetic modeling in Dynamic Contrast-Enhanced (DCE-)MRI has been introduced to non-invasively assess microvasculature in carotid atherosclerotic plaques, a marker for plaque vulnerability. The main model-parameter, K^{trans} , can be assessed in the outer region of the vessel (adventitia) or in the entire vessel wall (including plaque and adventitia) and already showed association with histology and features of plaque vulnerability, respectively. We investigated systematically the correlation between K^{trans} of these various regions of the vascular wall and their individual correlation with histology as gold standard.

Methods: 45 symptomatic patients with 30-99% carotid stenosis underwent 3T DCE-MRI (0.1mmol/kg Gadobutrol, 0.5ml/sec). Quantitative modeling was performed to determine K^{trans} of the entire vessel wall, adventitia, and plaque region, separately. For 10 patients, CD31 immunohistochemistry was performed on specimens (containing mainly plaque) removed during carotid endarterectomy to quantify the endothelial microvessel area.

Results: Adventitial K^{trans} showed weak correlation with plaque K^{trans} ($r = 0.64$, $p < 0.001$) and was 17.3% higher ($p < 0.001$), coinciding with decreased uncertainty in parameter estimation ($p = 0.015$). Significant positive correlation between the endothelial microvessel area and adventitial K^{trans} ($r = 0.854$, $p = 0.002$), but not from the plaque ($r = 0.438$, $p = 0.2$) was observed. Entire vessel wall K^{trans} showed intermediate results for the various analyses.

Discussion: Although K^{trans} assessed over various regions within the vascular wall are correlated, absolute values differ significantly. Adventitial K^{trans} seems to be a better measure for plaque microvasculature compared to other vascular regions, coinciding with a lower uncertainty in parameter estimation. Comparison with histology in a larger number of patients is recommended for definitive conclusions.

P2.2

ULTRASOUND SPECKLE TRACKING HELPS IDENTIFY VULNERABLE CAROTID PLAQUES

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Ultrasound Speckle Tracking, a novel technique used to assess regional mechanics of carotid wall and plaques. We hypothesized that vulnerable carotid plaques have higher intraplaque stretch which resulted in an increased difference in deformation between cap and core

Methods: Study population consisted of 39 patients with carotid atherosclerosis: 11 with acute atherothrombotic stroke and 28 asymptomatic patients with similar demographics and risk factors. For each plaque, maximum circumferential and longitudinal strain (Sc_{-Sl}) and strain rate (SR_{C-SRL}) were measured for cap, core and base. Plaque characteristics (echogenicity,

degree of stenosis, surface, etc) were assessed. All plaques were divided into hyperechogenic(19) and echolucent(20) ones.

Results: Echolucent plaques underwent significantly higher deformations than hyperechogenic ones ($Sc = 4.06$ vs 3.25 , $p < 0.05$) and they had significant difference in deformation between cap and core ($p < 0.05$) whereas hyperechogenic plaques had no difference in deformation between segments ($Sc = 5.2_4.2_2.8$ and $3.5_3.1_3.2$ for cap, core and base of echolucent and hyperechogenic plaques, respectively). Moderate negative correlations were observed between echogenicity and deformations ($r = -0.35$, $p < 0.001$ for cap_Sc). Symptomatic plaques had higher difference between cap and core Sl. Plaque internal deformation coefficient, $Cpid = [(cap_{-Sl} - core_{-Sl}) / (core_{-Sl} + base_{-Sl})] \times 100$ was developed to quantify the relative deformation of different plaque segments. Based on ROC-analysis, plaques with $Cpid > 22.2$ were associated with an ischemic event (sensitivity-55%, specificity-87%, $AUC = 0.693$, $p = 0.0485$). Logistic regression confirmed that $Cpid > 22.2$ is an independent predictor of plaque vulnerability, $OR = 3.7$, $95\% CI = 0.8-22.8$, controlling for age, gender, plaque length, degree of stenosis, echogenicity.

Conclusions: Mobility of echolucent plaques exceeds those of hyperechogenic ones. Difference in mobility between plaque segments may help identify plaque vulnerability.

P2.3

SUBCLINICAL ATHEROSCLEROSIS AND CARDIOVASCULAR RISK FACTORS: TEN YEARS OF EXPERIENCE WITH IMT PLUS® IN THE NETHERLANDS

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Purpose: Atherosclerosis has become a global disease and risk factor mitigation has been a priority in counties like the Netherlands. We assessed the impact of this new approach on cardiovascular subclinical atherosclerosis and cardiovascular risk factors.

Methods: A quantitative standardized sonographic carotid intima media thickness and plaque formation (IMTplus®). IMT plus® distribution was done in accordance with the previously published protocol. (A, being a value lower than the P50, < 0.700 mm; B, being a value between P50 and P90, 0,700 and 0,850 mm; C, being a value between P90 and P125, 0,851-0,948 mm ;D, being P125 and P200 with values between 0,948 -1,300 mm and an E, value above P200 $> 1,300$ mm; P means percentile). (Prevention Concepts® Database)

Results: Distribution of IMT Plus® categories in the Netherlands and VS The Netherlands (mean age 53 years, 60 % men) Total number of cases per category:

Total:N=18.703(100%);A:N=2685(14.4%);B:N=6425(34.4%);C:N=6600(35.3%);D:N=2372(12.7%);E:N=571(3.0%).

US (mean age 50 years 49% men) Total number of cases per category: Total:N=29.894 (100%);A:N=6001(15%);B:N=10403(26%);C:N=13199(34%);D:N=7888(19%);E:N=2403 (3%).

Conclusions: The benchmark of ten years of IMT Plus® results in the Netherlands with the US shows a different picture category A (normal risk), but a greater number of category B (25% increased risk) and a smaller amount of category D (100% increased risk) and category E (200% increased risk) in the Netherlands. The US still leads in the extent and severity of Subclinical Carotid Atherosclerosis but the Netherlands is rapidly catching up. Carotid IMTplus® remains a reliable surrogate to assess atherosclerosis development.

P2.4

FEASIBILITY OF AORTIC ARCH MECHANICS - A STUDY IN NORMAL SUBJECTS

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There are no data in the literature regarding aortic arch mechanics assessed with 2D speckle tracking (2D-ST) echocardiography.

Purpose: To study the feasibility of measuring vascular mechanics in the aortic arch with 2D-ST echocardiography and to define normal values.