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### **P1.26: AORTIC PULSE WAVE VELOCITY IN OBESE CHILDREN AND ADOLESCENTS**

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Parameters	CONTROLS		ATEN		AML		ENL		LOS	
GENDER	M (89)	F (42)	M (75)	F (39)	M (66)	F (47)	M (135)	F (60)	M (95)	F (47)
AGE	49 ± 7	47.5 ± 7	56 ± 8	56 ± 8	55 ± 8	54 ± 9	55 ± 8	56 ± 8	57 ± 8	55 ± 7
SBP mmHg	127 ± 14	118.5 ± 14	131 ± 14	131 ± 12	136 ± 12	133 ± 11	135 ± 13	132 ± 12	131 ± 12	133 ± 12
DBP mmHg	80 ± 10	75 ± 9	83 ± 9	81 ± 8	84 ± 8	80 ± 10	84 ± 7.5	81 ± 8	83 ± 7.5	82 ± 8
HR lpm	63 ± 12	71 ± 11	61 ± 11	62 ± 7	66 ± 10	68 ± 12	67 ± 15	69 ± 11	66 ± 11	67 ± 12
PP c mmHg	37 ± 8	43 ± 9	48 ± 11	56 ± 10	48 ± 14	51 ± 12	47 ± 12	52 ± 11	46 ± 14	55 ± 9
PP p mmHg	47 ± 8	43 ± 10	48 ± 10	50 ± 9	51.5 ± 9	52.5 ± 15	51 ± 10	51 ± 10	48 ± 10	51 ± 7.5
Aix c %	19 ± 9.5	31 ± 12	32 ± 11.5	43 ± 8	30 ± 12	41 ± 9	28 ± 14	38 ± 11	27 ± 11	41 ± 11
Aix p %	-30 ± 26.5	-7 ± 31	4 ± 3	24 ± 18	-5 ± 28	19 ± 20	-10 ± 36	18 ± 47	-13 ± 26	16.5 ± 27.5
PWV m/s	9 ± 2	9 ± 2	12 ± 9.5	10 ± 3	12 ± 2	10 ± 2	12 ± 2	10 ± 2	11 ± 2	10 ± 2

Ref: SBP: Systolic Blood Pressure DBP: Diastolic Blood pressure HR: Heart Rate PPc: Central Pulse Pressure PPp: Peripheral Pulse Pressure Aix c: Central Augmentation Index Aix p: Peripheral Augmentation Index PWV: Pulse Wave Velocity.

## P1.24

## ASSESSMENT OF RISK FACTORS IN CHRONIC AIRWAYS DISEASE EVALUATION (ARCADE)

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**Background:** Chronic obstructive pulmonary disease (COPD) is a multi-system disorder with important systemic co-morbidities. These include increased cardiovascular (CV) risk which accounts for 30-50% of deaths. Cross-sectional studies have identified increased arterial stiffness in COPD, however there is no validated prognostic CV risk predictor.

**Methods:** The ARCADE is a longitudinal study of up to 1500 patients with confirmed COPD. Assessments include pulmonary function (spirometry), arterial stiffness (aortic pulse wave velocity (PWV)), blood pressure (BP), blood biochemistry and 6-minute walking distance (6MWD). These assessments will be repeated after two and five years.

**Results:** Thus far 300 patients have been compared to 36 controls (table 1). Mean PWV, systolic BP, and HsCRP was higher in patients than controls, and lung function impaired in patients with COPD. These differences remained after adjustment for age. Although mean blood pressure was similar, on assessment more patients (n= 185, 62%) met the criteria for hypertension (>140/90mmHg) than controls (n=16, 44%). More patients with COPD were on treatment for hypertension (n= 138, controls = 3, p=<0.001) and hypercholesterolemia (n=107 controls = 7, p=0.04). In patients, PWV related to the number of co-morbidities (r=0.377, p<0.05).

**Conclusions:** This is the first study to evaluate the progression of the systemic components of COPD over the medium to longer term. The results to date confirm previous findings of elevated PWV and increased CV risk factors. The longitudinal assessments will inform the understanding of the rate and cause of arterial stiffness and other systemic components in COPD, and may guide therapeutic interventions.

Mean (SD)	COPD	Control	p
Age (years)	66 (8)	62 (10)	0.012
Gender M/F	150/150	18/18	0.508
FEV <sub>1</sub> %	56 (20)	102 (13)	<0.001
FEV <sub>1</sub> /FVC	0.53 (0.12)	0.77 (0.06)	<0.001
Peripheral Systolic BP (mmHg)	147 (19)	138 (18)	0.005
Peripheral Diastolic BP (mmHg)	82 (11)	80 (10)	0.345
Peripheral Mean Arterial Pressure (mmHg)	104 (12)	101 (12)	0.089
Heart Rate (bpm)	74 (11)	68 (10)	<0.001
PWV (m/s)	9.9 (2.5)	7.8 (1.3)	<0.001
HsCRP (mg/L)	6.4 (8.7)	3.0 (3.0)	<0.001

## P1.25

## IN OLDER ADULTS, SEDENTARY TIME IS ASSOCIATED WITH INCREASED BRACHIAL PULSE PRESSURE INDEPENDENT OF PHYSICAL ACTIVITY LEVELS AND AGE

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**Background:** Sedentary behaviour leads to increased blood pressure (BP), and regular physical activity reduces BP. However, the extent to which elevated BP associated with sedentary behaviour can be offset by regular physical activity is unknown, and was the aim of this study.

**Methods:** Study participants (n=637, aged 66.3±7years; 49% male) were from the Tasmanian Older Adult Cohort Study, which was a randomly selected community sample of older men and women aged 50-79 years. Average time spent per day in sedentary behaviour (e.g. sitting/lying) and physical activity (light, moderate and vigorous intensity) was determined by accelerometers (worn over 1 week). Brachial BP was measured by automated oscillometry.

**Results:** The average activity levels per day were: sedentary (584±94 min), light (227±72 min), moderate (32±25 min) and vigorous (1±4 min) intensity. Participants in the highest tertile of sedentary time had the highest pulse pressure (PP; p=.014) and highest prevalence of isolated systolic hypertension (p<.001). Sedentary time was significantly associated with PP (r=0.110; p=.005). This association remained significant on multiple regression analysis after adjustment for physical activity levels, sex, body mass index and presence of diabetes (β=.158; p=.005). Age was also associated with PP and this was both independent of, and partially mediated by, sedentary time.

**Conclusions:** The amount of time spent sedentary is independently associated with increased PP in older adults and could be one reason why PP increases with age. This suggests decreasing sedentary behaviour in older people could help to achieve better BP control, regardless of the level of physical activity.

## P1.26

## AORTIC PULSE WAVE VELOCITY IN OBESE CHILDREN AND ADOLESCENTS

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The global childhood obesity epidemic threatens future health due to a rise in cardiovascular disease. There is a need for identifying subclinical organ damage (SOD) markers when evaluating cardiovascular risk in the young since hard end points does not/rarely exist among adolescents. Aortic pulse wave velocity (aPWV) is an established marker of SOD in adults. Furthermore, studies on adults have shown that obesity is correlated with a higher aPWV. It is uncertain whether this relationship is manifest already in the young since high aPWV is regarded as a measure of chronic change to the vasculature. The present study assess aPWV in a cross-sectional survey where 100 obese children and adolescents, median age 12.7 years (range 10.1 to 18.9) are compared with 50 healthy gender and age matched individuals, median 12.9 years (10.3 to 17.9). Mean aPWV (SD; 95% CI) were in the obese group 4.52 m/s (0.53; 4.42 to 4.62) and in the control group 4.32 m/s (0.50; 4.17 to 4.47). Preliminary

unadjusted results analysed by unpaired t-test, shows that obese individuals have a higher aPWV of 0.2007 m/s compared with the control group ( $P = 0.0338$ , 95% CI: 0.39 to 0.02). When analysing data in correspondence with a European normal material obese children had an aPWV standard deviation score in the normal range for age and height although higher than the control group in the present study. This study shows that obesity is correlated to a higher aPWV although this effect may disappear after adjustment for possible confounders.

#### P1.27

##### NT-PROBNP AND VASCULAR CALCIFICATION IN AFRICAN AND CAUCASIAN MEN: THE SAFREIC STUDY

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**Background:** The N-terminal prohormone B-type natriuretic peptide (NT-proBNP) is a reliable marker of cardiac strain. In hypertensive heart disease, NT-proBNP levels increase and may lose its protective function. Simultaneously, the vasculature is also subject to hemodynamic stress, resulting in vascular matrix remodelling and stiffening which contribute to further cardiac alterations. Alkaline phosphatase (ALP) is a marker of osteoblast activity and is involved in vascular calcification. We explored the link between NT-proBNP and ALP in African and Caucasian men.

**Design and measurements:** This study included 128 African (mean age, 41.1 years) and 118 Caucasian (mean age, 36.4 years) men. Conventional measurements were acquired along with serum NT-proBNP and ALP.

**Results:** NT-proBNP correlated positively with ALP ( $r = 0.29$ ;  $p < 0.001$ ) in Africans, but inversely in Caucasians ( $r = -0.20$ ;  $p = 0.024$ ). After minimal adjustment (age, body mass index, SBP and arterial compliance), the positive significant correlation of NT-proBNP with ALP remained in African men ( $r = 0.225$ ;  $p = 0.014$ ), whereas significance was lost in Caucasian men. Multiple regression analyses confirmed the independent association of NT-proBNP with ALP in African men ( $R^2 = 0.37$ ;  $\beta = 0.248$ ;  $p = 0.005$ ), as well as in younger African men ( $R^2 = 0.26$ ;  $\beta = 0.375$ ;  $p < 0.001$ ;  $n = 96$ ), with no significance in Caucasians.

**Conclusions:** NT-proBNP is independently and positively associated with ALP in African men. This was however not evident in Caucasian men. These results suggest that African men are susceptible to early vascular calcification and may develop cardiac afterload prematurely.

#### P1.28

##### THE ACCUMULATION OF RISK FACTORS OF METABOLIC SYNDROME IS ASSOCIATED WITH THE INCREASE IN ARTERIAL STIFFNESS AMONG MIDDLE-AGED MALE INDUSTRIAL WORKERS

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Early detection of arterial dysfunction is important in preventing cardiovascular diseases. We evaluated the associations of the accumulated cardiovascular risk factors with the cardio-ankle vascular index (CAVI), a new indicator of arterial stiffness.

**Methods:** The study population consisted of 101 employees in the forest industry (49±8 years of age). CAVI was measured by PWV method (VaSera, Fukuda Denshi, Japan). International Diabetes Association (IDF) criteria for metabolic syndrome were used to dichotomize the cardiovascular (CV) risk variables (<http://www.idf.org/metabolic-syndrome>). Statistical analyses were performed by SPSS 20.0 for Windows (SPSS, USA). Number of risk factors was used as a grouping variable for group comparisons. Independent-Samples T Test was used to compare means and stepwise multiple regression to evaluate the independent risk factors affecting CAVI.

**Results:** There were no differences between number of risk factors and CAVI in women. Only the men ( $N = 72$ , 49±8 years of age) were included in further analyses. The CAVI of the men with 3 or 4 risk factors was significantly higher than the CAVI of the men without risk factors ( $p$ -values 0.025 – 0.0005). Men with elevated blood glucose level (B-Gluc) or arterial blood pressure (BP) had significantly higher CAVI than men with normal B-Gluc ( $p = 0.032$ ) and BP ( $p = 0.007$ ). In the regression analysis Age ( $\beta = 0.455$ ,  $p = 0.000$ ), B-Gluc ( $\beta = 0.237$ ,  $p = 0.038$ ), systolic blood pressure ( $\beta = 0.268$ ,  $p = 0.010$ ) and

waist circumference ( $\beta = -0.201$ ,  $p = 0.064$ ) explained 45.1 % of the variation in CAVI.

**Discussion:** Among middle-aged men the number of CV risk factors is an important determinant of cardiovascular health assessed by arterial stiffness. B-Gluc and BP may have a special negative effect on CAVI. Waist circumference seems to be more useful risk factor for arterial dysfunction in male workers than BMI.

#### P1.29

##### AN IGF2 RECEPTOR GENE POLYMORPHISM MODULATES BLOOD PRESSURE TRENDS OVER TIME IN TYPE 2 DIABETES

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**Rationale:** Previous studies have associated low circulating IGFBP-2 with diastolic BP in a cross-sectional population. We examined 1) the relation between IGFBP-2 and long term trends in blood pressure in a population with type 2DM and 2) the relation between blood pressure and SNPs from the IGFBP-2 and IGF2 receptor (*IGF2R*) gene.

583 individuals with T2DM (58.5% male;  $n = 341$ ) had repeated yearly cardiometabolic assessments between 2002 and 2009. We used a commercial ELISA (RayBio Inc) platform for IGFBP-2 measurement. Haplotype tagging SNPs (8 from *IGF2* gene, 12 from *IGF2R* gene and 2 from *IGFBP2* gene) were selected.

**Results:** High baseline IGFBP-2 ( $\beta = -1.52$  95% CI: -2.56, -0.49,  $p = 0.004$ ) was associated with a longitudinal decrease in diastolic BP over 8 years, adjusted for age, gender, diabetes duration, time effects, as well as IGF-I, IGF-II, IGFBP-1, IGFBP-3 and anti-hypertensive use. There was no association in a similar model using systolic BP. In mixed-effects regression models the SNP rs2014620 from the *IGF2R* gene (encoding the IGF-II receptor which degrades IGF-II) was associated with decreased diastolic BP over the 8-year period adjusted for age and gender ( $\beta = -0.252$ , 95% CI -0.14 to -0.298,  $p = 0.003$ ). Significance remained after gene-wise Bonferroni adjustment. This SNP rs2014620 was also nominally associated with higher baseline IGFBP-2 adjusted for age and gender ( $\beta = 0.119$ ,  $p = 0.011$ ).

**Conclusion:** We suggest that SNPs in the *IGF2R* gene may influence IGF-II bioavailability independently of IGF-II degradation, with the possibility that variations in this gene directly modulate longitudinal diastolic blood pressure trends.

#### P1.30

##### IN HIGH CVD RISK GROUP ARTERIAL FUNCTION MARKERS CORRELATE WEAKLY WITH PWV AND AIXHR75 AS EXCEPTIONS

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**Background:** With more recent publications it is becoming obvious that arterial wall function contributes to the cardiovascular disease (CVD) risk. Relatively few studies investigated high CVD risk subjects, where arterial wall function abnormalities are likely to be more pronounced with multiple risk factors. The aim of the study was to assess the relationship between arterial wall markers in a high CVD risk subjects.

**Methods:** A cross-sectional study included patients with metabolic syndrome but with no previous CVD. Arterial stiffness (aortic pulse wave velocity [PWV] augmentation index [Aix], carotid and ankle-brachial stiffness index [CSI and CAVI, respectively]), endothelial function (flow-mediated dilatation in brachial artery and finger [RHI]), and carotid intima-media thickness (CIMT) were measured. Univariate and multivariable association assessment between these parameters was performed.

**Results:** Among 3168 subjects (aged 55±5, 69% women) univariate analysis revealed that markers significantly ( $p < 0.01$ , Pearson  $r > 0.1$ ) associated with PWV and Aix are CAVI and RHI, and PWV correlates with Aix. CSI was significantly associated only with CIMT. No significant interaction between other independent variables was observed. Interestingly, 2/3 of markers revealed higher correlations for male compared to female group. Traditional risk factors (gender, age, blood pressure, BMI etc.) explained only 12-34% of variability for PWV, Aix, and CSI.

**Conclusion:** In this high CVD risk group we did not find a definite/strong correlation between most of the arterial markers investigated, possibly because they reflect different stage of the same process or due to varying impact of different factors. Stronger inter-correlation of the arterial markers was observed in men.