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Concordance among pulse wave velocity assessment methods: A network meta-analysis

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To the Editor: Arterial stiffness signifies early structural and functional changes in the arterial wall. Pulse wave velocity (PWV) stands out as the most validated method for noninvasive arterial stiffness quantification, serving as the gold standard for assessing aortic stiffness. PWV estimates the transit time of the pulse between waves at distinct sites in the vascular tree.[1]

The predominant method for PWV measurement involves simultaneous carotid-femoral tonometry using available devices. This entails placing two tonometers at the femoral artery and homolateral primitive carotid artery while the patient is in dorsal decubitus. The distance between these points is measured, and the device calculates the time separating the two wave endpoints, reporting PWV through specific formulas.[1]

However, tonometry-based PWV measurements are influenced by many factors such as the need for sophisticated equipment, trained personnel, procedural time, potential bias in patient positioning, and distance measurement inaccuracies. To address these challenges, alternative PWV measurement methods, including photoplethysmography, piezoelectricity, oscillometry, ultrasonography (US), and magnetic resonance imaging (MRI), have been proposed. The goal is to enhance user-friendliness, reduce interobserver variability, and minimize measurement time, making PWV assessment as a practical tool in clinical settings.[2]

While a previous comprehensive review qualitatively explored the validation of PWV assessment methods, a quantitative synthesis comparing PWV values across methods was lacking.[3] This study applies a network meta-analysis (NMA) approach to comprehensively analyze all available comparison studies among common PWV assessment methods. The NMA aimed to synthesize evidence about the concordance, measured as limits of agreement (LoA), between different assessment methods on PWV.

This report adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-NMA guidelines[4] and Cochrane Handbook recommendations, registered in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/, CRD42022334359). A systematic search in PubMed, Scopus, and Web of Science, from inception to April 2022, targeted articles comparing at least two PWV assessment methods. The comprehensive search strategy is available in Supplementary Table 1, http://links.lww.com/CM9/C65. Additionally, a review of reference lists from relevant articles was conducted to augment the systematic literature search.

Inclusion criteria encompassed cross-sectional studies comparing two or more PWV assessment methods, with no restrictions on participant types. Assessment methods included tonometry, piezoelectricity, oscillometry, MRI, US, photoplethysmography, or catheterism. Certain publication types such as review articles, editorials, comments, guidelines, and case reports, duplicates, studies with insufficient data for network meta-analysis, and studies comparing the same method with different devices were excluded. Two independent reviewers conducted the literature search, resolving disagreements through consensus or involving a third researcher.

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Data extracted from original reports covered various aspects, including publication details, study location, population characteristics, assessment methods, devices used, PWV index, and baseline PWV means. Methodological quality was assessed using the COSMIN Risk of Bias tool,[5] evaluating design and statistical standards. A four-point rating system determined the final quality assessment for each study. Two reviewers independently performed data extraction and quality assessment, with inconsistencies resolved through consensus or involvement of a third researcher. Agreement rate between reviewers was evaluated using kappa statistics.

The included studies were qualitatively summarized in a table detailing direct and indirect comparisons. The network meta-analysis followed the PRISMA-NMA guidelines,[4] including the following steps: (1) Utilization of a network geometry graph to visually represent evidence in the PWV network. (2) Consistency assessment, checking agreement between PWV values estimated from direct and indirect comparisons using the Wald test, with additional evaluation of local inconsistency. (3) Comparative assessment of the LoA for PWV values through random effects pairwise and network meta-analysis, along with random effects pairwise meta-analysis for correlation coefficients when sufficient studies were available. Statistical heterogeneity was assessed using the I^2 statistic. (4) Bland and Altman scatterplots were generated for PWV assessment method comparisons with at least four studies. (5) Relative rankings of treatments were determined based on LoA estimates, visually represented through rankograms. Additionally, the Surface under the Cumulative Ranking (SUCRA) was calculated for each PWV assessment method, simplifying their classification. (6) Sensitivity analyses were conducted to assess summary estimate robustness, and a network funnel plot was used to examine bias due to the small study effect. All analyses were conducted using Stata 15.0 (Stata, College Station, Texas, USA).

A total of 57 studies [Supplementary Figure 1, http://links.lww.com/CM9/C65] comparing different assessment methods on PWV values were identified [Supplementary Figure 2, http://links.lww.com/CM9/C65]. They were conducted in 25 countries across North America, Europe, Asia, South America, and Oceania, published between 2007 and 2021 [Supplementary Table 2, http://links.lww.com/CM9/C65]. Involved populations aged 5.9 to 79.0 years, with sample sizes ranging from 14 to 1162 participants across assessment methods. Fifty-one studies compared two methods, while six studies compared three or more methods.

Various devices were used, including SphygmoCor, PulsePen, Colin, etc., for tonometry; Complior, polyvinylidene fluoride piezoelectric sensor, and a prototype for piezoelectricity; Arteriograph, SphygmoCor XCEL, etc., for oscillometry; MR scanner, Tesla Magnetom AVANTO-scanner, etc., for MRI; eTRACKING, MyLab, LOGIQ P6, etc., for US; pOpmètre, PulseTrace PCA, etc., for photoplethysmography; and Fluid-filled catheters for catheterism. Baseline PWV ranged from 3.0 m/s to 12.8 m/s.

Among included studies, 93% (53/57) were of doubtful methodological quality, and 7% (4/57) were inadequate, assessed by the COSMIN Risk of Bias checklist. Interpretation caution is advised due to methodological shortcomings [Supplementary Table 3, http://links.lww.com/CM9/C65].

Triangular loops showed inconsistency in certain comparisons: oscillometry-piezoelectricity-US (inconsistency factor: 3.46; $P = 0.005$), photoplethysmography-piezoelectricity-tonometry (inconsistency factor: 2.40; $P = 0.112$), and MRI-oscillometry-piezoelectricity (inconsistency factor: 2.10; $P = 0.043$) [Supplementary Figure 3, http://links.lww.com/CM9/C65].

With tonometry as the gold standard, in network meta-analysis, piezoelectricity (LoA: –0.27 m/s, 95% CI: –0.82 to 0.28 m/s) and oscillometry (LoA: –0.33 m/s, 95% CI: –0.74 to 0.09 m/s) exhibited the narrowest LoAs on PWV [Supplementary Figure 4, http://links.lww.com/CM9/C65]. Pairwise meta-analysis indicated catheterism with the narrowest LoA (LoA: –0.20 m/s, 95% CI: –0.24 to –0.15 m/s; only one study) [Supplementary Table 4, http://links.lww.com/CM9/C65]. Bland and Alman scatterplots are shown in Figure 1 when in pairwise meta-analysis there were at least four studies.

Pairwise meta-analyses for correlation coefficients showed a very high correlation for the tonometry *vs.* piezoelectricity comparison ($r = 0.90$; 95% CI: 0.87, 0.92), a high correlation for the following comparisons: tonometry *vs.* US ($r = 0.70$; 95%CI: 0.49, 0.90), oscillometry *vs.* MRI ($r = 0.66$; 95% CI: 0.48, 0.84), tonometry *vs.* oscillometry ($r = 0.61$; 95% CI: 0.50, 0.71), tonometry *vs.* MRI ($r = 0.51$; 95% CI: 0.45, 0.58), and a moderate correlation for oscillometry *vs.* piezoelectricity comparison($r = 0.49$; 95% CI: 0.41, 0.58) [Supplementary Figure 5, http://links.lww.com/CM9/C65].

Tonometry ranked the highest (SUCRA: 85.2%), followed by photoplethysmography (SUCRA: 68.0%), piezoelectricity (SUCRA: 61.1%), catheterism (SUCRA: 58.3%), and oscillometry (SUCRA: 55.5%), US and MRI ranked the lowest (SUCRA: 19.3% and 2.6%, respectively) [Supplementary Figure 6, http://links.lww.com/CM9/C65].

Meta-regressions showed no age-associated differences [Supplementary Figure 7, http://links.lww.com/CM9/C65]. Sensitivity analysis indicated robust pooled estimates. Evidence of a small study effect was found in the tonometry *vs.* oscillometry comparison ($P = 0.006$) [Supplementary Figure 8, http://links.lww.com/CM9/C65].

This network meta-analysis offers a comprehensive comparison of common PWV assessment methods. In relation to tonometry, considered the gold standard, piezoelectric and oscillometric methods exhibit the narrowest LoAs on PWV, with a notably high correlation observed in tonometry *vs.* piezoelectricity comparison.

These results align with prior systematic reviews,[3] supporting piezoelectric devices as having the best correlation with tonometry. However, our study quantitatively endorses oscillometric devices showing a well agreement with tonometry, challenging past debates about their

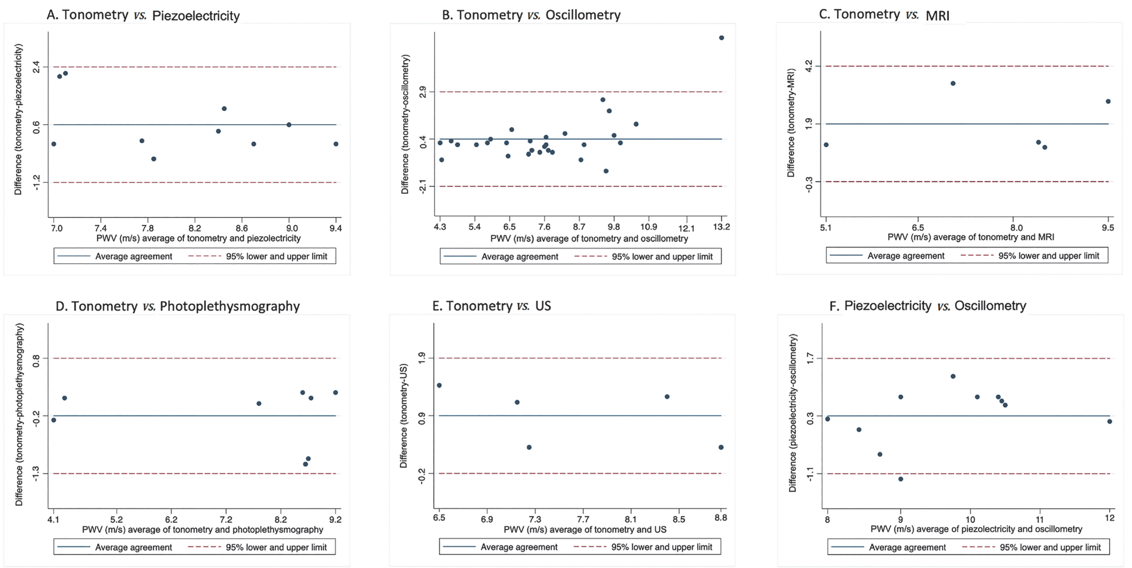

Figure 1: Bland and Altman scatterplots comparing PWV measurement methods. MRI: Magnetic resonance image; PWV: Pulse wave velocity; US: Ultrasonography.

clinical suitability. Although photoplethysmography and MRI showing good LoA values with tonometry, the included studies were fewer.

The limited implementation of PWV assessment in clinical practice is primarily due to the technical complexities associated with tonometry. This review suggests a potential shift in clinical practice, advocating for PWV oscillometric assessment due to its simplicity, reduced variability, and independence from specific distance measurements. Catheterism, compared to tonometry, exhibits the widest LoA, possibly attributed to its focus on aortic stiffness.

Tonometry serves as the reference method despite challenges associated with invasive PWV measurements. Other noninvasive methods, like MRI, photoplethysmography, and ultrasound, require further validation through extensive research.

Each PWV method presents distinct advantages and limitations, and their prognostic value varies with the specific disease under consideration. Tonometry proves valuable in predicting cardiovascular outcomes, especially in diseases like hypertension, coronary artery disease, and chronic kidney disease. Oscillometry shows promise in population studies for predicting cardiovascular risk, while the prognostic value of piezoelectricity is yet to be firmly established. Photoplethysmography demonstrates prognostic value in various populations, and MRI shows promise in diseases related to aortic stiffness and atherosclerosis. Ultrasound has been studied across different populations, while catheterism is more common in research or specialized clinical settings.

Acknowledging limitations, such as methodological biases, small sample sizes, and heterogeneous study populations, this review supports the clinical applicability of oscillometric PWV assessment due to its narrow LoA and high correlation with tonometry. Piezoelectric methods also emerge as a viable alternative. Caution is warranted in interpreting the findings, emphasizing the need for further studies with improved methodological designs to validate these conclusions.

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Conflicts of interest

None.

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