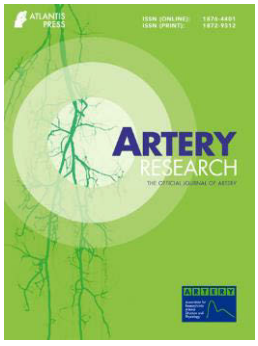

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2.2: GREATER BLOOD PRESSURE VARIABILITY IS ASSOCIATED WITH LOWER COGNITIVE PERFORMANCE – THE MAASTRICHT STUDY

Tan Lai Zhou, Abraham Kroon, Coen Stehouwer, Martin van Boxtel, Frans Verhey, Miranda Schram, Thomas van Sloten, Ronald Henry

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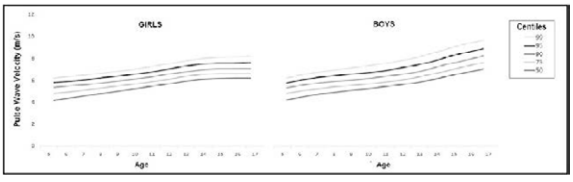
brachial artery with a clinically validated automatic sphygmomanometer (OMRON 705IT) and an appropriately sized cuff. Gender-specific percentiles were used for the definition of the individual BP phenotype. Carotid-femoral PWV was measured to all participants at the third clinical evaluation, with the 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]
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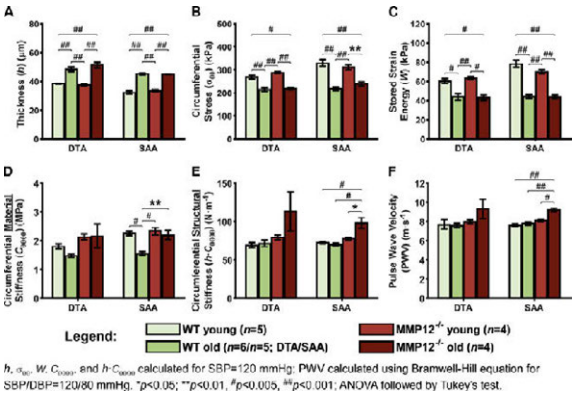
Background: Matrix metalloproteinase-12 (MMP12) may modulate arterial stiffening with age [1]. We aimed to study the effect of aging on biaxial arterial stiffness in wild-type (WT) and MMP12 knock-out (MMP12-/-) mice.

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.



h, $\sigma_{\theta,ref}$, W, $C_{\theta\theta,ref}$, and h·$C_{\theta\theta,ref}$ 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.

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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]
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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-

SD greater dBPV was associated with lower IPS (beta [SD difference]; 95% CI: -0.10;-0.20 to -0.00) and EF (-0.12; -0.22 to -0.01), and borderline associated with lower MF (-0.09; -0.20 to 0.01). A 1-SD greater sBPV, however, was not associated with IPS (-0.040; -0.14 to 0.06), or EF (-0.09; -0.20 to 0.022), but was borderline associated with lower MF (-0.11; -0.21 to 0.00). This effect of greater dBPV on cognitive performance is equivalent to ±3 additional years of ageing. The stronger association of dBPV than sBPV with cognitive performance may be explained by the fact that DBP is the main determinant of MAP. Excessive dBPV may then lead to inadequate cerebral perfusion. In conclusion, greater very short-to mid-term dBPV and, to a lesser extent, sBPV could be a modifiable risk factor for cognitive impairment.

2.3
OCCUPATIONAL, SPORT AND LEISURE RELATED PHYSICAL ACTIVITY HAVE CONTRASTING EFFECTS ON NEURAL BAROREFLEX SENSITIVITY. THE PARIS PROSPECTIVE STUDY III

Rachel Climie [1], Pierre Boutouyrie [1], Marie-Cecile Perier [1], Edouard Chaussade [2], Matthieu Plichart [2], Lucile Offredo [1], Catherine Guilbout [1], Thomas van Sloten [1], Frederique Thomas [3], Bruno Pannier [3], James Sharman [4], Stephane Laurent [5], Xavier Jouven [6], Jean-Philippe Empana [7]
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[7]*INS, France*

Background: Physical activity (PA) is beneficial for baroreflex sensitivity (BRS), but it is unclear whether the type of PA has similar effects on the neural (nBRS) or vascular (carotid stiffness) components of BRS. We sought to determine this in healthy adults from a community- based study via assessment of occupational (OPA), sport (SPA), leisure (LPA) and total PA (TPA).
Methods: In 8649 adults aged 50 to 75 years, resting nBRS (estimated by low frequency gain, from carotid distension rate and heart rate) and carotid stiffness were measured by high-precision carotid echotracking. PA was self-reported using the Baecke questionnaire, which distinguishes OPA, SPA, LPA and TPA. The associations between PA and nBRS and carotid stiffness were quantified using multivariate linear regression analysis. Analyses were conducted separately in the working and non- working population.
Results: In working adults (n = 5039), OPA was associated with lower nBRS function (p = 0.026) and borderline higher carotid stiffness (p = 0.08). When stratified by education, this association remained only in those with less than tertiary education. SPA was associated with higher nBRS (p = 0.0005) and borderline lower carotid stiffness (p = 0.052). Neither LPA nor TPA was associated with nBRS or carotid stiffness. In non-working adults (n = 3610), SPA and TPA were both associated with lower carotid stiffness (p = 0.012 and p = 0.020), but not nBRS. LPA was not associated with either parameter.
Conclusion: Occupation-related PA is associated with lower nBRS function and higher carotid stiffness, especially in those with lower education. Higher amounts of sport-related PA are associated with higher nBRS and lower carotid stiffness.

2.4
CENTRAL SYSTOLIC BLOOD PRESSURE PROVIDES ADDITIONAL INFORMATION IN RISK PREDICTION IN HEMODIALYSIS PATIENTS

Christopher C. Mayer [1], Julia Matschkal [2], Pantelis A. Sarafidis [3], Stefan Hagmair [1], Georg Lorenz [2], Susanne Angermann [2], Matthias C. Braunisch [2], Marcus Baumann [2], Uwe Heemann [2], Christoph Schmaderer [2], Siegfried Wassertheurer [1]
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Background: Association of Ambulatory Blood Pressure Monitoring (ABPM) with mortality depends on cardiac function in hemodialysis patients. Evidence for the predictive power of central Systolic Pressure (cSBP) is inconclusive. Thus, this study aimed to investigate the additional information of ambulatory cSBP in risk prediction in a cohort of hemodialysis patients.
Methods: Within the ISAR-study cohort, 344 hemodialysis patients underwent 24 h ABPM on the dialysis day. All-cause and cardiovascular mortality served as endpoints. Risk prediction was performed using Cox regression in patients with or without atrial fibrillation (AF) or heart failure (HF) for peripheral (pSBP) and central systolic pressure calibrated with peripheral systolic and diastolic pressure (cSBP1) or peripheral mean and diastolic pressure (cSBP2).
Results: During a mean follow-up of 37.6 (17.5 SD) months, 115 patients died, of whom 47 due to cardiovascular reasons. In patients with AF or HF, a negative association to mortality could be observed, independent of pressure location and calibration (see Table). In patients without AF or HF, these associations were to the opposite directions and cSBP2 was superior to pSBP and cSBP1 for all-cause (pSBP: HR = 1.01, p = 0.30; cSBP1: HR = 1.00, p = 0.77; cSBP2: HR = 1.01, p = 0.06) and cardiovascular (pSBP: HR =1.03, p = 0.02; cSBP1: HR = 1.02, p = 0.06; cSBP2: HR = 1.03, p = 0.003) mortality. This circumstance was confirmed in multivariable analysis combining pSBP and differences between pSBP and cSBP (see Table).
Conclusions: This study provides evidence for the additional information of central systolic blood pressure and its dependency on calibration in risk prediction in hemodialysis patients. Further studies are needed to confirm these findings.

		AForHF (n = 105)		noAForHF (n = 239)	
		HR	p	HR	p
All-cause Mortality		*59 events*		*56 events*	
Univariate	pSBP	0.97 (0.96, 0.98)	<0.001	1.01 (0.99, 1.03)	0.30
	cSBP1	0.97 (0.95, 0.98)	<0.001	1.00 (0.98, 1.02)	0.77
	cSBP2	0.97 (0.96, 0.99)	<0.001	1.01 (1.00, 1.03)	0.06
	pSBP-cSBP1	0.93 (0.85, 1.01)	0.09	1.10 (1.04, 1.17)	<0.001
	pSBP-cSBP2	1.01 (0.97, 1.05)	0.59	0.95 (0.91, 0.98)	0.005
Multivariable	pSBP	0.97 (0.95, 0.99)	<0.001	1.00 (0.98, 1.01)	0.60
	pSBP-cSBP1	1.01 (0.92, 1.12)	0.80	1.11 (1.04, 1.19)	0.002
	pSBP	0.97 (0.96, 0.98)	<0.001	1.00 (0.99, 1.02)	0.79
	pSBP-cSBP2	1.00 (0.96, 1.04)	0.83	0.95 (0.91, 0.99)	0.009
Cardiovascular Mortality		*20 events*		*27 events*	
Univariate	pSBP	0.95 (0.93, 0.98)	<0.001	1.03 (1.00, 1.05)	0.02
	cSBP1	0.95 (0.93, 0.97)	<0.001	1.02 (1.00, 1.05)	0.06
	cSBP2	0.96 (0.94, 0.98)	<0.001	1.03 (1.01, 1.05)	0.003
	pSBP-cSBP1	0.88 (0.74, 1.02)	0.08	1.12 (1.03, 1.20)	0.006
	pSBP-cSBP2	1.01 (0.94, 1.07)	0.87	0.93 (0.88, 0.98)	0.006
Multivariable	pSBP	0.95 (0.93, 0.98)	<0.001	1.02 (0.99, 1.04)	0.22
	pSBP-cSBP1	0.98 (0.81, 1.19)	0.87	1.08 (0.98, 1.18)	0.12
	pSBP	0.95 (0.93, 0.98)	<0.001	1.02 (1.00, 1.04)	0.12
	pSBP-cSBP2	0.98 (0.91, 1.05)	0.59	0.94 (0.89, 1.00)	0.04

Table: Univariate and multivariable hazard ratios (95% confidence intervals) per mmHg increase and significance levels (p) for all-cause and cardiovascular mortality. Abbreviations: pSBP, peripheral systolic pressure; cSBP, central systolic pressure (1=brachial systolic and diastolic pressure calibration; 2= brachial mean and diastolic pressure calibration); HR, hazard ratio; AF, atrial fibrillation; HF, heart failure.

2.5
DOES WAVE REFLECTION PROTECT THE MICROVASCULATURE FROM HIGH PULSE PRESSURE?

Avinash Kondiboyina [1,2], Joe Smolich [3,2], Michael Cheung [3,2,4], Berend Westerhof [5], Nico Westerhof [5], Jonathan Mynard [1,2,6]
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Background: Wave reflection (caused by a stiffness increase from large to small arteries) has been considered to protect against high microvasculature Pulse Pressures (mPP) (1). However, according to transmission line theory, Transmission (T) and Reflection (R) coefficients are proportional (T = 1+R), implying that reflection would not be protective. Proximal arterial stiffening with aging is associated with reduced Total Arterial Compliance (TAC) and increased forward Pressure (Pfw). We hypothesized that a high TAC and low Pfw, rather than high R, are responsible for protection from mPP.
Methods: We constructed a fractal arterial tree containing 5008 vessels across 14 generations (fractal exponent 2.76, asymmetry ratio 0.8). Wave speed in each vessel was prescribed to achieve a uniform reflection coefficient (R = -0.025, 0, 0.025 or 0.05) at every junction, achieved by progressively stiffening distal vessels while keeping aortic wave speed constant ("distal-stiffening") or by progressively stiffening proximal vessels while