



Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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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To cite this article: Dean Picone*, Petr Otahal, Martin Schultz, James Sharman (2015) 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, Artery Research 12:C, 41–41, DOI: <https://doi.org/10.1016/j.artres.2015.10.010>

To link to this article: <https://doi.org/10.1016/j.artres.2015.10.010>

Published online: 7 December 2019

arterial wall properties. Current cPWV 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 cPWV.

Methods: Aortic blood pressure was measured using a validated transfer function from a brachial cuff waveform together with cPWV in 27 subjects (15 female, 36 ± 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 ± 8 mmHg, supine 70 ± 8 mmHg, $p < 0.001$). Hydrostatic change in pressure across the carotid-femoral path added a further difference of 19 ± 2 mmHg ($p < 0.001$). Standing cPWV was 7.3 ± 2.2 m/s and supine cPWV 5.2 ± 1.3 m/s ($p < 0.001$). The resulting pressure sensitivity of cPWV 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 cPWV and blood pressure in the standing and supine position provides a method of calculation of pressure sensitivity of cPWV that could be easily implemented in any research laboratory or clinic and may provide predictive information beyond either cPWV 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

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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 ± 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-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 cPWV were associated mutually independently with narrower retinal arterioles; aPWV introduction in the model of cPWV, improved model's R^2 ($p = 0.012$). Similar discriminatory ability of 24 hr aPWV and of cPWV to detect the presence of retinal arteriolar narrowing was found.