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### **P4.46: RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, DIASTOLIC FUNCTION AND GLYCEMIC CONTROL IN HEALTHY SUBJECTS**

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320-row CT scanner, and compared them with 101 Caucasians matched for age, gender and coronary risk factors.

**Results:** CAC prevalence was similar in the two groups (56.4% SA, 47.5% CA;  $p=0.25$ ) but mean CAC score (CACS) ( $p<0.0001$ ) and mean number of affected segments ( $p=0.0001$ ) were significantly higher in S.Asians, in whom also 3 vessel disease (VSD) (25.7% SA, 5.9% CA;  $p=0.0004$ ) and obstructive CAD (stenosis  $>50\%$  in any branch) were more common (19.8% SA, 5.76% CA;  $p=0.0041$ ). In patients  $\leq 50$  years old ( $n=37$ ), no significant difference was found between the two groups in mean CAC score ( $p=0.28$ ), affected segments number ( $p=0.12$ ) or CAD severity ( $p=0.684$ ) and extent ( $p=0.514$ ). In individuals  $>50$  years old, the CAC severity was higher in S.Asians (Table 1) as was the number of affected segments ( $p=0.001$ ).

**Conclusions:** Symptomatic S.Asians have more diffused coronary artery calcification, age plays an important role in this difference.

#### P4.43

##### ACUTE, INDUCED INFLAMMATION AFFECTS ARTERIAL LOAD

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Acute, systemic inflammation may contribute to a shift in ventricular-vascular coupling (VVC), quantified by the ratio of arterial load (Ea) to ventricular elastance (Elv). Fitness is associated with reduced systemic inflammation which may affect VVC. We determined the effect of acute systemic inflammation on VVC in young, healthy adults and evaluated the impact of fitness on this outcome. We tested 21 adults ( $m=15$ , mean age=25 yr, mean body surface area = 2.05m<sup>2</sup>) before and at 24 and 48 hr post influenza vaccination (inflammatory stimulus). Ventricular volumes were measured by ultrasound from the 4-chamber apical view. Applanation tonometry was used to measure end-systolic pressure (ESP). Arterial load was calculated as ESP/stroke volume (SV) and Elv was calculated as ESP/end-systolic volume (ESV). Treadmill VO<sub>2</sub> max was used to quantify fitness. A repeated measures (1 x 3) ANOVA was used with VO<sub>2</sub> max as a covariate, and Spearman's correlation used to assess relationships between variables. Ea increased at 48 hr post-vaccination (from 1.19 to 1.13 to 1.32 mmHg/ml),  $p<0.05$ , but Elv did not change at either time point ( $p>0.05$ ), resulting in an increase in VVC from 0.49 to 0.53 to 0.52,  $p<0.05$ , at 24 and 48 hr post vaccination. At 48 hr post-vaccination, the change in Ea was ( $r=0.45$ ,  $p<0.05$ ) related to VO<sub>2</sub> max. There were no significant changes in blood pressure. Thus, acute inflammation increased arterial load but not ventricular elastance, independent of changes in blood pressure. This increased VVC, and higher fitness was associated with greater inflammation induced changes in arterial load.

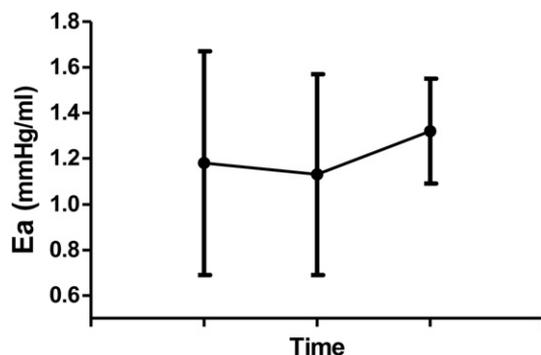


Figure 1 Ea (mmHg/ml) at baseline and at 24 and 48 hr post-inflammation. \* indicates  $p<0.05$  from baseline value

#### P4.44

##### REGIONAL ARTERIAL STIFFNESS ASSESSED BY POPMETRE® IN PATIENTS WITH CAROTID PLAQUES

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**Purpose:** To date, regional arterial stiffness can be easily evaluated using pOpmetre® (Axelife SAS – France), a new device measuring the pulse wave transit time (TT) between the finger (TTf) and the toe (TTt). The aim was to evaluate the relationship between the pOpmetre® indices and the presence of carotid plaques.

**Methods:** In 66 consecutive patients with risk factors (40 men aged  $54 \pm 2$  years; 26 women aged  $49 \pm 3$  years), the difference between TTt and TTf (Dt-f) and the pulse wave velocity (PWVt = Constant\*Height\_Patient / Dt-f in m/s) were measured by pOpmetre®. Doppler ultrasound imaging assessed presence of carotid plaques. The local aortic stiffness (AoStiff) was evaluated by the Physioflow® system.

**Results:** No statistical difference was found between the group of patients with carotid plaques ( $n=23$ ) and the rest of patients for Ankle-Brachial Index (ABI:  $1.13 \pm 0.02$  vs  $1.17 \pm 0.03$ ), systolic and diastolic blood pressure ( $83.8 \pm 2.1$  vs  $86.2 \pm 2.9$ ;  $131.2 \pm 2.7$  vs  $137.3 \pm 3.7$ ). The first group was older than the second one ( $59 \pm 2$  yrs vs  $49 \pm 2$  yrs,  $p<0.002$ ) with a larger intima media thickness ( $0.70 \pm 0.02$  vs  $0.63 \pm 0.01$ ,  $p=0.003$ ), a higher AoStiff and PWVt ( $10 \pm 1.0$  vs  $8 \pm 1.0$  m/s,  $p<0.03$ ;  $10.97 \pm 0.97$  vs  $8.84 \pm 0.43$  m/s,  $p<0.02$ ) and a shorter Dt-f ( $57.9 \pm 6.2$  vs  $70.4 \pm 3.2$  ms,  $p<0.02$ ). PWVt ( $r=0.49$ ,  $p<0.0001$ ) and Dt-f ( $r=0.54$ ,  $p<0.0001$ ) were correlated with age. **Conclusion:** Although we found no difference in ABI and arterial pressure, the data reveals an increased in local and peripheral arterial stiffness (pOpmetre®) for patients with carotid plaques.

#### P4.45

##### SUBTHERAPEUTIC, LOW-DOSE FLUVASTATIN IMPROVES FUNCTIONAL AND MORPHOLOGICAL ARTERIAL WALL PROPERTIES IN APPARENTLY HEALTHY, MIDDLE-AGED MALES

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**Objective:** Early arterial wall changes are already present in the apparently healthy, middle-aged population and continuously progress with age. The aim of our study was to investigate whether 30 days low-dose fluvastatin treatment could improve and reverse these arterial changes that are primarily associated with ageing, in otherwise healthy middle-aged males.

**Methods:** In a double blind, randomized study, 50 middle-aged males received either placebo or fluvastatin (10mg) for 30 days. Brachial artery flow-mediated dilation (FMD), pulse wave velocity (PWV) and  $\beta$ -stiffness of the common carotid artery were measured on the 1st, 14th and 30th day of the study using an Aloka instrument by integrated eTracking.

**Results:** In 77% of subjects, impaired endothelial function was revealed at inclusion in the study. All the parameters were improved already after 14 days, and after 30 days of treatment FMD improved by  $91.5 \pm 15.6\%$ , while PWV and  $\beta$ -stiffness improved by  $6.2 \pm 1.1\%$  and  $10.7 \pm 1.5\%$ , respectively (all  $P<0.001$ ). After therapy discontinuation, the beneficial effects progressively decreased, but were still detectable after 5 months. During the study the lipid profile remained unchanged, thus the beneficial effects obtained were attributed to the pleiotropic effects of fluvastatin.

**Conclusions:** We found that subtherapeutic low-dose fluvastatin (10mg daily; 30 days) considerably improves and reverses early functional and morphological arterial wall impairments that are present in apparently healthy, middle-aged males. It might be supposed that such a new and original approach could be valuable in cardiovascular prevention.

#### P4.46

##### RELATIONSHIP BETWEEN ARTERIAL STIFFNESS, DIASTOLIC FUNCTION AND GLYCEMIC CONTROL IN HEALTHY SUBJECTS

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Insulin resistance with its associated metabolic derangements is associated with cardiovascular disease. It is unknown if lesser degrees of this metabolic derangement are associated with early vascular functional or structural changes. Our aim is to examine the relationship between glycemic indices and early vascular dysfunction in healthy subjects.

For this study 109 male and 117 female, lifelong non-smoking, normotensive subjects ( $40 \pm 11$  years, BMI  $25.6 \pm 3.9$  kg.m<sup>2</sup>) 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  $5.02 \pm 0.46$  mmol.L<sup>-1</sup> and  $4.96 \pm 1.09$  mmol.L<sup>-1</sup>. Mean CIMT, carotid compliance & distensibility, PWV and MV E/A were  $0.52 \pm 0.07$  mm,  $15.86 \pm 13.15$  m<sup>2</sup>.kPa.10<sup>-7</sup> &  $49.09 \pm 34.95$  kPa.10<sup>-3</sup>,  $7.03 \pm 1.23$  m.s<sup>-1</sup> and  $43.46 \pm 18.65$  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,  $22.8 \pm 0.4$  years) (N=11), young sedentary (YS,  $23.3 \pm 0.3$  years) (N=11), elderly healthy trained (ET,  $50.6 \pm 1.0$  years) (N=12) and elderly sedentary subjects (ES,  $47.7 \pm 0.9$  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 ( $70.38 \pm 6.0$  % of precooling value) when compared to the YS ( $41.23 \pm 7.6$  %) (Dunnett's test,  $p < 0.01$ ). In contrast, there was no significant difference in LDF response to cold in YT ( $49.60 \pm 9.3$  %) and ET ( $53.65 \pm 8.2$  %). **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  $61 \pm 10$  years and a BMI von  $30 \pm 6$  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 $\beta$ -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