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### **P4.3: PHYSICAL ACTIVITY IS ASSOCIATED WITH LOWER ARTERIAL STIFFNESS IN OLDER ADULTS: RESULTS OF THE SAPALDIA 3 COHORT STUDY**

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**Methods:** From the outpatient hypertensive cohort (N=773) two groups were chosen – (1) white coat effect patients “WCHT” with systolic office blood pressure (OSBP) > 140 mmHg, and 24-hour systolic blood pressure < 130 mmHg; and (2) patients with normal OSBP but 24-hour SBP > 130 mmHg “MHTN”. Anthropometric measurements, together with basic cardiovascular risk factors and target organ damage assessment were performed.

**Results:** In univariate analyses age, weight, BMI, waist circumference, as well as biochemical markers (total cholesterol, HDL, LDL-C, triglycerides, glucose levels) were comparable between the groups (P=NS, for all comparisons). MHTN patients presented with more pronounced target organ damage markers (eGFR, LVH, IMT) except for cfPWV (11.4 vs. 9.6 m/s for WCHT vs. MHTN, respectively; P<0.001). Nevertheless, the multivariate analysis adjusted to the levels of OSBP, HR and age showed marked attenuation of the observed PWV difference (P=0.84 for the model).

**Conclusion:** Single time office pulse wave velocity measurement in white coat effect presenting patients may not be a sufficient tool for the accurate assessment of subclinical damage. Thus sequential PWV measurement or other methods should be considered in this group of patients.

### P3.21

#### ASSOCIATIONS OF INSULIN-LIKE GROWTH FACTOR AND ITS BINDING PROTEIN-2 AND 3 WITH BLOOD PRESSURE AND ARTERIAL STRUCTURE AND FUNCTION IN HYPERTENSIVE PERIMENOPAUSAL WOMEN

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IGFs and their binding proteins are increasingly recognized as important in understanding the pathogenesis of cardiovascular disease. During the transition from premenopause to postmenopause, many women experience weight gain, hence we hypothesized that circulating growth hormones can play a role in the pathogenesis of hypertension and subclinical organ damage in perimenopausal women.

The study included 152 women with newly diagnosed, never treated hypertension and 40 normotensive age-matched controls (mean age 51.73±1.82 years). In all subjects 24-hr ABPM, carotid ultrasound with measurement of intima-media thickness (IMT), and carotid-femoral pulse wave velocity (PWV) measurement (Sphygmocor) were performed. Serum levels of IGF-I, IGFBP2 and IGFBP3 and were measured using an immunochemical assay.

**Results:** Postmenopausal women (n=93) did not differ from premenopausal (n=99) in respect to mean arterial pressure (normotensive 85.2±5.6 vs 84.4±4.9 mmHg; hypertensive 99.5±5.9 vs 98.8±5.3 mmHg). Hypertensive women had significantly lower IGFBP-2 level than normotensive (162±83 vs 273±101 ug/l, p<0.001), groups did not differ in IGF and IGFBP3 concentration. IGFBP2 was the independent predictor of blood pressure in the examined group. In multivariate regression analysis after adjustment to age and BMI – IGFBP2 remained significantly negatively correlated to BP ( $\beta$ =-0.33, p=0.001). Odds ratio for hypertension per SD decrease in IGFBP2 was 3.43 (95% CI 1.65–7.13). IGFBP2 was independently of BP related with PWV ( $\beta$ =-0.22, p=0.05) but not with IMT ( $\beta$ =-0.14, p=0.22).

**Conclusions:** In perimenopausal women decreased IGFBP2 level may play a role in the blood pressure regulation. Further longitudinal studies are needed to elucidate the cardioprotective role of IGFBP2.

### P4.1

#### ARTERIAL STIFFNESS IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW

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**Background:** Arterial stiffness is increased with chronic inflammatory disorders. The reduction of inflammation by immunomodulatory therapy is associated with a restoration of arterial function.

**Objectives:** To determine whether carotid-femoral pulse wave velocity (cf-PWV) is increased in subjects with inflammatory bowel disease (IBD).

**Data sources:** A systematic literature search for arterial stiffness in IBD was performed using PubMed and Google Scholar databases (last accessed on 11 June 2015). The search terms were “arterial stiffness,” “vascular stiffness”

or “pulse wave velocity” in combination with “inflammatory bowel disease,” “inflammatory bowel diseases,” “Crohn’s disease” or “ulcerative colitis.” Study eligibility criteria. Inclusion criteria included peer-reviewed publications reporting original data; a minimum of 10 subjects tested; and cf-PWV measured via validated devices.

**Participants:** Adults with IBD.

**Methods:** Publications with titles or abstracts appearing to meet the inclusion criteria were selected for detailed review. These articles were reviewed by two authors according to PRISMA 2009 guidelines.

**Results:** A total of 9 cross-sectional studies met the inclusion criteria (234 patients with Crohn’s disease (CD), 342 with ulcerative colitis (UC) and 435 control patients). One study only included patients with UC. Arterial stiffness was significantly increased in subjects with IBD in 8 studies and slightly but not significantly increased in subjects with IBD in one study.

**Conclusions:** Current cross-sectional studies suggest that arterial stiffness is increased in IBD subjects. Longitudinal studies are required to confirm preliminary data showing a reversibility of arterial stiffening by anti-TNF-alpha therapy. Systematic review registration number: CRD42015017364.

### P4.2

#### CORONARY RISK IN RELATION TO GENETIC VARIATION IN MEOX2 AND TCF15 IN A FLEMISH POPULATION

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**Aims:** In mice, MEOX2/TCF15 heterodimers are highly expressed in heart endothelial cells and are involved in the transcriptional regulation of lipid transport. We investigated whether coronary heart disease (CHD) in humans is associated with variation in these genes.

**Methods and results:** In 2027 participants enrolled in the Flemish Study on Environment, Genes and Health Outcomes (51.0% women; mean age 43.6 years), we genotyped SNPs in MEOX2 and TCF15, measured baseline cardiovascular risk factors, and recorded CHD incidence. Over 15.2 years (median), CHD occurred in 106 participants. For SNPs, we contrasted minor-allele heterozygotes and homozygotes (variant) vs. major-allele homozygotes (reference) and for haplotypes carriers vs. non-carriers. Sex- and age-standardised CHD rates were higher in MEOX2 rs10777, rs12056299, rs7787043, rs4532497, rs1050290 variants, in MEOX2 GTCCGC haplotype carriers (prevalence, 16.5%), but lower in MEOX2 rs6959056 variants (P ≤ 0.04, adjusted for multiple testing). In multivariable-adjusted analyses, the corresponding hazard ratios were ≥1.50 (P ≤ 0.049), 1.77 (P = 0.0054) and 0.62 (P = 0.025), respectively. None of four TCF15 SNPs was associated with coronary risk (P ≥ 0.29). However, CHD risk associated with MEOX2 rs4532497 was confined to TCF15 rs12624577 variant allele carriers (P for interaction = 0.011). The MEOX2 GTCCGC haplotype significantly improved the prediction of CHD over and beyond traditional risk factors and was associated with similar population-attributable risk as smoking (18.7% vs. 16.2%).

**Conclusions:** In randomly recruited Flemish, genetic variation in MEOX2, but not TCF15, is a strong predictor of CHD. Further experimental studies should elucidate the underlying molecular mechanisms.

### P4.3

#### PHYSICAL ACTIVITY IS ASSOCIATED WITH LOWER ARTERIAL STIFFNESS IN OLDER ADULTS: RESULTS OF THE SAPALDIA 3 COHORT STUDY

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We examined cross-sectional associations of self-reported PA intensities with arterial stiffness in elderly Caucasians of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA). Mixed central and peripheral arterial stiffness was measured oscillometrically by the cardio-ankle vascular index (CAVI) and brachial-ankle pulse wave velocity (baPWV). The self-reported International Physical Activity Questionnaire (IPAQ) long version was administered to classify each subject's PA level. We used univariable and multivariable mixed linear and logistic regression models for analyses in 1908 persons aged 50 years and older. After adjustment for several confounders moderate, vigorous and total PA were inversely associated with CAVI ( $p=0.02-0.03$ ). BaPWV showed negative and marginally significant associations with vigorous and moderate PA (each  $p=0.06$ ), but not with total PA ( $p=0.28$ ). Increased arterial stiffness (CAVI $\geq 9$ , upper tertile) was inversely and significantly associated with vigorous PA (Odds Ratio (OR)=0.65, 95% Confidence Interval (CI): 0.48-0.88), and marginally significantly with total PA (OR=0.76, 95% CI: 0.57-1.02) and moderate PA (OR=0.75, 95% CI: 0.56-1.01). The odds ratio for baPWV $\geq 14.4$  was 0.67 (95% CI: 0.48-0.93) across the vigorous PA levels, and was non-significant across the total (OR=0.91, 95% CI: 0.66-1.23) and moderate PA levels (OR=0.94, 95% CI: 0.69-1.28). In this general Caucasian population of older adults higher levels especially of vigorous PA were associated with lower arterial stiffness. These data support the importance of PA for improving cardiovascular health in elderly people.

#### P4.4

##### INHIBITION OF ARTERIAL CALCIFICATION BY MATRIX GLA PROTEIN AS DETERMINANT OF RENAL FUNCTION IN THE GENERAL POPULATION

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**Background:** Carboxylation of matrix Gla protein (MGP), a vitamin K dependent process, activates the protein to a powerful inhibitor of arterial calcification. Circulating dephosphorylated and uncarboxylated MGP (dp-ucMGP) and total uncarboxylated MGP (t-ucMGP) are associated with macrovascular disease. The association with microcirculatory disease remains unknown.

**Methods:** In 1174 randomly recruited Flemish (51.4% women; mean age, 38.2 years), we studied the estimated glomerular filtration rate (eGFR) and microalbuminuria, as prototypes of microcirculatory traits, in relation to dp-ucMGP and t-ucMGP. In multivariable linear and logistic regressions, we expressed effect sizes for a doubling of the biomarkers, while accounted for anthropometric characteristics, lifestyle, risk factors and use of medications.

**Results:** Among all participants, geometric means of dp-ucMGP and t-ucMGP were 3.68 mg/L and 45.2 mg/L, respectively. In relation to dp-ucMGP (figure), eGFR decreased by 1.57 mL/min/1.73 m<sup>2</sup> ( $p=0.015$ ), while the risk of renal dysfunction (eGFR <60 mL/min/1.73 m<sup>2</sup>) increased by 19% ( $p=0.022$ ) with a 43% trend in the same direction ( $p=0.069$ ) for microalbuminuria (albumin-to-creatinine ratio  $\geq 3.5$  mg/mmol in women and  $\geq 2.5$  mg/mmol in men). In relation to t-ucMGP (figure), eGFR increased by 1.89 mL/min/1.73 m<sup>2</sup> ( $p=0.041$ ) with no changes in the risks of renal dysfunction or microalbuminuria ( $p\geq 0.12$ ).

**Conclusion:** In the general population, eGFR is inversely correlated with dp-ucMGP, a marker of vitamin K deficiency, whereas the opposite is the case for t-ucMGP, a marker of prevalent arterial calcification.

#### P4.5

##### VASCULAR HEALTH ASSESSMENT OF THE HYPERTENSIVE PATIENTS (VASOTENS) REGISTRY: RATIONALE, DESIGN AND METHODS OF AN INTERNATIONAL REGISTRY FOR AMBULATORY BLOOD PRESSURE AND ARTERIAL STIFFNESS TELEMONITORING

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**Background:** Ambulatory (A) blood pressure (BP), central BP and pulse wave velocity (PWV) are parameters recommended by hypertension guidelines for estimating BP control and vascular impairment. Recent advances in technology made available devices allowing combined non-invasive estimation of these parameters over the 24-h during ABPM. However, at present, there is limited evidence on the usefulness of such an approach for routine hypertension management.

**Objective:** We recently launched an investigator-initiated, international, multicenter, observational, prospective study aiming at: i) evaluating non-invasive 24-h ABP and arterial stiffness estimates (through 24-h pulse wave analysis, PWA) in hypertensive subjects; ii) assessing the changes in estimates following treatment; iii) weighing the impact of 24-h PWA on target organ damage and cardiovascular prognosis; iv) assessing the relationship between arterial stiffness, BP absolute level and variability, and prognosis.

**Methods:** Approximately 2000 subjects, referred to 20 hypertension clinics for routine diagnostic evaluation and follow-up of hypertension, will be recruited. Data collection will include ABPM, performed with a device allowing simultaneous non-invasive assessment of BP and arterial stiffness (BPLab), and clinical data (including cardiovascular outcomes). A web-based telemedicine platform will be used for data collection. Subjects will visit the centers at 6-12 month intervals. First follow-up results are expected to be available in the next 2-years.

**Conclusions:** The results of the VASOTENS Registry will help defining the normalcy thresholds for current and future indices derived from 24-h PWA, according to outcome data. They will also provide supporting evidence for the inclusion of such evaluation in recommendations on hypertension management.

#### P4.6

##### GREATER CAROTID CIRCUMFERENTIAL WALL STRESS IS ASSOCIATED WITH INCIDENT CARDIOVASCULAR DISEASE IN INDIVIDUALS WITH TYPE 2 DIABETES – THE HOORN STUDY

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**Introduction:** Arterial remodeling is an adaptive phenomenon aimed at maintaining circumferential wall stress (CWS) within operating limits. It is characterized by widening of the inter-adventitial diameter (IAD) and increases in intima-media thickness (IMT). This process is maladaptive when CWS increases despite remodeling. Type 2 Diabetes (T2D) is associated with increased carotid CWS, but its association with cardiovascular disease (CVD) is unknown.

**Methods:** The cohort consisted of 277 individuals with normal glucose metabolism (NGM), 162 with impaired glucose metabolism (IGM) and 131 with T2D (age 69.6  $\pm$  6.4, 51.0% women, systolic pressure 141.9  $\pm$  20.6 mmHg, bmi 26.9  $\pm$  3.5 kg/m<sup>2</sup>, prior CVD 50.1%). Carotid arterial properties (IAD, IMT, lumen diameter (LD)) were quantified by ultrasonography. CWS was calculated as PP-LD/(2IMT), where PP is the brachial pulse pressure. A morbidity and mortality register was kept on all individuals.