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### **P1.07: A LONGITUDINAL PILOT STUDY OF AORTIC STIFFNESS IN COPD**

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## P1.04

## IMPACT OF WEIGHT-REDUCTION ON ARTERIAL STIFFNESS IN OBESE CHILDREN AND ADOLESCENTS: A ONE YEAR FOLLOW-UP STUDY

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**Introduction:** Recently, in a cross-sectional study, we have found arterial stiffness assessed as carotid-femoral pulse wave velocity (cfPWV) to be reduced in obese children and adolescents. Therefore, we wanted to investigate whether weight-reduction influenced cfPWV independently of blood pressure (BP).

**Methods:** One hundred obese patients with age 10-18 years newly referred to the Children's Obesity Clinic were investigated before and after one year of lifestyle intervention. CfPWV and augmentation index at heart rate 75 (AIx@HR75) were measured non-invasively using the SphygmoCor device. Weight-reduction was defined as  $\Delta$ BMI z score  $<0$ . [ClinicalTrials.org](http://ClinicalTrials.org) NCT01310088.

**Results:** Seventy-three of initial 104 patients were followed up (period: median 364 days (IQR 364-371)).  $\Delta$ BMI z score was mean  $-0.26 \pm 0.41$  ( $P < 0.0001$ ) in the total group, whereas fifty-five (75.3%) patients responded to treatment. Patients were divided by  $\Delta$ BMI z score tertiles into high-, low- and non-responders. No difference was found in clinic BP in the total group at follow up or across responders ( $P = NS$ ).  $\Delta$ cfPWV was higher in the total group at follow up ( $0.26 \pm 0.47$  m/s,  $P < 0.0001$ ) with no difference across responders ( $P = 0.87$ ). Furthermore,  $\Delta$ cfPWV showed no relationship with  $\Delta$ BMI z score ( $P = 0.82$ ), neither when adjusting for gender, baseline age, heart rate and mean arterial pressure ( $P = 0.99$ ). Similar,  $\Delta$ AIx@HR75 was higher at follow up ( $2.77 \pm 9.91$ ,  $P = 0.020$ ) with no difference across responders ( $P = 0.42$ ).

**Conclusion:** No effect of weight-reduction was found on measures of arterial stiffness. In this respect, the higher arterial stiffness at follow up seems age-related.

## P1.05

## AORTIC PULSE WAVE VELOCITY BUT NOT AUGMENTATION INDEX IS ASSOCIATED WITH ASYMPTOMATIC CAROTID ATHEROSCLEROSIS

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**Objectives:** To study the association between aortic stiffness, assessed by a single arm cuff oscillometric method, and asymptomatic carotid atherosclerosis (ACA) in a healthy population.

**Methods:** We studied 234 normotensive subjects without known cardiovascular disease or diabetes ( $125 \pm 9 / 75 \pm 8$  mm Hg,  $51 \pm 11$  years, 58% women) attending voluntary health screening. Aortic pulse wave velocity (PWVao) and augmentation Index (Aix) were measured with an Arteriograph. ACA (by ultrasonography) was defined as a  $\geq 1.0$  mm echogenic plaque and/or a focal  $\geq 1.3$  mm increase of intima-media thickness.

**Results:** Asymptomatic ACA was present in 60 subjects (26%). There were differences between subjects with and without ACA (all  $P < 0.001$ ) in stiffness parameters (PWVao  $9.6 \pm 1.6$  vs  $8.2 \pm 1.3$  m/s, Aix  $34.8 \pm 12.9$  vs  $25.7 \pm 14.5\%$ ), and age ( $59 \pm 9$  vs  $48 \pm 10$  years, respectively), but not in systolic and diastolic blood pressure ( $126 \pm 8$  vs  $124 \pm 9$ , and  $76 \pm 7$  vs  $75 \pm 8$  mm Hg, respectively). In a logistic regression analysis performed to define factors related to ACA (including age, gender, smoking, body mass index, systolic blood pressure, heart rate, Aix, and PWVao), age, smoking, and PWVao remained independently related (all  $P < 0.05$ ) to ACA. The optimal threshold of PWVao to identify ACA was 8,7 m/s; details are shown below.

**Conclusions:** PWVao measured with the Arteriograph in an apparently healthy normotensive population is independently related to ACA, while Aix is not. We suggest that Aix might be related to an early stage of atherosclerosis, whereas PWVao is a more specific marker of macrovascular atherosclerosis.

	Value	95% Confidence Interval
Sensitivity	0.72	0.59–0.82
Specificity	0.71	0.64–0.77
Positive predictive value	0.45	0.36–0.56
Negative predictive value	0.88	0.81–0.92
Relative risk	3.77	2.29–6.19
Odds ratio	6.1	3.19–11.68

## P1.06

## CARDIO-ANKLE VASCULAR INDEX (CAVI) IS AN INDEPENDENT PREDICTOR OF DEATH IN MAINTENANCE HEMODIALYSIS PATIENTS

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**Objects:** The purpose of this study was to calculate robust quantitative estimates of the predictive value of cardio-ankle vascular index, (CAVI) for future all-cause mortality in hemodialysis patients.

**Subjects and methods:** A total of 163 hemodialysis patients (102 males and 61 females, mean age  $60 \pm 11$  years), who had the examination of CAVI between 2004 and 2005 at Mihama Narita Clinic, Chiba, Japan, were included and followed up for 80 months. Those had diabetes mellitus (27.0%), hypertension (77.3%) or/and dyslipidemia (36.8%). CAVI was measured using Vaseta1500 (Fukuda Denshi. Co.LTD).

**Results:** Among 163 hemodialysis patients, 51 deaths were observed in 6.5 years. Causes of death were heart disease (37.3%), brain stroke (19.6%), infection (17.6%), suffocation (3.9%) and others. In subjects with death, higher CAVI ( $9.3 \pm 1.8$  vs.  $8.3 \pm 1.2$ ), mean age ( $65 \pm 12$  vs.  $57 \pm 10$  years) and prevalence of diabetic nephropathy (43.1 vs. 19.6%) were observed.

COX proportional-hazards regression analysis of the association between death and clinical variables showed that high CAVI ( $\geq 10$ ) independently increased the risk of death with OR of 2.605 (95% CI 1.321-5.141,  $P = 0.006$ ). OR of Diabetic nephropathy was 2.027 (95% CI 1.102-3.727,  $P = 0.023$ ) and OR of elderly ( $\geq 65$  years) was 3,152, (95% CI 1.758-5.649,  $P < 0.0001$ ).

Kaplan-Meier curves for cumulative survival in hemodialysis patients stratified by severity of CAVI ( $8 >$ ,  $9 >$ ,  $10 >$ ,  $10 <$ ) showed that the survival rates on the patients with higher CAVI groups were significantly low ( $P = 0.002$ , Log-rank test).

**Conclusion:** CAVI is an independent predictor of death in hemodialysis patients.

## P1.07

## A LONGITUDINAL PILOT STUDY OF AORTIC STIFFNESS IN COPD

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**Background:** Increased arterial stiffness has been established in patients with COPD (1). However, the changes in aortic stiffness over time and contributing factors are still unknown. We hypothesise that there would be a significant change in aortic stiffness in COPD over one year.

**Methods:** Aortic pulse wave velocity (PWV) was measured using the SphygmoCor device at baseline and after one year in 30 (14 males) patients with stable COPD and 10 (6 males) controls, they free from cardiovascular diseases. Spirometry, peripheral and central blood pressure, body composition and serum creatinine were also determined as well as heart rate, smoking status and number of exacerbations per year.

**Results:** Of the patients, 16 (10 male) showed increased aortic PWV (progressor) from their baseline measurements, mean (SD) 1.70 (2.1) m/s, which related to serum creatinine  $r = 0.66$ ,  $p = 0.01$ . There was no change in PWV in the remaining (non-progressor). Both groups were similar in age, FEV<sub>1</sub>%, blood pressure or mean arterial pressure (MAP). The difference in aortic stiffness between progressor and non-progressor in COPD remained significant after adjustment for MAP, heart rate, smoking status and number of exacerbations,  $R^2 = 0.71$ ,  $p < 0.001$ . The changes over one were greater in patients than controls, 1.70 (0.92) vs 0.85 (0.77) m/s, respectively,  $p < 0.001$ .

**Conclusion:** The increase in aortic stiffness in subset COPD patients was independent of conventional risk factors. The relationship of aortic PWV with

creatinine may indicate subclinical organ damage with a greater risk of cardiovascular disease.

#### P1.08

##### DETERMINANTS OF VASCULAR DAMAGE IN SYSTEMIC LUPUS ERITHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is associated with increased cardiovascular risk and early vascular aging. The aim of the study was to evaluate aortic and carotid stiffness, central blood pressure (BP) and wave reflection in women with SLE, in order to identify whether different vascular districts are similarly influenced by disease duration, activity and organ damage.

**Methods:** Medical and pharmacological history were collected. Disease activity and organ damage were evaluated by ECLAM e SLICC/ACR-DI scores, respectively. Pulse Wave Velocity (PWV) and Augmentation Index (AI) were acquired by applanation tonometry, whereas carotid intima-media thickness (IMT) and stiffness were obtained by an automated image analysis system.

**Results:** 46 SLE women were enrolled (age 41±10years, BP 116±16/76±9 mmHg). Mean disease duration was 17±9years, ECLAM 0,9±1, SLICC 0,9±1,5. PWV(7,4±1,5 m/s) was related to age (r=0.52, p<0,001), mean BP (r=0.59, p<0.001), SLICC (r=0.44, p=0,01). AI (22,5±10,6%) was related to age (r=0.58,p<0,001), mean BP (r=0.50,p<0.001), SLICC (r=0.60,p<0,001), cumulative corticosteroid dose (CCD,r=0.40,p=0.03). Carotid IMT was related only to age (r=0.45, p=0.006). Carotid stiffness was related to age(r=0.68,p<0.001), AI (r=0.54,p<0.001), disease duration (r=0.45,p<0.03), CCD (0.52, 0.01). In multiple regression models adjusted for confounders, SLICC remained an independent predictor of PWV (p=0.04,r<sup>2</sup>=0.13) and AI (p=0.04, r<sup>2</sup>=0.16). Conversely, CCD (p<0.001,r<sup>2</sup>=0.25) and SLICC (p=0.02,r<sup>2</sup>=0.01) were independent predictors of carotid stiffness.

**Conclusions:** In a cross-sectional analysis of a cohort of SLE patients, increased arterial stiffness and wave reflection are independently associated with disease-specific organ damage, but not with disease activity or duration; carotid stiffness is also selectively compromised by chronic corticosteroid use.

#### P1.09

##### MILD COGNITIVE IMPAIRMENT IS ASSOCIATED WITH SYSTEMIC VASCULAR DYSFUNCTION

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**Aim:** To evaluate vascular function and structure in subjects with mild cognitive impairment (MCI).

**Methods:** 58 MCI and 22 controls (age 74±5vs75±4years, men 45vs59% p=ns) were recruited. Endothelial function in the brachial artery (BA) was studied by flow-mediated dilation (FMD) and response to glyceryl trinitrate, (GTN), while large artery stiffness was measured as carotid-femoral pulse wave velocity (PWV).

**Results:** MCI and controls had a similar prevalence of established CV disease (14vs13%,p=ns) and traditional CV risk factors (hypertension 50vs54%, diabetes 13vs5%, dyslipidemia 28vs48%, smoking 4vs9%, p=ns for all). MCI showed higher blood pressure (BP) values than controls (pulse pressure 70±16vs62±12mmHg, mean BP 97±9vs91±8 mmHg, p<0.05 for both). PWV tended to be higher in controls compared to MCI (11.0±2.2vs9.9±2.4 m/s, p=0.07) but the difference was not significant after considering mean BP as covariate. MCI and controls showed similar BA diameter baseline shear rate (SR) and response to GTN. In MCI hyperemic SR and SR area under the curve were significantly lower (1591±831vs1175±673s<sup>-1</sup>, 29.7±15,8\*10<sup>3</sup>vs 21.1±14.9\*10<sup>3</sup>, p<0.05 for all) and time to peak was delayed compared to controls (50±16 s59±16s, p<0.05). Mean FMD values, allometrically corrected for baseline BA diameter, were significantly reduced in MCI (4.5±2.9vs2.7±2.9%, p<0.01). The difference remained significant after considering age, mean BP, and SR area under the curve as covariates (p<0.01).

**Conclusions:** Patients with MCI showed a significant reduction in conduit artery endothelial function as well as in microcirculatory function. These data

support the hypothesis that impaired systemic vascular function might hamper cognitive function.

#### P1.10

##### BENEFICIAL EFFECT OF SEQUENTIAL NEPHRON BLOCKADE OF CENTRAL PRESSURE AND LARGE ARTERY REMODELLING IN RESISTANT HYPERTENSION

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**Objective:** We have previously shown that combined renin-angiotensin system blockade (RB) was less effective than sequential-nephron blockade (SNB) for controlling BP in resistant hypertension (RH). Whether this is accompanied with an improvement in the mechanical properties of large arteries is unknown.

**Design and method:** Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) >135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. Central pulse pressure (CPP) and carotid-femoral pulse wave velocity (PWV) were measured by applanation tonometry. High-resolution echotracking system (Walltrack<sup>®</sup>) was used to measure carotid artery diameter (Dcca), wall thickness (WT), circumferential wall stress (CWS), and stiffness. All parameters were measured at baseline and week 12.

**Results:** Baseline clinical characteristics did not differ between groups. dASBP decreased more in SNB (-19±12 mmHg) vs RB (-8±13 mmHg, p<10-6), either for CPP [SNB (-12.8±16.9 mmHg) vs RB (-1.0±9.3 mmHg, p<0.006)] after adjustment on baseline CPP and delta MeanBP. CCA stiffness and PWV decreased similarly in both groups. Dcca decreased more in SNB (-267±46 µm) vs RB (-7.8±39 µm, p=0.01) after adjustment on baseline D and delta ASBP. WT did not differ and CWS decreased more in SNB (-15.2±16.5 kPa) vs RB (-5.2±12.6 kPa, P=0.001).

**Conclusions:** In RH pts, a ttt strategy based on SNB improved CPP to a greater extent than a RB strategy. This may lead to a better target organ damage prevention and CV outcome. SNB improved CWS. Whether this effect is due aldosterone blockade or sodium depletion remains to be investigated.

#### P1.11

##### TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE

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**Objective:** We previously showed that sequential-nephron blockade (SNB) was more effective than combined renin angiotensin system blockade (RB) for controlling BP in patients with resistant hypertension (RH). We assessed medication adherence (MA) on the antihypertensive (AHT) response to SNB/RB with a new combined scoring system.

**Design and method:** Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) ≥135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. MA was scored as: (i) plasma Irb concentration; (ii) urinary AcSDKP/creatinine ratio (UR); (iii) last medication intake before visit (LMI); and (iv) pill counting (PC, %). 1 point of MA score was attributed to Irb >20ng/ml, UR >4nmol/mmol, LMI <24h, PC >80%. MA was defined as low (LMA, score ≤2), intermediate (IMA, score =3), and optimal (OMA, score =4).

**Results:** Among 164 pts: 82 had OMA (46 SNB/36 RB), 52 IMA (23 SNB/29 RB) and 30 LMA (13 SNB/17 RB) (NS). LMA pts were younger than SAs pts (50±11 vs. 56±10 yrs, p<0.011). In OMA pts, the difference in dASBP/dADBP between SNB vs RB was significant (-11 [-17 ; -6]/-6 [-9 ; -2] mmHg, p<0.0001/p=0.0025), favoring SNB, whereas in LMA pts the difference between the two groups did not reach significance (-6 [-19 ; 7]/-1 [-10 ; 7] mmHg, p=0.352/p=0.7096).