

# Standardization of Arterial Stiffness Measurements Make Them Ready for Use in Clinical Practice

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## CAROTID-FEMORAL PULSE WAVE VELOCITY IS THE GOLD STANDARD FOR NONINVASIVE MEASUREMENT OF ARTERIAL STIFFNESS

Arterial stiffness can be measured as regional stiffness expressed as pulse wave velocity (PWV), local stiffness expressed as distensibility coefficient or PWV, and systemic stiffness. Many devices are commercially available to measure arterial stiffness of different vascular territories. However, not all vascular territories have shown predictive value for cardiovascular events.<sup>1,2</sup> Predictive value has been shown for the local stiffness of the carotid artery (CA) and the femoral artery (FA).<sup>2,3</sup> Arterial segments with predictive value are the carotid-femoral, brachial-ankle, cardio-ankle, and the aortic arch segments.<sup>2</sup> Carotid-femoral PWV (cfPWV) also has “incremental” value, above and beyond classical risk scores. It can reclassify patients into higher and lower risk categories.<sup>1</sup> Therefore, arterial stiffness should be determined noninvasively by the measurement of cfPWV. This has been recommended by the 2010 guideline for assessment of cardiovascular risk in asymptomatic adults of the American College of Cardiology Foundation and the American Heart Association (AHA), the 2013 guidelines for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension (ESH), and the 2015 AHA recommendations for improving and standardizing vascular research on arterial stiffness.<sup>1,4</sup>

## THE METHOD TO MEASURE cfPWV SHOULD BE STANDARDIZED

To calculate PWV, the path length traveled by the pulse wave and the transit time have to be measured. A large majority of devices adequately measure transit time, but many different ways have been proposed as best noninvasive estimate of the path length traveled by the pulse. The most frequently used distance estimates are shown in Table 1. Using magnetic resonance imaging, the traveled path length for cfPWV was

measured as the arterial length from the ascending aorta to the measurement point at the FA minus the length from the ascending aorta to the measurement point at the CA.<sup>5</sup> In that study with adult Europeans, 80% of the full carotid-femoral (CA-FA) distance appeared the best estimate. The full CA-FA distance overestimates the traveled path length and cfPWV by 25%, while the subtracted distance using the suprasternal notch (SSN; SSN-to-FA minus SSN-to-CA) underestimates the traveled path length by about 10%. This lack of standardization makes it impossible to compare cfPWV data from studies using different distance definitions, to compare cfPWV data with stiffness at other vascular territories, to correctly interpret data in clinical practice or to use a single cutoff value. Indeed, a cutoff value of 10 m/s using the 80% CA-FA distance method is equivalent to 12.5 m/s when using the full CA-FA distance as advised in the Complior manual and is equivalent to 8.94 m/s when using the SSN-subtracted distance as advised in the Sphygmocor manual.

In the present issue of this Journal, Sugawara *et al.*<sup>6</sup> present the results of a similar magnetic resonance imaging study and found the 80% CA-FA distance also being the best estimate of the effective path length in Japanese adults. In addition, a similar underestimation of 9% was found for the SSN-subtracted distance. After applying a conversion factor of 1.1, the SSN-subtracted distance correlated very well with the 80% CA-FA distance. The study by Sugawara *et al.* supports the consensus document of the Artery Society, the ESH Working Group on Vascular Structure and Function and the European Network for Noninvasive Investigation of Large Arteries to promote 80% of the full CA-FA distance as the standard method for cfPWV measurement.<sup>7</sup>

The 2015 AHA recommendations for vascular research on arterial stiffness also recommend the use of the 80% CA-FA distance, but at the same time also promote the use of the SSN-subtracted distance. Authors find this recommendation quite strange, as by recommending 2 different methods, standardization is lost. It was argued that cfPWV using the SSN-subtracted distance correlates very

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**Table 1.** Comparison of MRI measured path length with different tape measure distances

	Distance mean (SD) (cm)	Tape measure minus reference distance (cm) <sup>a</sup>	Tape measure deviation from reference distance (%) <sup>b</sup>
(AA-FA)-(AA-CA)	50.7 (4.2)		
Reference distance <sup>c</sup>			
(CA-FA)-(SN-CA)	48.3 (4.1)	-2.35 (3.8)	-4.73
(CA-FA)-(SSN-CA)	53.0 (4.1)	2.32 (3.8)	+4.54
(SN-FA)-(SN-CA)	35.9 (4.3)	-14.77 (3.9)	-29.19
(SSN-FA)-(SSN-CA)	45.5 (4.5)	-5.11 (3.5)	-10.26
(SSN-UMB) + (UMB-FA)	57.7 (4.5)	7.15 (4.0)	+13.81
(CA-FA)	63.6 (4.4)	12.99 (4.2)	+25.44
[(SSN-UMB) + (UMB-FA)]-(SN-CA)	42.3 (4.7)	-8.18 (4.1)	-16.57
[(SSN-UMB) + (UMB-FA)]-(SSN-CA)	47.0 (4.7)	-3.51 (4.1)	-7.30
(CA-FA) × 0.8	50.9 (3.5)	0.26 (3.8)	+0.39
Body height/4 + 7.28	50.2 (2.3)	-0.50 (3.9)	-0.99
Body height × 0.29	49.8 (2.6)	-0.90 (4.0)	-1.78

Abbreviations: AA, ascending aorta; CA, carotid artery; FA, femoral artery; MRI, magnetic resonance imaging; SN, sternal notch; SSN, suprasternal notch; UMB, umbilicus.

<sup>a</sup>Tape measure: the body surface distance measured by tape measure.

<sup>b</sup>Deviation is calculated as (mean tape measure distance)/(mean reference distance) × 100.

<sup>c</sup>Reference distance is the traveled path length measured by MRI.

Adapted from the studies of Huybrechts *et al.* and Van Bortel *et al.*<sup>5,7</sup>

well with true aortic PWV (from aortic valve to aortic bifurcation) measured invasively.<sup>4</sup> However, the pathway of cfPWV substantially differs from the true aortic pathway: cfPWV also contains the more muscular (stiffer) iliac arteries and lacks the highly distensible (less stiff) ascending aorta and part of the aortic arch up to the branching off of the brachiocephalic artery. This also explains why true aortic PWV is lower than cfPWV. Although it might be hypothesized that true aortic PWV may have better predictive value than cfPWV, these epidemiologic data are lacking. In addition, true aortic stiffness can only be measured invasively and is therefore not suitable for use in daily clinical practice. Because of these arguments and because SSN-subtracted distance requires 2 distance measurements which can increase the error of the measurement, it is the authors' position that the SSN-subtracted distance should not be recommended as alternative distance method for cfPWV assessment.

A possible source of error in the calculation of cfPWV arises from the fact that from the branching off of the brachiocephalic artery, the pulse wave travels in opposite directions: up to the measurement point at the CA and down to the measurement point at the FA. Upon arrival of the pulse wave at the CA, it also traveled further down in the descending aorta. By subtracting these 2 pathways, both the studies by Huybrechts *et al.*<sup>5</sup> and Sugawara *et al.*<sup>6</sup> assume an identical PWV in the brachiocephalic-to-CA and aortic arch-to-descending thoracic aorta segments, which may not be the case as discussed earlier.<sup>8</sup> The potential error can be estimated using published data: assuming (i) an average length of the brachiocephalic-to-CA of 11.7 cm;<sup>5</sup> (ii) that PWV in the brachiocephalic-to-CA

segment equals CA PWV (6.50 m/s in normotensives, 7.48 m/s in hypertensives);<sup>9</sup> and (iii) PWV in the aortic-arch-to-descending-aorta segment equals PWV of the aortic arch close to the branching off of the brachiocephalic artery (4.88 m/s and 6.70 m/s, respectively).<sup>10</sup> When using the 80% CA-FA distance to calculate cfPWV, these assumptions lead to an underestimation of cfPWV of 5.0% in normotensives, and of 1.4% in hypertensives. With the same assumptions, use of the SSN-subtracted distance would underestimate cfPWV by 15.1% and 11.9%, respectively. The error, however, is likely to be much less as arterial stiffness presumably increases gradually, with the average stiffness of the brachiocephalic-to-CA being lower than CA stiffness and the aortic-arch-to-descending-aorta stiffness being higher than the stiffness of the aortic arch near the brachiocephalic branching.

Measurements in the magnetic resonance imaging study by Huybrechts *et al.* were done at the right body side. Bossuyt *et al.* found the traveled path length in the same subjects at the left side 1 cm shorter than at the right body side.<sup>11</sup> The consensus document advised to perform measurements preferentially at the right body side.<sup>7</sup> Alternatively, the standard distance at the left side can be reduced by 1 cm. This small left-right difference of about 2%, which might not be clinically relevant, has also been found in another study in Europeans.<sup>12</sup> However, Sugawara did not find any left-right difference in the Japanese population.<sup>13</sup>

Finally, to avoid much larger inaccuracies than those mentioned above, it should be underlined that recommendations for user procedures as described earlier in guidelines like the consensus document<sup>7</sup> should be followed.

# EIGHTY PERCENT OF THE FULL CA-FA DISTANCE SHOULD BE USED AS STANDARD DISTANCE TO CALCULATE STANDARD cfPWV IN DAILY CLINICAL PRACTICE

The available data, in Europeans and Japanese, indicate that the effective path length for calculation of cfPWV is best estimated as 80% of the full CA-FA distance. For that standard, a consensus was reached for a cutoff value of 10 m/s, which represents about 4% of risk for a first major cardiovascular event in the next 8 years in the Framingham study.<sup>7,14</sup> In addition, reference values have been published for cfPWV based on the 80% CA-FA distance.<sup>15</sup> These reference values show mean, median, and percentiles for different age and blood pressure categories. The availability of percentiles opens opportunities to investigate whether the trend in patient's percentiles is more predictive than a general cutoff value. To interpret these cfPWV data or apply the cutoff value, cfPWV should first be converted to the standard cfPWV. This can be done using Table 1 or by using the calculator.

## A CALCULATOR TO CONVERT ARTERIAL STIFFNESS DATA AND TO PROVIDE PATIENT'S PERCENTILE

To promote the use of arterial stiffness in clinical practice and to facilitate further research in arterial stiffness, a web-based calculator has been developed which can be used free of charge (<http://bit.do/referencevalues>).<sup>16</sup> The application calculates cfPWV and local carotid and femoral stiffness. In addition, the calculated stiffness value is compared to the appropriate reference values database<sup>14,17,18</sup> and the patient's stiffness percentile is given. cfPWV is calculated for the distance used and for the standard distance. The calculator can also convert a measured cfPWV to the standard cfPWV based on the 80% CA-FA distance. For local stiffness measurements, the calculator corrects for the echotracking device used, the distance of the measurement point proximal to the bifurcation (flow divider) and it converts distensibility into PWV using the Bramwell–Hill equation. Authors invite readers to use the calculator and to send suggestions for further improvement to authors.

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## DISCLOSURE

The authors declared no conflict of interest.

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