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P4.50: EFFICACY OF THE COMBINATION OF β -BLOCKER BISOPROLOL AND IF INHIBITOR IVABRADINE IN PATIENTS WITH STABLE ANGINA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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For this study 109 male and 117 female, lifelong non-smoking, normotensive subjects (40 ± 11 years, BMI 25.6 ± 3.9 kg.m²) were recruited from general population. Subjects with abnormal glycemic responses after an oral glucose tolerance test (OGTT) were excluded. High resolution B-mode ultrasound images (HD7XE, Philips, U.K) of the common carotid artery were used to measure carotid intima-media thickness (CIMT) and calculate carotid compliance/distensibility. Central aortic blood pressure and pulse wave velocity (PWV) were measured using applanation tonometry (Sphygmocor & Vicorder, Skidmore Medical, U.K). Early/late mitral valve filling velocity (MV E/A) was used to assess cardiac diastolic function (Vivid 7 Dimension, GE, USA). Mean fasting and plasma glucose and post OGTT glucose were 5.02 ± 0.46 mmol.L⁻¹ and 4.96 ± 1.09 mmol.L⁻¹. Mean CIMT, carotid compliance & distensibility, PWV and MV E/A were 0.52 ± 0.07 mm, 15.86 ± 13.15 m².kPa.10⁻⁷ & 49.09 ± 34.95 kPa.10⁻³, 7.03 ± 1.23 m.s⁻¹ and 43.46 ± 18.65 respectively.

	PSBP	PDBP	cSBP	cDBP	24h-SBP	24h-DBP	24h-cSBP	24h-cDBP
Baseline	144±12	84±8	130±11	85±8	131±10	78±9	119±11	80±10
Week 8	138±15	83±7	125±11	84±8	127±8	74±9	113±7	77±9
p	0,0285	0,231	0,013	0,366	0,0067	0,0152	0,0025	0,077

P=peripheral, S=systolic, D=diastolic, BP=blood pressure, c=central, 24-h= ambulatory 24-h mean

Spearman's analysis revealed significant correlations between fasting blood glucose and carotid compliance & distensibility (-0.2205 , $p < 0.0238$; -0.2615 , $p < 0.007$), MV E/A ratio (-0.3722 $p < 0.0001$) and PWV (0.1666 , $p < 0.0127$). No significant correlation with CIMT was observed (0.0614 , $p < 0.4983$).

These results indicate that the vascular disease continuum exists in association with metabolic derangement even in the "normal" ranges.

P4.47 THE ROLE OF PHYSICAL TRAINING ON ARTERIAL AND ARTERIOLAR AGING

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Introduction: Aging affects macro and microvessels. The aim of present work was to determine if regular physical training could diminish age related changes in cardiovascular system and vascular reactivity.

Methods: Heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP), stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR) and laser-Doppler flux (LDF) were monitored at rest and during cooling of one hand for six minutes at 15°C. We examined four groups of subjects: young healthy trained (YT, 22.8 ± 0.4 years) (N=11), young sedentary (YS, 23.3 ± 0.3 years) (N=11), elderly healthy trained (ET, 50.6 ± 1.0 years) (N=12) and elderly sedentary subjects (ES, 47.7 ± 0.9 years) (N=11).

Results: There were statistically significant differences in HR, DBP, SV, CO and TRP among groups at rest. However, resting LDF did not vary among groups. During cooling there was significantly smaller LDF decrease in the group of ES (70.38 ± 6.0 % of precooling value) when compared to the YS (41.23 ± 7.6 %) (Dunnett's test, $p < 0.01$). In contrast, there was no significant difference in LDF response to cold in YT (49.60 ± 9.3 %) and ET (53.65 ± 8.2 %). **Conclusions:** Physical training partially prevents changes in cardiovascular function and microvascular reactivity in the elderly subjects. HR and SBP did not rise with ages as did DBP and TRP. Training prevented falling in SV but not in CO. HR was significantly lower in ET than YT. Training successfully prevented decrease in cutaneous microvascular response to cold in the elderly.

P4.48 SUPERIOR PERIPHERAL AND CENTRAL BLOOD PRESSURE (BP) CONTROL AFTER SWITCHING HYPERTENSIVE TYPE 2 DIABETIC PATIENTS WITH UNCONTROLLED HYPERTENSION UNDER RAMIPRIL/HCT TO PERINDOPRIL/INDAPAMIDE

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The aim of the present study was to compare the change from baseline BP (office, 24-h ABPM, central BP) in uncontrolled, hypertensive typ 2 Dm patients under ramipril/HCT after switching therapy to a dose-equivalent

fixed combination of perindopril/indapamide Investigator initiated, non-randomized, one arm study. Typ 2 Dm, males and females >18, with previously uncontrolled hypertension as defined by a sitting office BP $\geq 130/80$ mmHg (office BP). Triplicate office BP was measured with a validated, fully automatic, oscillometric upper arm device (ESH guidelines; Microlife watch BP office). 24-h-ABPM (Central and peripheral BP) was measured with a validated device at baseline and after 8 weeks therapy (Mobilograph, IEM, Germany) Central BP in the clinic was measured at baseline and after 4 and 8 weeks therapy according to the recommendations of the ESH working group on Large Arteries (Sphygmocor, Atcor)

Results: Up to now 18 patients with a mean age of 61 ± 10 years and a BMI von 30 ± 6 were included. Mean daily dosage of Ramipril/HCT was $5.3/22.2$ mg, the respective dosage after changing to Perindopril/Indamide was $5.97/1.49$.

Switching hypertensive Typ 2 diabetic patients with uncontrolled hypertension under Ramipril/HCT to Perindopril/Indapamide resulted mainly in superior systolic blood pressure control. This effect was persistent for central BP as well as for 24-h-ABPM.

P4.49 RELATION BETWEEN ARTERIAL STIFFNESS AND COMPONENTS OF AMBULATORY BLOOD PRESSURE IN CHILDREN WITH HYPERTENSION AND CHRONIC KIDNEY DISEASE

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Arterial stiffening may be both the cause and consequence of an increase in blood pressure but the blood pressure components implicated in the inter-relationship may differ. The blood pressure component caused by stiffening is pulse pressure (PP). By contrast, passive stiffening resulting from distension of the arterial wall would be expected to relate most closely to mean arterial blood pressure (MAP) at the time of measurement and stiffening related to structural change to relate to longer term MAP and/or pulse pressure (PP). The objective of the present study was to examine the relation between arterial stiffness as measured by carotid-femoral pulse wave velocity (PWV) and components of blood pressure (MAP and PP) at the time of the measurement of PWV (PWV BP) and over a 24 hour period in children with hypertension and chronic kidney disease (CKD). Children (n=45, 12 female, 27 with CKD, 11 with hypertension, 7 controls) were aged 6-17 years with mean±SD blood pressure $113 \pm 17/62 \pm 15$ mmHg. PWV was measured by ECG referenced carotid-femoral tonometry (SphygmoCor system, Atcor Medical, Australia). PWV was more closely correlated with MAP than with PP ($R=0.38$, $P < 0.01$ and $R=0.26$, $P=0.08$ for 24h MAP and PP respectively) and more closely correlated with 24h MAP than with day-time, night-time or clinic MAP ($R=0.26$, 0.20 and 0.29 respectively). In children with CKD and hypertension, PWV is most closely associated with 24h MAP and likely to be secondary to increased MAP.

P4.50 EFFICACY OF THE COMBINATION OF β -BLOCKER BISOPROLOL AND IF INHIBITOR IVABRADINE IN PATIENTS WITH STABLE ANGINA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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The study was aimed to assess the efficacy and safety of treating coronary heart disease (CHD) patients complicated with Chronic Obstructive Pulmonary Disease (COPD) using the combination of tolerable doses of beta-blocker bisoprolol and inhibitor If-channel ivabradine, compared with

bisoprolol alone. **PARICIPANTS:** 50 patients with stable angina and COPD were included (88% men, mean age 62.8±7.2 years). All patients received bisoprolol, the dose of which was titrated until the clinical signs of intolerance. Then, the patients were randomized into two groups: patients of the first group continued to take bisoprolol and patients of the second group were added ivabradine (5–15 mg).

Results: Combination therapy resulted in further decrease of heart rate (HR) to an average of 62±4 bpm over 6 month of follow-up. This was associated with additional decrease of the number of angina attacks (by 4.7±4.4 per week vs. 2.5±4.7, $p<0.05$) and increase of quality of life ($p<0.05$). Only in combination therapy group there was also the decrease of broncholytics consumption (from 2.9±3.2 to 1.9±2.7 per week, $p<0.05$). Pulse wave velocity (PWV) estimated by Arteriograph (TensioClinic «Meditech») decrease significant in both groups, but no difference delta PWV between groups.

Conclusion: The combination of tolerable doses of bisoprolol and ivabradine is safe and allows to achieve adequate HR decrease. This is associated with maximal antianginal effect, decrease in the need for broncholytic therapy, improvement of the quality of life compared with the treatment with bisoprolol alone. We did not find the influences of ivabradine on the arterial stiffness.

P4.51

NONINVASIVE EVALUATION OF STRUCTURAL AND FUNCTIONAL CHANGES IN THE HEART AND LARGE ARTERIES IN PATIENTS WITH PRIMARY ALDOSTERONISM

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Background Only few studies, in small groups of patients, have evaluated large arteries alterations in primary aldosteronism(PA). In addition, the assessment of cardiac and vascular involvement has not been simultaneously performed.

Aim of the study was to evaluate cardiac, vascular and renal complications in patients with PA.

Patients and Methods: 70 patients with PA(age 49±6years,27 F) and 70 essential hypertensives (EH) matched for age, sex, BMI and BP, underwent laboratory examinations, cardiac and carotid ultrasound and PWV.

Results: no differences in age, sex, BMI, BP and HR were observed. Cholesterol was lower in PA (195±37 vs 215±33 mg/dl, $p<0.05$); no difference in tryglicerides, glucose and uric acid was observed. In PA eGFR(MDRD) was greater in comparison to EH(96±22 vs 89±17mL/min/1.73m², $p=0.05$). LV mass index(LVMI) and relative wall thickness(RWT) were significantly greater in PA vs EH(LVMI 42±13 vs34±7 g/m².7, $p<0.001$ and RWT 0.34±0.08 vs 0.31±0.04, $p<0.001$). At TDI Emvel was significantly lower, and Evel/Em vel was significantly higher in PA (9.5±2.9 vs 10.5±2.7, $p<0.05$ and 9.2±4.4 vs 7.6±2.7, $p<0.05$, respectively). No difference was observed in carotid prevalence of thickening or plaques and in IMT (Meanmax 1.02±0.25 vs 0.98±0.18, p ns, CBMMax 1.05±0.26 vs 1.01±0.16, p ns), as well as in PWV(10.8±2.1 vs 10.8±1.6 m/sec, p ns).

Conclusions: In this large group of patients with PA a significant increase in LVMI and concentric geometry, associated with a worse diastolic function were observed. Opposite to previous findings, no difference in aortic stiffness and carotid structure was observed.

P4.52

CORONARY ARTERY DISEASE AND STROKE IN TYPE 2 DIABETIC PATIENTS: POSSIBLE ROLE OF A RAISED CENTRAL PULSE PRESSURE

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Background: Whether large artery static and dynamic properties are different in type 2 diabetics with coronary or cerebrovascular disease (DM-CVD) as compared to patients free of clinical complications (DM) is debated. **Aim:** To evaluate common carotid (CCA) IMT, local and aortic stiffness in DM-CVD as compared to DM and controls (CTRL).

Methods: thirty-five nondiabetic normotensive CTRL, 130 diabetics without complications (DM) and 25 diabetics with CAD and/or previous stroke/TIA (DM-CVD) (Tab 1) underwent radiofrequency (RF)-based ultrasound (QIMT® and QAS®, Esaote) of CCA, that provides automatic measurement of far-wall IMT, local stiffness (β -index) and contour wave analysis yielding local pulse pressure (PPc). Carotid-femoral pulse-wave velocity (PWV) was also measured (Complior).

Results: Adjusting for sex, age and smoking habit, CTRL and diabetics differed significantly ($p<0.05$) in PWV (9.0±1.9 vs. 11.4±2.5 m/s), CCA IMT (619±146 vs. 736±169 μ m) and PPc (37±9 vs. 46±14 mmHg), but not in β -index (10.1±2.9 vs. 12.5±4.9; $p=0.23$). Within diabetics, after adjustment for confounders, DM-CVD showed higher ($p<$ at least 0.05) PPc but not CCA IMT, β -index and brachial PP (PPb) than DM (Tab 2).

Table 1.

Groups	Age	BMI	Glycemia	SBPb	PPb
CTRL	56±8*	26±4*	88±10*	123±12*	46±8*
DM	62±8	29±5	146±42	136±18	57±16
DM-CVD	66±7	29±4	138±42	136±23	62±18

Table 2.

Groups	PWV	IMT	β -index	SBPc	PPc
CTRL	9.0±1.9*	619±146*	10.1±2.9*	115±12*	37±9*
DM	11.3±2.4	726±173	12.4±4.3	123±16	44±13°
DM-CVD	12.0±3.5	794±129	14.6±6.8	127±19	52±16

*: $p<0.05$ in CTRL vs DM and DM-CVD; °: $p<0.05$ in DM vs DM-CVD

Conclusions: central PP appears to be the only structural/functional large artery measure significantly different in diabetic patients with or without cardiovascular complications, despite similar glucose levels and BMI. Contour wave analysis by ultrasound provides additional information beyond IMT and local stiffness indices.

P4.53

IMMEDIATE EFFECTS OF SUBMAXIMAL EFFORT ON PULSE WAVE VELOCITY IN PATIENTS WITH MARFAN SYNDROME

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Marfan syndrome (MS) is a dominant autosomal disease caused by mutations in chromosome 15, the locus controlling fibrillin 1 synthesis, and may exhibit skeletal, ocular, cardiovascular, and other manifestations. Pulse wave velocity (PWV) is used to measure arterial elasticity and stiffness and is related to the elastic properties of the vascular wall. Since the practice of exercise is limited in MS patients, it was of interest to analyze the acute effect of submaximal exercise on aortic distensibility using PWV and other hemodynamic variables in patients with MS with either mild or no aortic dilatation. PWV and physiological variables were evaluated before and after submaximal exercise in 33 patients with MS and 18 controls. PWV was 8.51 ± 0.58 at rest and 9.10 ± 0.63 m/s at the end of exercise ($P = 0.002$) in the group with MS and 8.07 ± 0.35 and 8.98 ± 0.56 m/s in the control group, respectively ($P = 0.004$). Comparative group analysis regarding PWV at rest and at the end of exercise revealed no statistically significant differences. The same was true for the group that used β -blockers and the one that did not. The final heart rate was 10% higher in the control group than in the MS group ($P = 0.01$). Final systolic arterial pressure was higher in the control group ($P = 0.02$). PWV in MS patients with mild or no aortic dilatation did not differ from the control group after submaximal effort.