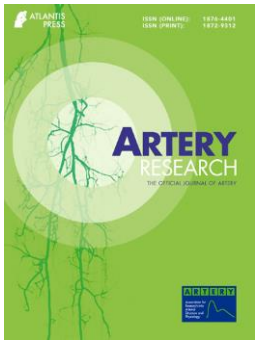


Artery Research

ISSN (Online): 1876-4401 **ISSN (Print): 1872-9312**
Journal Home Page: https://www.atlantis-press.com/journals/artres

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

Bart Spronck, Abhay B. Ramachandra, Jakub Toczek, Jinah Han, Mehran Sadeghi, Jay D. Humphrey

To cite this article: Bart Spronck, Abhay B. Ramachandra, Jakub Toczek, Jinah Han, Mehran Sadeghi, Jay D. Humphrey (2018) 2.1: KNOCK-OUT OF MATRIX METALLOPROTEINASE-12 EXACERBATES COMPROMISED MECHANICAL HOMEOSTASIS IN ARTERIAL AGING, Artery Research 24:C, 69–69, DOI: https://doi.org/10.1016/j.artres.2018.10.024

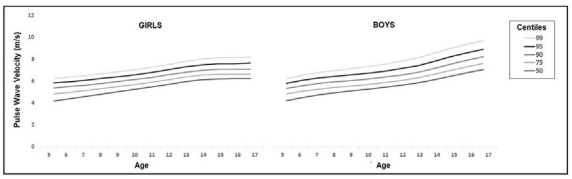
To link to this article: https://doi.org/10.1016/j.artres.2018.10.024

Published online: 7 December 2019

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

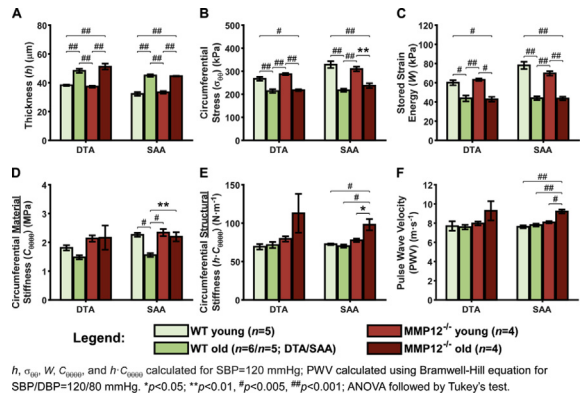
2.1
KNOCK-OUT OF MATRIX METALLOPROTEINASE-12 EXACERBATES COMPROMISED MECHANICAL HOMEOSTASIS IN ARTERIAL AGING

Bart Spronck [1], Abhay B. Ramachandra [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 ± 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.



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-