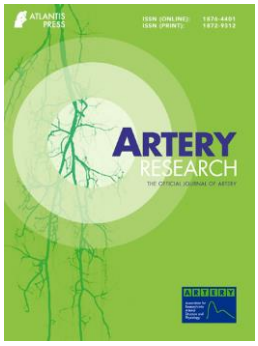

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2.4: AMBULATORY AORTIC STIFFNESS, INDEPENDENTLY OF STATIC, ASSOCIATES WITH NARROWER RETINAL ARTERIOLAR CALIBERS IN HYPERTENSIVES: THE SAFAR STUDY

Evaggelia K. Aissopou*, Antonios A. Argyris, Efthimia G. Nasothimiou, George D. Konstantonis, Konstantinos Tampakis, Nikolaos Tentolouris, Miltiadis Papathanassiou, Panagiotis G. Theodossiadis, Theodoros G. Papaioannou, Coen D.A. Stehouwer, Petros P. Sfik

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arterial wall properties. Current cfPWV measurement does not differentiate between effects of blood pressure and arterial wall properties. Animal studies show that the blood pressure sensitivity of arterial PWV is indicative of blood vessel remodeling. Measurement of this parameter in humans requires a forced change in blood pressure, as can be achieved by Valsalva maneuver. This study investigated a simplified method of measurement of pressure dependency of cfPWV.

Methods: Aortic blood pressure was measured using a validated transfer function from a brachial cuff waveform together with cfPWV in 27 subjects (15 female, 36 $\pm$ 19 years) in both the standing and supine position. The additional change in hydrostatic pressure across the carotid-femoral path length was estimated using body surface distances.

Results: Diastolic blood pressure changed for all subjects (standing 83 $\pm$ 8 mmHg, supine 70 $\pm$ 8 mmHg, $p < 0.001$). Hydrostatic change in pressure across the carotid-femoral path added a further difference of 19 $\pm$ 2 mmHg ($p < 0.001$). Standing cfPWV was 7.3 $\pm$ 2.2 m/s and supine cfPWV 5.2 $\pm$ 1.3 m/s ($p < 0.001$). The resulting pressure sensitivity of cfPWV ranged from 2.7 to 39.4 cm/s/mmHg and had a correlation with age (0.2 cm/s/year, $R^2 = 0.35$, $p < 0.001$).

Conclusions: Measuring cfPWV and blood pressure in the standing and supine position provides a method of calculation of pressure sensitivity of cfPWV that could be easily implemented in any research laboratory or clinic and may provide predictive information beyond either cfPWV or blood pressure alone.

2.2
RE-REFLECTION OF BACKWARD PROPAGATING WAVES LEADS TO AMPLIFICATION OF THE FORWARD PRESSURE WAVE IN WAVE SEPARATION ANALYSIS

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Introduction: In wave separation analysis, the pressure wave is decomposed into a single forward and backward component, which actually compounds all forward and backward propagating waves. We hypothesize that, in particular in presence of early reflections as in aortic coarctation, re-reflection of backward propagating waves at the ventricular-arterial interface amplifies the forward wave component.

Methods: We set up a 3D fluid-structure interaction model of the aorta based on MRI scans of a healthy volunteer. With the healthy model as reference, we introduced a 25 mm narrowing section in the descending thoracic aorta to model an aortic coarctation, with coarctation index (CI) 0.65 and 0.5. Inflow and outflow boundary conditions were kept constant to allow studying the isolated effect of the coarctation. Aortic root pressure and flow waveforms were extracted and subjected to wave intensity and wave separation analysis.

Results: The presence of the coarctation increased systolic pressure by 10 mmHg and 41 mmHg for CI 0.65 and 0.5, respectively. Wave separation analysis indicated that this increase in blood pressure was about equally due to an increase in the amplitude of both the forward and backward pressure wave. Wave intensity analysis - though only after separating into forward and backward wave intensity - revealed that the amplification of the forward pressure wave is caused by re-reflection of backward waves at the level of the aortic valve.

Conclusion: We conclude that wave separation analysis might overestimate the incident pressure wave component because of re-reflection of backward waves at the aortic valve.

2.3
TESTING RIVA-ROCCI'S BASIC ASSUMPTIONS BY SYSTEMATIC REVIEW AND META-ANALYSIS TO DETERMINE THE TRUE DIFFERENCE BETWEEN AORTIC AND BRACHIAL INVASIVE BLOOD PRESSURE

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Background: The Riva-Rocci brachial blood pressure (BP) method purported to measure aortic BP, and this remains the cornerstone thesis of clinical BP measurement. However, few studies have confirmed this thesis with direct BP measurements. This study aimed to determine the true differences in aortic and brachial BP by systematic review and meta-analysis of invasive (intra-arterial) data.

Methods: Five online databases and several offline techniques were used to search for studies that reported simultaneous or sequentially recorded intra-arterial aortic and brachial BP. Differences in systolic BP (SBP) and diastolic BP (DBP) were calculated as brachial minus aortic values.

Results: Data from 12 studies (from 1956 to 2013), totalling 399 participants (aged 57.3 [95% CI: 52.2, 62.4] years, 76.9% male) met inclusion criteria. Brachial SBP was significantly higher than aortic SBP (pooled SBP difference estimate = 7.99 [95% CI: 5.30, 10.7] mmHg, $p<0.001$; $I^2 = 93.3\%$). However, there was only a minimal decrease in DBP between the aorta and brachial artery (pooled DBP difference estimate = -0.67 [95% CI: -1.67, 0.32] mmHg, $p = 0.18$; $I^2 = 79.7\%$). Heterogeneity in SBP differences between studies was modestly explained by age ($R^2 = 5.7\%$), but not by sex, measurement method (simultaneous or sequential) or type of catheter (fluid-filled or micromanometer [$R^2 = 0\%$ all]).

Conclusion: Although only minimal difference in DBP, brachial SBP is significantly higher than aortic SBP, with substantial variability in the magnitude of SBP difference. This questions the Riva-Rocci assumption of brachial BP being representative of aortic BP, and could have accuracy implications for BP assessment using the brachial cuff method.

2.4
AMBULATORY AORTIC STIFFNESS, INDEPENDENTLY OF STATIC, ASSOCIATES WITH NARROWER RETINAL ARTERIOLAR CALIBERS IN HYPERTENSIVES: THE SAFAR STUDY

Evaggelia K. Aissopou [1,*], Antonios A. Argyris [1], Efthimia G. Nasothimiou [1], George D. Konstantonis [1], Konstantinos Tampakis [1], Nikolaos Tentolouris [1], Miltiadis Papathanassiou [2], Panagiotis G. Theodossiadis [2], Theodoros G. Papaioannou [3], Coen D. A. Stehouwer [4,5], Petros P. Sfikakis [1], Athanassios D. Protogerou [1,5]
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Background: Arterial stiffness measured under static conditions reclassifies significantly cardiovascular (CV) risk and associates with organ damage, including narrower retinal arterioles. However, arterial stiffness exhibits diurnal variation, thus single static stiffness recordings do not correspond to the "usual" 24 hr, awake and asleep average arterial stiffness. We aimed to test the hypothesis that ambulatory 24 hr, awake and asleep aortic (a) pulse wave velocity (PWV) associate with retinal vessel calibers, independently of confounders and of static arterial stiffness, in hypertensive individuals free from diabetes and CV disease.

Methods: Digital retinal images were obtained (181 individuals, age: 53.9 $\pm$ 10.7 years, 55.2% men) and retinal vessel calibers were measured with validated software to determine central retinal arteriolar and venular equivalents (CRAE and CRVE, respectively); ambulatory (24 hr, awake, asleep) and static office aPWV were estimated by Mobilo-O-Graph; and static office carotid-femoral (cf) PWV by SphygmoCor.

Results: Regression analysis performed in 320 gradable retinal images showed that, after adjustment for confounders: (i) ambulatory aPWV was significantly associated with narrower retinal arterioles but not with venules; (ii) asleep aPWV had stronger associations with CRAE than awake aPWV; (iii) both ambulatory aPWV and cfPWV were associated mutually independently with narrower retinal arterioles; aPWV introduction in the model of cfPWV, improved model's R^2 ($p = 0.012$). Similar discriminatory ability of 24 hr aPWV and of cfPWV to detect the presence of retinal arteriolar narrowing was found.

Conclusion: Ambulatory aPWV, estimated by an operator-independent method, provides additional information to cfPWV regarding the associations of arterial stiffness with the retinal microcirculation.

2.5
IN SINGLETONS BORN AT TERM, LOWER GESTATIONAL AGE IS ASSOCIATED WITH INCREASED AORTIC PULSE WAVE VELOCITY IN YOUNG ADULTHOOD: THE NORTHERN IRELAND YOUNG HEARTS PROJECT (NIYHP)

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Decreases in the mean gestational age of babies born at term have been reported over the past decade in several developed countries, linked to increases in the rates of planned births by labour induction and/or pre-labour caesarean sections. In contrast to the effects of pre-term birth, the extent to which lower gestation age within the 'at-term' range (i.e. $\geq$37−$\leq$42 weeks) affects individuals' cardiovascular heath is largely unknown, however. We have therefore examined the association between gestational age (obtained from the Northern Ireland Child Health Services' records) and aortic pulse wave velocity (aPWV) in 351 young adults from the NIYHP (50.4% women, mean age of 22.4 $\pm$ 1.6 years, all singletons and born at term, 98% with birth weight>2.5 kg). In analyses adjusted for age, sex, birth weight (in SDs relative to UK's 1990 reference), birth order, breast-feeding, maternal and paternal age at child's birth, and social economic status, we found that each week increase in gestational age was significantly associated with lower levels of aPWV [standardized ß = −0.11 (95% CI:−0.21;−0.01, p = 0.039)]. Additional adjustments for individuals' adult BMI and mean arterial pressure did not appreciably affect this association. None of the other birth covariates were independently associated with aPWV. These findings suggest that lower gestational age, even within the at-term range, may be a key determinant of early vascular ageing as each additional week conferred benefits. This aspect may have been neglected by the over-simplistic characterization of individuals as 'born at-term' and may have clinical implications for policies around planned deliveries, given the current trends.

2.6
PULSE WAVE VELOCITY AND GAIT PERFORMANCE IN OLDER SUBJECTS

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Background: Arterial stiffening is an age-related change and is a well-known cardiovascular risk factor but its association with physical decline is rarely evaluated.
The aim of this analysis was to assess the association of arterial stiffness as carotid-femoral pulse wave velocity (PWV) with gait performance in older subjects.
Methods: PWV was measured with Complior device. In all subjects was assessed: gait speed (V), Timed Up&Go test (TUG), handgrip strength, personal (ADL) and Instrumental Activities of Daily Living (IADL). Body composition was assessed with DXA, nutritional status with Mini Nutritional Assessment. Standard blood laboratory tests and markers of inflammation (hsCRP, IL-6, pentraxin3-PTX3, osteoprotegerin-OPG, TNFα soluble receptor2-sTNFR2) were determined.
Results: Mean age of 69 subjects (53—96 yrs) was 72.5 $\pm$ 9.8 yrs. Mean number of diseases was 5.3 $\pm$ 2.2, and of used medications was 7.0 $\pm$ 2.5. Subjects with PWV < 10 m/s and $\geq$10 m/s did not differ in systolic (SBP) and diastolic blood pressure, heart rate, number of diseases and medications, IADL, ADL, handgrip strength. Patients with PWV < 10 m/s were younger (67.8 $\pm$ 6.4vs74.8 $\pm$ 10.4 yrs; p = 0.004), had higher V (1.02 $\pm$ 0.31vs0.798 $\pm$ 0.23 m/s; p = 0.006), lower TUG (9.69 $\pm$ 2.6vs11.81 $\pm$ 4.56; p = 0.02), higher mdrd (76.3 $\pm$ 21.4 vs 62.87 $\pm$ 20.3 ml/min/m^2) and lower legs' fat content (LEfat) (6433.1 $\pm$ 1934.2vs 8046.4 $\pm$ 3187.5g; p = 0.047). PWV correlated positively with age (r = .47, p < 0.0001), TUG (r = 0.26, p = 0.037), negatively with V (r = −0.37, p = 0.003), handgrip strength (r = −0.30, p = 0.015), ADL (r = −0.28, p = 0.02).
In multiple regression analysis gait speed was negatively associated with PWV (β = −0.37; p = 0.0075), female gender (β = −0.36; p = 0.045) and TUG (β = −0.443; p = 0.0038), and positively with Hb (β = 0.30; p = 0.045), PTX3 (β = 0.608; p = 0.001), sTNFR2 (β = 0.374; p = 0.035).
Conclusions: Artery stiffness, apart from female gender and inflammation, may be associated with poorer gait performance in older subjects.

3.1
PREDIABETES IS ASSOCIATED WITH IMPAIRED RETINAL VASODILATION: THE MAASTRICHT STUDY

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Aim: Type 2 diabetes (DM2) causes microvascular dysfunction (MVD). In addition, MVD can contribute to insulin resistance, predisposing to DM2. This hypothesis predicts that MVD should be present in impaired glucose metabolism (IGM; prediabetes). However, population-based studies of MVD and glucose metabolism are not available. We investigated this using the retinal arteriolar dilator response to flicker light.
Methods: In a population-based study (n = 2205), we determined retinal %-dilation (Dynamic Vessel Analyzer; Imedos, Germany) and glucose metabolism status (OGTT; classified as normal (NGM), IGM or DM2). Differences were compared with multivariable regression adjusted for age, sex, BMI, smoking, systolic-BP, lipid profile, retinopathy, (micro)albuminuria, the use of lipid-modifying and/or blood-pressure-lowering medication and prior cardiovascular disease.
Results: 1263 individuals had NGM (42% men, aged 58 $\pm$ 8 years (mean $\pm$ SD)), 336 IGM (61% men, aged 61 $\pm$ 7 years) and 606 (due to oversampling) DM2 (69% men, aged 63 $\pm$ 8 years). Arteriolar %-dilation was median 3.51, IQR 1.47 to 5.95, range −5.69 to +19.71. %-dilation (mean $\pm$ SD) was 4.42 $\pm$ 3.45 in NGM, 3.77 $\pm$ 3.06 in IGM, and 3.26 $\pm$ 3.27 in DM2. Adjusted analyses showed decreased %-dilation in IGM (β = −0.461, p = 0.03) and DM2 (β = 0.559, p = 0.01) vs NGM.
Conclusion: IGM and DM2 are associated with reduced flicker-light-induced retinal arteriolar dilation, independently of major cardiovascular risk factors. These findings support the concept that MVD precedes and thus may contribute to DM2.

3.2
ORIGINS OF THE BACKWARD TRAVELING WAVE IN THE ARTERIAL TREE

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Backward traveling waves, an important determinant of central haemodynamics, are usually regarded as being due to reflections from discontinuities in the arterial tree. However, consideration of a single tube model of the arterial with a single site of reflection shows that a backward pressure wave may be generated by elastic recoil of large arteries, in which case the magnitude of the backward wave is proportional to that of the forward wave. A 55-segment 1-D model of the arterial which allows reflection as a continuum along the arterial tree and, for a given prescribed aortic flow, generates physiological aortic pulse waveforms was used to examine the relation of the backward to forward pressure waves in 4107 "virtual subjects" with arterial parameters spanning the physiological range. Backward pressure wave was closely correlated with the forward wave (R = 0.931, P < 0.001). Clinical data was obtained by carotid tonometry and aortic Doppler sonography during modulation of cardiovascular function in healthy volunteers (n = 13, age 46.5 $\pm$ 10.1 years with inotropic, vasopressor and vasodilator drugs (dobutamine, norepinephrine phentolamine and nitroglycerin). The magnitude of backward pressure was highly correlated with forward pressure over a range 5—15 mmHg (R = 0.824, P < 0.001) with a constant ratio of backward to forward wave magnitude except during treatment with nitroglycerin, a vasodilator known to be highly selective for large muscular arteries. These numerical and experimental data suggest that backward pressure waves can