1.6: AORTIC PULSE WAVE VELOCITY IN PORTUGUESE CHILDREN AND ADOLESCENTS – RESULTS FROM THE PORTUGUESE VASCULAR PHENOTYPE IN CHILDREN AND ADOLESCENTS (PORT-VASPH) COHORT

Telmo Pereira, João Maldonado, Margarida Carvalho

[2]*Lund University, Department of Clinical Sciences, Skane University Hospital, Jan Waldenstroms gata 15, Level 5, S-20502, Malmö, Sweden*

Background: This study aims to translate two arterial measurements, aortic Pulse Wave Velocity (aPWV) and carotid Intima-Media Thickness (cIMT), into a combined Vascular Ageing Index (VAI), to evaluate the predictive power of VAI and utilize it to identify a sub-group with Healthy Vascular Ageing (HVA).
Methods: In all, 2718 subjects were included from the CV arm of the Malmö Diet Cancer study (median age 72 years, 62.2% females). Median follow-up for CV events (N = 269) was 6.5 years. VAI was created by a function that combined aPWV and cIMT. Cox regressions for aPWV, cIMT and VAI, adjusted for conventional CV risk factors, were carried out. aPWV and cIMT were mutually adjusted for while VAI was analyzed separately. Model improvements for a model of conventional CV risk factors were assessed using Harrell's c-statistic and continuous Net Reclassification Index (NRI).
Results: Cox regression Results: (fully adjusted model): 1 SD of log-(aPWV), HR: 1.22 (95% CI: 1.03−1.42, P = 0.010), 1 SD of log (cIMT), HR: 1.29 (95% CI: 1.13−1.47, P < 0.001), 1 SD of log-VAI, HR: 1.43 (95% CI: 1.22−1.68, P < 0.001) (Figure1). C-statistics: 0.715 (conventional risk factor model), 0.721 (+aPWV), 0.734 (+aPWV and cIMT) and 0.732 (+VAI). NRI showed a significant (P < 0.001) improvement for classification of event-free subjects when adding aPWV and cIMT or VAI.
Conclusion: VAI added marginally to prediction of CV events. However, the classification of subjects who remained free from CV events was significantly improved.

CV event incidence by aPWV and cIMT
Based on Kaplan-Meier estimates
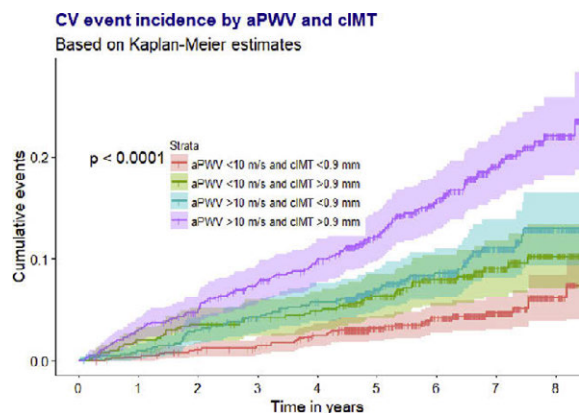
1.4

PROGNOSTIC VALUE OF PROXIMAL AORTA LONGITUDINAL STRAIN IN MARFAN SYNDROME

Andrea Guala [1], Jose Rodríguez-Palomares [1], Aroa Ruiz-Muñoz [1], Minerva Gandara [1], Violeta Sanchez [2], Alberto Forteza [3], David Garcia-Dorado [4], Artur Evangelista [4], Gisela Teixido-Tura [1]
[1]*Hospital Vall d'Hebron, Department of Cardiology, VHIR, Universitat Autònoma de Barcelona, Barcelona, Spain*
[2]*University Hospital 12 de Octubre, Madrid, Spain*
[3]*Hospital Puerta del Hierro, Madrid, Spain*
[4]*Hospital Vall d'Hebron, Department of Cardiology, VHIR, Universitat Autònoma de Barcelona, Barcelona, Spain*

Background: Aortic root dilation and type A aortic dissection are the most common cardiovascular complications of Marfan syndrome (MFS). Current clinical management of MFS patients relies on a close follow-up of aortic root diameter and preventive aortic root surgery in case of severe or fast-progressing dilation. However, as the capacity of aortic diameter to predict type A aortic dissection is limited, new non-invasive biomarkers to improve risk stratification are needed. We investigated the capacity of proximal aorta circumferential and longitudinal strain and ascending aorta distensibility to predict aortic root diameter dilation and occurrence of major cardiovascular events in Marfan patients.
Methods: Eighty-seven Marfan patients without previous cardiac/aortic surgery or dissection were prospectively included in a multicenter follow-up. Proximal aorta longitudinal and circumferential strain and distensibility were computed from baseline CMR.

Results: During a follow-up of 81.6 ± 17 months, 11 patients underwent elective aortic root replacement, and 2 experienced type A aortic dissections. Mean dilation rate was 0.65 ± 0.67 mm/year and z-score growth rate 0.07 ± 0.13 1/year. In multivariable analysis, proximal aorta longitudinal strain but not circumferential strain and distensibility were independent predictors of diameter growth-rate (p = 0.001, p = 0.385 and p = 0.381, respectively), z-score growth-rate (p = 0.018, p = 0.515 and p = 0.484, respectively) and major cardiovascular events (p = 0.018, p = 0.064 and p = 0.205, respectively) corrected for demographic and clinical characteristics and baseline aortic root diameter.
Conclusions: In Marfan syndrome, proximal aorta longitudinal strain is an independent predictor of aortic root dilation and major cardiovascular events beyond aortic root diameter and established risk factors.

1.5

DEEP VASCULAR PHENOTYPING IN PATIENTS WITH FIBROMUSCULAR DYSPLASIA

Rosa Maria Bruno [1,2], Louise Marais [2], Hakim Khettab [3], Aurélien Lorthioir [3], Xavier Jeunemaitre [4,2], Stèphane Laurent [3,2], Pierre Boutouyrie [3,2], Michel Azizi [3]
[1]*University of Pisa, Italy*
[2]*INSERM U970, Paris, France*
[3]*APHP, Hôpital Européen Georges Pompidou, Paris, France*
[4]*APHP, Hôpital Européen Georges Pompidou, France*

Background: Fibromuscular dysplasia (FMD) is a non-atherosclerotic, non-inflammatory vascular disease involving medium-sized muscular arteries, whose pathophysiology is still unknown.
Objectives: We aimed at identifying systemic vascular alterations in usually non-affected arteries of patients with multifocal renal FMD by a deep imaging-based phenotyping.
Methods: This cross-sectional study included FMD patients (n = 50, 84% hypertensives), age-, sex and BP-matched patients with primary hypertension (PH, n = 50) and healthy normotensive subjects (HS, n = 50). Brachial artery (BA) endothelium-dependent flow-mediated dilation (EDD) and endothelium-independent vasodilation (EID) were studied. Aortic stiffness was assessed by carotid-to-femoral pulse wave velocity (PWV). We quantified abnormal echographic patterns in the common carotid wall by the triple signal score. Common carotid Young's incremental elastic modulus (Einc)/ stress curves were also plotted.
Results: FMD patients had impaired EID compared to PH and HS (p = 0.008, after adjustment for confounders p = 0.002), smaller BA diameter but comparable EDD and PWV. The prevalence of triple signal score >6 was 56%, 40%, 24% in FMD, PH and HS respectively (p = 0.005). FMD, but not PH, was significantly associated with triple signal (beta = 0.143, p = 0.022, r2 = 0.058). Impaired EDD was only present in FMD patients with triple signal score >6 (p for interaction=0.047). For a given stress value of 80 kPa, Einc was higher in the presence of a triple signal score >6, especially in FMD patients.
Conclusions: Non-affected musculo-elastic and muscular arteries in patients with multifocal renal FMD exhibit a cluster of functional and structural abnormalities, while elastic arteries are preserved. Triple signal in FMD may identify a distinct vascular phenotype.

1.6

AORTIC PULSE WAVE VELOCITY IN PORTUGUESE CHILDREN AND ADOLESCENTS − RESULTS FROM THE PORTUGUESE VASCULAR PHENOTYPE IN CHILDREN AND ADOLESCENTS (PORT-VASPH) COHORT

Telmo Pereira [1], João Maldonado [2,3], Margarida Carvalho [3]
[1]*Polytechnic Institute, Coimbra Health School, Portugal*
[2]*Polytechnic Institute, Coimbra Health School, Portugal*
[3]*Clínica da Aveleira, Coimbra, Portugal*

Introduction: The PORT-VASPh Cohort was designed to contribute to a better understanding of vascular function in children and adolescents, mostly focusing PWV and other complementary aspects of arterial hemodynamics.
Methods: The PORT-VASPh cohort is a prospective and observational study, with 953 children and adolescents enrolled, 40% females, age ranging from 5 to 17 years (mean age: 12.08 ± 2.92 years). The overall health profile for each participant was defined based on three clinical evaluations, in which blood pressure (BP) was measured under standard conditions over the

brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. Carotid-femoral PWV was measured to all participants at the third clinical evaluation, with the Complior SP device, complying with the methodological recommendations. All participants were evaluated by the same experienced clinician.

Results: Mean PWV was 6.20 ± 0.95 m/s and was higher in males compared with females (6.31 ± 0.97 m/s vs 6.02 ± 0.89, respectively; $p < 0.0001$). Gender-specific percentile tables, accounting for age, were obtained from the normotensive participants (n = 758), as depicted in Figure 1. The determinants of PWV were assessed through linear regression. In a multivariable model, age, gender, blood pressure and family history of cardiovascular disease were significantly associated with PWV.

Conclusion: In children and adolescents, aortic PWV is strongly influenced by age, gender, BP and genetics, in line with the available evidences in adult populations. Further studies are needed towards a thorough understanding of the arterial dynamics at these ages.
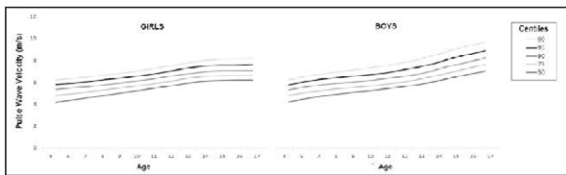
Oral Session II — Young Investigator Award

2.1
KNOCK-OUT OF MATRIX METALLOPROTEINASE-12 EXACERBATES COMPROMISED MECHANICAL HOMEOSTASIS IN ARTERIAL AGING

Bart Spronck [1], Abhay B. Spronck [1], Jakub Toczek [2,3,4], Jinah Han [2,3,4], Mehran Sadeghi [2,3,4], Jay D. Humphrey [1,5]

[1]Department of Biomedical Engineering, Yale University, New Haven, CT, USA
[2]Cardiovascular Molecular Imaging Laboratory, Section of Cardiovascular Medicine and Yale Cardiovascular Research Center, Yale School of Medicine, New Haven, CT, USA
[3]Veterans Affairs Connecticut Healthcare System, West Haven, CT, USA
[4]Yale Cardiovascular Research Center, New Haven, CT, USA
[5]Vascular Biology and Therapeutics Program, Yale School of Medicine, New Haven, CT, USA

Background: Matrix metalloproteinase-12 (MMP12) may modulate arterial stiffening with age [1]. We aimed to study the effect of aging on biaxial arterial stiffness in wild-type (WT) and MMP12 knock-out (MMP12-/-) mice.

Methods and Results: After euthanasia, descending thoracic (DTA) and suprarenal abdominal (SAA) aortas of young and old, WT (ages 21 ± 0 and 103 ± 1 weeks; mean $\pm$ SE) and MMP12-/- (13 ± 0 and 52 ± 0 weeks) male mice were dissected and cannulated on glass pipettes in a computer-controlled biaxial testing device. Pressure-diameter tests were performed at 95%/100%/105% of estimated in vivo stretch; axial force-length tests at pressures of 10/60/100/140 mmHg. Data were fitted using a four-fiber constitutive model [2]. WT and MMP12-/- blood pressures were comparable (133/88 vs. 126/93 mmHg; SBP/DBP; telemetry); WT aging did not influence blood pressure [3]. All metrics are therefore presented at a common pressure (figure). At first sight, MMP12-/- aging resembles WT aging: increased wall thickness (figure, panel A) leading to decreased circumferential stress (B) and decreased stored strain energy (C) [3-5]. However, in WT aging, circumferential material stiffness decreased, which did not occur in MMP12-/- (D). Structural stiffness and pulse wave velocity remained constant in WT mice but increased in MMP12-/- (E-F).

Discussion: Our findings suggest that in both WT and MMP12-/-, mechanical homeostasis with aging was compromised, a finding that was exacerbated with MMP12-/-. MMP12-/- was previously reported to reduce age-associated stiffening [1]. This contradictory finding may be explained by the use of atomic force microscopy in [1] (measuring compressive stiffness) versus our use of tensile biaxial testing.
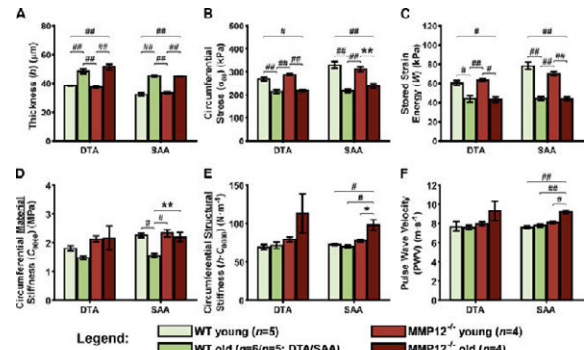
h.C_θθθθ, W, C_θθθθ, and h·C_θθθθ calculated for SBP=120 mmHg; PWV calculated using Bramwell-Hill equation for SBP/DBP=120/80 mmHg. *p<0.05; **p<0.01, #p<0.005, ##p<0.001; ANOVA followed by Tukey's test.

References

1. Liu SL, Bae YH, Yu C, Monslow J, Hawthorne EA, Castagnino P, Branchetti E, Ferrari G, Damrauer SM, Pure E, Assoian RK. Matrix metalloproteinase-12 is an essential mediator of acute and chronic arterial stiffening. Sci Rep. 2015;5:17189.
2. Ferruzzi J, Bersi MR, Humphrey JD. Biomechanical phenotyping of central arteries in health and disease: advantages of and Methods: for murine models. Ann Biomed Eng. 2013;41:1311-1330.
3. Ferruzzi J, Madziva D, Caulk AW, Tellides G, Humphrey JD. Compromised mechanical homeostasis in arterial aging and associated cardiovascular consequences. Biomech Model Mechanobiol. 2018; [in press].
4. Ferruzzi J, Bersi MR, Uman S, Yanagisawa H, Humphrey JD. Decreased elastic energy storage, not increased material stiffness, characterizes central artery dysfunction in fibulin-5 deficiency independent of sex. J Biomech Eng. 2015;137.
5. Ferruzzi J, Bersi MR, Mecham RP, Ramirez F, Yanagisawa H, Tellides G, Humphrey JD. Loss of Elastic Fiber Integrity Compromises Common Carotid Artery Function: Implications for Vascular Aging. Artery Res. 2016;14:41-52.

2.2
GREATER BLOOD PRESSURE VARIABILITY IS ASSOCIATED WITH LOWER COGNITIVE PERFORMANCE — THE MAASTRICHT STUDY

Tan Lai Zhou [1,2], Abraham Kroon [3,2], Coen Stehouwer [3,2], Martin van Boxtel [4], Frans Verhey [4], Miranda Schram [3,2,5], Thomas van Sloten [6,7,2], Ronald Henry [3,2,5]

[1]Dept. of Internal Medicine, Maastricht University, Maastricht, the Netherlands
[2]Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, the Netherlands
[3]Dept. of Internal Medicine, Maastricht University Medical Centre, Maastricht, the Netherlands
[4]School for Mental Health and Neuroscience, Dept. of Psychiatry & Neuropsychology, Maastricht University, Maastricht, the Netherlands
[5]Heart and Vascular Centre, Maastricht University Medical Centre, Maastricht, the Netherlands
[6]Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Paris, France
[7]INSERM, UMR-S970, Paris Cardiovascular Research Center, Department of Epidemiology and Department of Arterial Mechanics, Paris, France

An increasing number of individuals will face age-related cognitive difficulties, as life expectancy has increased globally. It is therefore important to identify modifiable risk factors for cognitive impairment. Very short- to mid-term blood pressure variability (BPV) may be such factor, as it may cause cerebral ischemia via various mechanisms. To this end, we investigated whether greater diastolic (dBPV) and systolic BPV (sBPV) are cross-sectionally associated with memory function (MF; n = 1804), information processing speed (IPS; n = 1793), and executive function (EF; n = 1780), in 40- to 75-year-old individuals from The Maastricht Study. A composite BPV-index was derived by standardizing and averaging within-visit, 24-hour and 7-day BPV. We performed linear regression with adjustments for age, sex, educational level, 24-hour DBP or SBP, and cardiovascular risk factors. We found that a 1-