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01.02: GEOMETRIC AND ELASTIC PROPERTIES OF THE COMMON CAROTID ARTERY IN VASCULAR EHLERS-DANLOS SYNDROME PATIENTS WITH IDENTIFIED COL3A1 MUTATIONS

K.T. Ong, S. Laurent, J. Perdu, H. Plauchu, D. Germain, P. Collignon, G. Georgesco, E. Bozec, B. Laloux, J. De Backer, X. Jeunemaitre, P. Boutouyrie

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species cannot be exposed to an average calculated shear stress value. The cells have to be studied under the shear stress conditions they are exposed to in real live.

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Abstracts

ORAL PRESENTATIONS

01.01

LOW BONE MINERAL DENSITY IS ASSOCIATED WITH GREATER AORTIC PULSE-WAVE VELOCITY IN WOMEN: THE NORTHERN IRELAND YOUNG HEARTS PROJECT (NIYHP)

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Background & Aims: Associations between low bone mineral density (BMD) and increased arterial stiffness have been suggested as a potential mechanism explaining the increased cardiovascular risk observed in osteoporosis. We have therefore examined, in a population of young adults: 1) whether BMD was associated with stiffness of central (i.e. aorta) and peripheral (i.e. upper and lower limbs) arterial segments; and 2) whether any such associations were similar in men and women.

Methods: Subjects were 274 (128 women) young adults (mean age of 23 yrs), participating in the NIYHP. BMD (in g/cm³) of the lumbar spine and the femoral neck were measured by means of DXA. Arterial stiffness was assessed by measuring pulse wave velocity (PWV, in m/s) in 3 arterial segments using a non-invasive optical method.

Results: After adjustment for potential confounders (i.e. age, height, MAP, physical activities' peak strain, smoking and alcohol, calcium and vitamin D intake) BMD of both the lumbar spine [$\beta = -0.67$ (95%CI: -1.27; -0.07), $p = 0.029$] and the femoral neck [$\beta = -0.69$ (-1.16; -0.22), $p = 0.005$] were inversely associated with aortic PWV in women, but not in men; further adjustment for other cardiovascular risk factors did not attenuate these associations [$\beta = -0.61$ (-1.19; -0.04) and $\beta = -0.58$ (-1.04; -0.13), for BMD of the lumbar spine and femoral neck, respectively]. No significant associations were found between BMD and PWV of the upper and lower limbs, however.

Conclusions: Young women, but not men, with lower BMD have increased aortic stiffness. Pathophysiological mechanisms underlying these associations, notably already observed in young age, need to be further explored.

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01.02

GEOMETRIC AND ELASTIC PROPERTIES OF THE COMMON CAROTID ARTERY IN VASCULAR EHLERS-DANLOS SYNDROME PATIENTS WITH IDENTIFIED COL3A1 MUTATIONS

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Background: Vascular Ehlers-Danlos syndrome (vEDS), an autosomal dominant inherited disorder of connective tissue, results from mutations in the gene encoding type III procollagen (COL3A1), can present with spontaneous arterial rupture or dissection. Diagnostic is based on the clinical criteria. Mutations of COL3A1 gene may be identified in about 60% case. Our study is to compare arterial geometric and elastic properties in vSED patients with identified COL3A1 mutations (COL3A1+) to unidentified COL3A1 mutations (COL3A1-).

Methods: 53 vEDS patients diagnosed by clinical criteria with no previous β -blocker were included in the cross-sectional study. Mutations of COL3A1

gene was identified in 32 patients. Arterial parameters were determined with high-resolution echo-tracking system coupled with applanation tonometry. Quantitative variables were compared by general linear model ANOVA. **Results:** Demographic data did not differ between COL3A1+ and COL3A1- patients. Patients with COL3A1- were significantly older than COL3A1+ patients (+7 yrs, $p < 0.05$). Heart rate, SBP, MBP, brachial PP, central PP, carotid diameter, distensibility, Young's elastic modulus, carotid-femoral pulse-wave velocity were not significantly different between two groups. Carotid intima-media thickness (IMT) was significantly lower (-18%, $p < 0.001$) in COL3A1+ than COL3A1- patients. Carotid circumferential wall stress ($\sigma\theta$) was higher (+35%, $p < 0.001$) in COL3A1+ than COL3A1- patients. After adjustment for age and blood pressure, these differences remained significant.

Conclusions: vSED patients with COL3A1+ have a lower carotid IMT associated with a higher $\sigma\theta$ than COL3A1- patient. These results reveal the role of $\sigma\theta$ in the pathogenesis of the vascular lesions and confirm the gold-standard of identifying COL3A1 mutations in the diagnostic of this syndrome.

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01.03

CAROTID-FEMORAL PULSE WAVE VELOCITY IS NOT INDEPENDENTLY RELATED TO INTIMA-MEDIA THICKNESS IN MIDDLE AGED WOMEN

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Carotid-femoral pulse wave velocity (PWV), a measure of central arterial stiffness and carotid intima-medial thickness (CIMT), thought to be a measure of subclinical atherosclerosis, are predictors of future cardiovascular events, recommended for risk stratification. Their relationship, however, remains poorly characterised. We sought to determine the association between PWV, CIMT and atherosclerotic plaque at the carotid and femoral artery and the heritability of PWV and CIMT. The study population consisted of 496 female twins (112 monozygotic (MZ), 135 dizygotic (DZ), mean age (interquartile range) 58 (53-64) years, from the TwinsUK cohort. PWV was determined using the SphygmoCor system (Atcor Australia) and CIMT measured 1 cm proximal to the flow divider by B-mode ultrasound. Plaque was quantified according to its presence at the carotid and femoral artery. Multiple regression analysis was used to examine the relation between PWV, CIMT and plaque. Heritability was determined from intra-class correlations. In multiple regression analysis incorporating age, mean arterial pressure (MAP) and heart rate (HR), PWV was not significantly positively correlated with CIMT, indeed there was a weak but significant negative correlation between PWV and CIMT (standardised regression coefficient $\beta = -0.13$, $P < 0.05$). PWV was weakly positively associated with plaque ($\beta = 0.13$, $P < 0.01$). Heritability of PWV (adjusted for HR and MAP) and CIMT (adjusted for MAP, total cholesterol and HDL-cholesterol) was 0.34 and 0.57 respectively. These results confirm high heritability of CIMT but suggest that it is largely independent of PWV which may be influenced more by environmental factors. Combining measures of CIMT and PWV might improve risk stratification.

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01.04

REFERENCE VALUES FOR ARTERIAL STIFFNESS

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Objectives: The implementation of arterial stiffness measurements in clinical practice is hampered by methodological differences in PWV definitions and the absence of reference values. This study reports reference values for pulse wave velocity (PWV) in a population of 24,482 subjects originating from 13 European centres.

Methods: PWV values presented are valid for direct carotid-femoral distance measurement (L_{direct}) and transit time determined by the algorithm of intersecting tangents ($\Delta t_{intersecting tangent}$). PWV was converted using statistical models for estimation of L_{direct} and $\Delta t_{intersecting tangent}$ if required. PWV relevant clinical data were available in 13,919 without current antihypertensive therapy. Subjects were divided into age deciles (<30, 30-39, 40-49, 50-59, 60-69, 70-79, ≥ 80 years) and for each age category a box-percentile plot was constructed.

Results:

Conclusions: The data presented form a solid base for establishing reference values according to age group valid for a European population.