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P4.2: CORONARY RISK IN RELATION TO GENETIC VARIATION IN MEOX2 AND TCF15 IN A FLEMISH POPULATION

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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

Agnieszka Olszanecka ^{*}, Kalina Kawecka-Jaszcz, Danuta Czarnecka
Jagiellonian University Medical College, 1st Department of Cardiology, Interventional Electrophysiology and Hypertension, Krakow, Poland

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 (β =−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 (β =−0.22, p=0.05) but not with IMT (β =−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

Luca Zanolì ^{1,*}, Stefania Rastelli ¹, Jean-Philippe Empana ², Pierre Boutouyrie ², Stephane Laurent ², Pietro Castellino ¹

¹University of Catania, Catania, Italy

²HEGP, AP-HP, INSERM U970, Paris, France

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

Wen-Yi Yang ¹, Thibault Petit ¹, Lutgard Thijs ¹, Zhen-Yu Zhang ¹, Lotte Jacobs ¹, Azusa Hara ¹, Fang-Fei Wei ¹, Erika Salvi ², Lorena Citterio ³, Yu-Mei Gu ¹, Judita Knez ¹, Nicholas Cauwenberghs ¹, Matteo Barcella ², Cristina Barlassina ², Paolo Manuta ³, Tatiana Kuznetsova ^{1,*}, Daniele Cusi ², Peter Verhamme ¹, Aernout Luttun ¹, Jan Staessen ^{1,4}

¹University of Leuven, Leuven, Belgium

²University of Milan, Milan, Italy

³University Vita-Salute Raffaele, Milan, Italy

⁴Maastricht University, Maastricht, The Netherlands

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

Simon Endes ^{1,*}, Emmanuel Schaffner ^{2,3}, Seraina Caviezel ^{2,3}, Julia Dratva ^{2,3}, Christine S. Autenrieth ^{2,3}, Miriam Wanner ⁴, Brian Martin ⁴, Daiana Stolz ⁵, Marco Pons ⁶, Alexander Turk ⁷, Robert Bettschart ⁸, Christian Schindler ^{2,3}, Nino Künzli ^{2,3}, Nicole Probst-Hensch ^{2,3}, Arno Schmidt-Trucksäss ¹

¹Department of Sport, Exercise and Health, Div. Sports and Exercise Medicine, University of Basel, Basel, Switzerland

²Swiss Tropical and Public Health Institute, Basel, Switzerland

³University of Basel, Basel, Switzerland

⁴Physical Activity and Health Working Unit, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland