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### **P4.3: INFLUENCE OF GENDER ON AORTIC STIFFNESS IN COPD**

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## P3.11

## CAROTID INTIMA-MEDIA THICKNESS IS POSITIVELY ASSOCIATED WITH SUBCHRONIC PERSONAL EXPOSURE TO BLACK CARBON: A STUDY IN A PANEL OF HEALTHY ADULTS

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**Background:** Research shows an association between particulate air pollution exposure and cardiovascular morbidity and mortality, with atherosclerosis as an implied underlying mechanism. The accurate assessment of personal exposure is a major challenge in epidemiological research since it is strongly related to time-activity patterns. We investigated carotid intima-media thickness (CIMT) in association with subchronic personal exposure to black carbon (BC) in a panel of healthy adults.

**Methods:** Personal BC exposure of 54 participants (92.3% female; mean age 40.7 years) was measured during one average workweek as a proxy for subchronic exposure. Within this week, the CIMT of each participant was measured ultrasonographically on two separate days. The effect of personal BC exposure on CIMT was estimated using mixed models adjusted for covariates including gender, age, exposure to secondhand smoke and general health indicators.

**Results:** The analyses showed a strong positive association between CIMT and personally measured BC. An interquartile range (320.8 ng/m<sup>3</sup>) higher personal BC exposure was associated with a 40.7 μm (95% CI: 16.0 to 65.5 μm; p=0.0026) thicker CIMT. Each year increase in age was associated with a 5.02 μm (3.30 to 6.74; p<0.0001) thicker CIMT, suggesting that an IQR higher personal BC exposure is equivalent to 8 years of ageing.

**Conclusion:** Based on individually measured BC exposures in a relatively young cohort of healthy nurses, our results suggest a larger impact of BC on CIMT than reported so far for other measures of pollution, including particulate matter.

## P3.12

## BLOOD PRESSURE CHANGES IN ASSOCIATION WITH PERSONAL BLACK CARBON EXPOSURE ARE NOT MEDIATED THROUGH MICROCIRCULATORY RESPONSES

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Exposure to ambient particulate matter and elevated blood pressure are risk factors for cardiovascular morbidity and mortality. Microvascular changes might be an important pathway in the association between air pollution and blood pressure. The objective of the study was to evaluate the role of the retinal microcirculation in the association between black carbon exposure and blood pressure.

A total of 56 healthy adults were provided with a μ-aethalometer for one week to measure personal exposure to black carbon. Blood pressure and retinal microvasculature were measured on average on four different days (range: 2-4) during this week.

Mean black carbon exposure was 866 ± 425 ng/m<sup>3</sup> and ranged from 201 ng/m<sup>3</sup> to 2415 ng/m<sup>3</sup>. An interquartile range increase (313 ng/m<sup>3</sup>) in black carbon exposure was associated with a 2.80 mm Hg (95% CI: 1.12 to 4.49, p<0.01) increase in systolic blood pressure and a 2.48 mm Hg (95% CI: 1.21 to 3.74, p<0.001) increase in diastolic blood pressure. These associations were independent of individual characteristics and time varying factors. Mediation analysis failed to reveal an effect of retinal microvasculature in the association between blood pressure and black carbon.

In conclusion, we found a positive association between blood pressure and personal black carbon exposure in healthy adults. This finding adds evidence to the association between black carbon exposure and cardiovascular health effects, with elevated blood pressure as a plausible intermediate effector. Our results suggest that the association between a person's usual blood pressure and black carbon exposure operates independent of the microcirculation.

## P4.1

## IMPACT OF AGE AND GENDER ON THE DETERMINANTS OF PULSE PRESSURE AND ISOLATED SYSTOLIC HYPERTENSION

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Age-related increases in pulse pressure (PP) across the adult age-span, and the development of isolated systolic hypertension (ISH), the extreme form of high PP, are often presumed due to age-related arterial stiffening. However, stroke volume (SV) is a key physiological determinant of PP, but the impact of SV on age-related changes in PP and ISH is unclear. We sought to quantify the impact of age on the physiological determinants of PP and ISH.

Detailed haemodynamic data including blood pressure (BP), SV and aortic pulse wave velocity (aPWV) were available in 5496 individuals (2470 males), aged between 18-92 years. Data were stratified by gender. ISH was defined as SBP≥140mmHg and DBP<90mmHg.

SV and aPWV were independently associated with PP (P<0.001 for both) and there was a strong interaction with age, where PP and aPWV increased significantly across the adult age-span (P<0.001 for both) but SV declined significantly with increasing age (P<0.001). In younger individuals (<30 years), SV, but not aPWV, was associated with increasing quartiles of PP in both males and females (P<0.001 for both) and was elevated in subjects with ISH versus normotensives (P<0.001). However, the opposite pattern was evident in older individuals, with aPWV rather than SV associated with high PP and ISH (P<0.001 for all comparisons).

The haemodynamic mechanisms underlying elevated PP and ISH change across the adult life-span. Moreover, due to the age-related decline in SV, PP may underestimate the true age-related increase in aortic stiffness.

## P4.2

## THE CARDIOVASCULAR RISKS PROFILES AND CENTRAL HEMODYNAMICS IN SURVIVORS OF ADULTHOOD CANCER WHO HAVE ANNUAL HEALTH CHECK-UP IN JAPAN

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**Objective:** This cross-sectional study was conducted to examine whether the risk profile for cardiovascular disease (CVD) and central hemodynamics, an independent marker for CVD, are not worsened in cancer survivors (CanS), who have annual health check-up, as compared to age-adjusted subjects without cancer (SWC).

**Design:** A cross-sectional cohort study.

**Setting:** Japan

**Participants:** From June 1, 2006, through November 30, 2007, Japanese subjects (4813 men and 3500 women) who had annual health check-up at the Health Care Center of Tokyo Medical University.

**Main Outcomes and Measures:** The prevalence rate of subjects quit smoking, hypertension, diabetes mellitus, hypercholesterolemia, and metabolic syndrome. Radial augmentation index (rAI) and the second peak of radial pressure wave form (SP2), marker of central hemodynamics

**Results:** In both genders, the age-adjusted prevalence rate of hypertension and that of metabolic syndrome were lower in the CanS (127 men and 127 women) than in the SWC (p < 0.05). These variables were significant determinants for the elevation of SP2. Then, age-adjusted SP2 was also lower in the CanS (109.2 mmHg) than in the SWC (110.4 mmHg)(p < 0.05).

**Conclusions and Relevance:** In Japanese male and female CanS who have annual health check-up, the risk profiles for CVD were not worsened and might be rather preferable as compared to SWC. Such preferable profiles might provide beneficial effects on central hemodynamics especially in male survivors. Thus, in Japan, CanS with the mind and condition to have annual health check-up may have rather preferable pathophysiological profiles with the prevention of CVD.

## P4.3

## INFLUENCE OF GENDER ON AORTIC STIFFNESS IN COPD

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**Background:** Male patients with chronic obstructive pulmonary disease (COPD) are at greater risk of cardiovascular (CV) events than females<sup>1</sup>.

Aortic stiffness is an independent predictor of adverse CV outcomes and elevated in COPD<sup>2</sup>. However, the influence of gender on aortic stiffness in COPD has not been established. We hypothesized that males with COPD would have greater aortic stiffness than females.

**Methods:** As part of the ARCADE study, we assessed 500 patients with COPD confirmed by spirometry and 150 comparators. Aortic pulse wave velocity (PWV) was evaluated using the sphygmoCor device. Other assessments included body composition, blood pressure, heart rate, number of exacerbations, smoking history and C-reactive protein and fibrinogen.

**Results:** Patients and comparators were similar in age, BMI and gender. Males with COPD (255) had greater aortic PWV mean (SD)10.2 (2.7) than females, 9.5 (2.4),  $p=0.003$ . However, they were similar in age, FEV<sub>1</sub>%, BMI, peripheral and central blood pressure indices, heart rate, number of exacerbations, smoking history and inflammatory biomarkers,  $p>0.05$ . The difference remained after controlling for age and peripheral mean arterial pressure (Adjusted R<sup>2</sup>=26%, F=6.15,  $p=0.014$ ). The gender difference was not evident in the comparator group.

**Conclusion:** Males with COPD had greater aortic stiffness compared to the females, independent of traditional cardiovascular risk factors. The increased aortic stiffness may explain the high incidence of fatal and non-fatal cardiac events in the male patients, which may offer a therapeutic target.

1) Agusti et al. 2010. *Respir Res.* 11:122.

2) Vlachopoulos et al. 2010. *J Am Coll Cardiol.* 55(13):1318-1327.

#### P4.4

##### DOPPLER INDEXES OF LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC FLOWS AND CENTRAL PULSE PRESSURE IN RELATION TO RENAL RESISTIVE INDEX IN A GENERAL POPULATION

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**Background:** The cardio-renal interaction occurs via hemodynamic and humoral factors. Non-invasive assessment of renal hemodynamics is currently possible by assessment of renal resistive index (RRI) derived from intrarenal Doppler arterial waveforms. So far, only limited information is available regarding the relationship between RRI and cardiac hemodynamics in the general population. We investigated these associations in randomly recruited subjects from a Flemish population.

**Methods:** In 171 participants (48.5% women; mean age, 52.2 years), using conventional pulsed wave Doppler, we measured RRI (mean, 0.60) and left ventricular outflow tract (LVOT) and transmitral (E and A) blood flow peak velocities and its velocity time integrals (VTI). Using carotid applanation tonometry, we measured central pulse pressure (cPP) and arterial stiffness indexes such as augmentation pressure and carotid-femoral pulse wave velocity.

**Result:** In stepwise regression analysis, RRI independently and significantly increased with female sex, age, body weight, brachial pulse pressure and use of  $\beta$ -blockers, whereas it decreased with body height and mean arterial pressure. In multivariable-adjusted models with cPP and arterial stiffness indexes as the explanatory variables, we observed a significant and positive correlation of RRI only with cPP ( $P<0.0001$ ). Among the Doppler indexes of left ventricular blood flow, RRI was significantly and positively associated with LVOT and E peak velocities ( $P\leq 0.012$ ) and VTIs ( $P\leq 0.010$ ).

**Conclusions:** We demonstrated that in unselected subjects RRI was significantly associated with cPP and left ventricular systolic and diastolic Doppler blood flow indexes. Our findings imply that in addition to the anthropometric characteristics, cardiac hemodynamic factors influence the intrarenal arterial Doppler waveform patterns.

#### P4.5

##### CHARACTERISTICS AND DETERMINANTS OF THE SUBLINGUAL MICROCIRCULATION IN A FLEMISH POPULATION

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**Background:** Endothelial glycocalyx (EG) acts as a protective barrier. Decrease of sublingual perfused boundary region (SPBR) reflects EG loss. We aimed to assess reproducibility of SPBR and to determine its determinants in a general population.

**Methods:** In 281 subjects randomly recruited in a Flemish population, we measured SPBR using by GlycoCheck software. SPBR is the distance between the median red blood cell column width and the estimated outer edge of the red blood cell perfused lumen. We standardized SPBR to medians of haematocrit and density of perfused capillaries. In 42 participants, we computed repeatability coefficients (RC) expressing bias as percentage of maximal biological variation. We searched for significant ( $p<0.05$ ) correlates of SPBR using stepwise regression.

**Results:** In 281 subjects (mean age, 51.2y; 53.0% women), SPBR averaged 1.80 $\mu$ m. RCs for intra- and inter-observer variability were  $\geq 53.4\%$ . Of 14 potential covariables, only age and mean arterial pressure (MAP) and use of diuretics correlated with SBPR ( $p\leq 0.049$ ). Changes in SPBR associated with a 1-SD increments in age (+16.6y) and MAP (+11.3mmHg) were -58.2nm and -35.5nm, while SPBR was 97.7nm wider in diuretic users. Disregarding 140 patients with albuminuria, hypertension, diabetes, and cardiovascular disease, the 5th and 95th percentiles of SPBR across age (<30y to  $\geq 50$ y) ranged from 1.54 $\mu$ m to 1.43 $\mu$ m and from 2.52 $\mu$ m to 2.28 $\mu$ m, respectively.

**Conclusion:** SPBR variability is high probably because of physiological factors, because imaging is software controlled. The inverse association of SPBR with age and MAP might reflect a defense mechanism in the presence of these cardiovascular risk factors.

#### P4.6

##### PULSATILE AND STEADY BLOOD PRESSURE COMPONENTS IN RELATION TO ENVIRONMENTAL LEAD EXPOSURE IN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2003-2010

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In view of the declining environmental lead exposure in the US, we analyzed the National Health and Nutrition Examination Survey (2003-2010) for association of pulsatile and steady BP components and hypertension (HT) with blood lead (BPb). The 12,725 participants included 21.2% Blacks, 20.5% Hispanics, 58.4% Whites, and 48.7% women. Blacks compared with non-Blacks had higher SBP, DBP, and mean arterial pressure (MAP) (126.5 vs. 123.9; 71.9 vs. 69.6; and 90.1 vs. 87.7mmHg, respectively) and higher HT prevalence (44.7 vs. 36.8%). SBP, DBP and MAP (123.3 vs. 125.5; 68.9 vs. 71.2; and 87.1 vs. 89.3mmHg) were lower in women than men with no significant sex difference in PP and HT prevalence ( $P\geq 0.11$ ). BPb was lower in Whites than non-Whites (1.46 vs. 1.57 $\mu$ g/dL) and in women than men (1.25 vs. 1.80 $\mu$ g/dL). In multivariable analyses of all participants, BPb doubling was associated with higher ( $P\leq 0.0007$ ) SBP, DBP and MAP (0.76 [CI, 0.38-1.13]; 0.43 [0.18-0.68]; and 0.54 [0.29-0.79]mmHg, respectively) with no change in PP ( $P=0.063$ ) or the odds of HT ( $P=0.11$ ). Associations with BPb were nonsignificant ( $P\geq 0.09$ ) for SBP in women and for DBP and MAP in non-Whites. Among men, SBP increased with BPb ( $P\leq 0.060$ ) with effect sizes associated with BPb doubling ranging from +0.65mmHg in Whites to +1.61mmHg in Blacks. For SBP and PP, interactions of ethnicity and sex with BPb were all significant ( $P\leq 0.027$ ). In conclusion, small and inconsistent effect sizes in the associations of BP with BPb likely exclude current environmental lead exposure as a major HT cause in the US.

#### P4.7

##### RELATIONSHIP OF DIFFERENT CARDIOVASCULAR TISSUE BIOMARKERS WITH ESTABLISHED RISK FACTORS AND FRAMINGHAM RISK SCORE IN MIDDLE-AGE SUBJECTS WITHOUT CARDIOVASCULAR EVENTS

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The relations between emerging biomarkers of preclinical CV disease and established risk algorithms are not well defined.

**Aim:** this study evaluated the relationships of various tissue CV biomarkers with Framingham risk score (FRS) and its individual determinants.

**Methods:** in 435 subjects without previous cardiovascular events (287 males, mean age 58 $\pm$ 11, 56% diabetics (DM), 48% treated for hypertension (HBP), 51% with dyslipidemic treatment, 27% smokers), we measured radio-frequency based (QIMT® and QAS®, Esaote) carotid intima-media thickness (IMT), wave speed (WS) and local pulse pressure (cPP), carotid-femoral pulse wave velocity (PWV; Complior), LV mass index (LVMI) and relative wall thickness (RWT).