Carotid-femoral pulse wave velocity assessment using novel cuff-based techniques: comparison with tonometric measurement

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Background: Carotid-femoral pulse wave velocity, a predictor of cardiovascular outcome, is conventionally measured using a tonometer sequentially placed upon the carotid and femoral arteries, gated using an electrocardiogram. Leg cuff detection of the femoral pulse removes the need for signal gating, reduces the time required for a single measurement, but gives different pulse wave velocity values to tonometric analysis. A novel algorithm to correct for the transit time and distance related to the additional femoral segment was applied to the cuff-based approach in this study.

Method: Eighty-eight individuals were recruited across four centres and carotid-femoral pulse wave velocity measured in triplicate using two operators with both a tonometer-based device and a device using an inflated thigh cuff with and without the use of the novel algorithm. Comparison was made by Bland–Altman and regression analysis.

Results: The unadjusted cuff-based approach gave lower pulse wave velocity values than the tonometer-based approach (6.11 ± 1.27 and 7.02 ± 1.88 m/s, P < 0.001). With application of the algorithm, the cuff-based device gave similar pulse wave velocity values (7.04 ± 1.72 m/s) as the tonometer-based approach (P = 0.86). Analysis of covariance with age showed a difference between the tonometer and cuff-based methods (P < 0.001), with a dependence upon age (P = 0.004). The adjusted cuff-based method gave similar results to the tonometer-based method (P = 0.94), with no dependence upon age (P = 0.46).

Conclusion: This study provided validation of a cuff-based assessment of carotid-femoral pulse wave velocity against the universally accepted tonometric method. Adjusting the cuff-based method for the additional femoral segment measured gives results comparable to the tonometer-based method, for which the majority of population data exist to date.

Keywords: aortic stiffness, arterial compliance, device validation, hemodynamics, measurement, pulse wave velocity

Abbreviation: cfPWV, carotid-femoral pulse wave velocity

INTRODUCTION

Carotid-femoral pulse wave velocity (cfPWV) is increasingly used in population studies [1–3] and is recommended by the European Society of Hypertension for use in the management of hypertension [4]. As a result, there is a demand for devices that accurately and easily measure cfPWV. The majority of cfPWV population data have been collected using sequential recording of the carotid and femoral pulse using applanation tonometry [2,5]. The two waveforms are synchronized using a simultaneously recorded ECG. This technique is widely used but does require a certain degree of operator skill to accurately acquire the pulses. Applanation tonometry also takes some time to acquire the two signals sequentially and is intrusive in that it requires palpation of the femoral pulse near the groin.

The use of an inflated cuff around the upper leg to acquire the femoral pulse permits hands free, minimally intrusive, user-independent acquisition of the femoral pulse, simultaneously with carotid tonometer applanation. Simultaneous, in place of sequential measurement of the pulses, along with elimination of the use of ECG leads, is estimated to reduce the time of measurement by slightly more than 50%. However, previous results have shown that leg cuff based measurement of cfPWV underestimates PWV compared with the tonometer-based technique, especially at higher values of cfPWV [6]. This may be due to the inclusion of a longer femoral segment of artery in the cuff-based approach (Fig. 1), the cuff being lower down the leg than the inguinal site of tonometric acquisition of the
femoral pulse. This study aimed to investigate the cuff-based technique of cfPWV measurement and applied an algorithm to adjust for the additional femoral segment measured. Both techniques were compared with the tonometer-based technique. Results of this study constitute a validation of the novel SphygmoCor XCEL (AtCor Medical, Sydney, New South Wales, Australia) cuff-based device that employs such an algorithm to adjust for the femoral segment measured.

MATERIALS AND METHODS

Participants
The method for comparison of cfPWV techniques adhered to the ARTERY Society guidelines [7]. Individuals recruited for the study were equally distributed across three age ranges (18–30, 30–60 and greater than 60 years) with at least 25 individuals in each range, each containing a minimum of 40% men and 40% women. Participants were excluded if they were pacemaker dependent, not in sinus rhythm, pregnant, had a BMI greater than 30 kg/m² or had known carotid or femoral artery stenosis. Recruitment and measurement was conducted across four centres: Macquarie University, Sydney, Australia; University of Peru-gia, Perugia, Italy; Hôpital Européen Georges Pompidou, Université Paris Descartes, Paris, France; Addenbrooke’s Hospital, Cambridge University, Cambridge, UK. Ethics approval was received from the ethics bodies of the respective institutions and the study was conducted with the understanding and the consent of each participant.

Carotid-femoral pulse wave velocity measurement
The standard for comparison was taken as cfPWV measured by the conventional or ‘classic’ SphygmoCor device (software version 9; AtCor Medical), which allows sequential recording of the pulse at the carotid and femoral site by applanation tonometry, gating these two signals using the QRS complex of a simultaneously recorded ECG. The SphygmoCor XCEL device (software version 1; AtCor Medical) records the cfPWV between the diastolic foot of the carotid waveform, recorded by tonometric applanation, and the diastolic foot of the simultaneously recorded femoral pulse, detected using the volume displacement waveform measured in a cuff placed around the upper thigh, inflated to subdiastolic pressure.

The diastolic foot of the femoral and carotid waveforms in both the XCEL and the tonometer-based PWV assessment devices was defined as the point of intersection of lines of fit during late diastole and early systole, often referred to as the intersecting tangents method. The transit time (t) of the pulse was measured as the time between the diastolic feet of the carotid and femoral pulse for the cuff-based device (t_C) and the tonometer-based device (t_T).

Arterial path length (Fig. 1) for the cuff-based assessment of cfPWV (PWV_C) was estimated by measuring the linear distance from the suprasternal notch to the top of the cuff at the centre line of the leg, approximately at the location of the femoral artery (d_{sfC}), and subtracting the distance from the suprasternal notch to the location wherein the carotid pulse could be palpated (d_{sc}). Distance for the tonometer-only based assessment of cfPWV (PWV_T) was measured as the linear distance from the suprasternal notch to the site where the femoral pulse could be palpated and measured with the tonometer (d_{sfT}), minus the linear distance from the suprasternal notch to the site where the carotid pulse could be palpated (d_{sc}). cfPWV was calculated as the measured distance divided by the transit time (Eqs. 1–2).

\[
PWV_C = \frac{d_{sfC} - d_{sc}}{t_C} \tag{1}
\]

\[
PWV_T = \frac{d_{sfT} - d_{sc}}{t_T} \tag{2}
\]

An algorithm, built into the SphygmoCor XCEL device, corrects for two possible sources of difference in cfPWV measurement from the tonometer-based technique. First, the transit time was reduced by a constant (k_T) associated with the delay in the transmission and registration of the volume displacement pulse from the cuff to the pressure sensor and the recording circuitry in the device. The value of k_T was ascertained by AtCor Medical. Second, the transit time and distance were reduced in an attempt to subtract the segment of artery between the femoral site wherein a tonometer is usually used and the location of the leg cuff. The distance was reduced by an operator-measured distance from the site wherein the femoral pulse can be palpated to the top of the cuff (d_{fTfC}, Fig. 1). The transit time was reduced by a constant factor (k_2) multiplied by this femoral distance. The constant factor, k_2, was derived from an average femoral transit time per unit distance measured in a separate group of 15 individuals (six women, 34 ± 10 years of age, 24–64 years old). The adjusted cfPWV (PWV_{CA}) was calculated according to Eq. (3).

\[
PWV_{CA} = \frac{d_{sfC} - d_{sc} - d_{fTfC}}{t_C - k_T - k_2 \cdot d_{fTfC}} \tag{3}
\]
Cuff-based pulse wave velocity measurement

Statistical analysis was conducted using the statistical package, R (Version 2.15.0) [9]. All results are given as mean ± SD, unless otherwise stated.

RESULTS

Ninety-eight individuals were recruited across the four centres (29 from Sydney, 41 from Perugia, 22 from Paris, six from Cambridge). As required by the ARTERY Society guidelines, individuals with a BMI greater than 30 kg/m² were excluded (n = 10). The remaining 88 individuals (45 male) had a mean age of 46 ± 20 years, were evenly distributed amongst the three designated age groups and had an even balance of men and women in each group (Table 1).

The mean transit time for the cuff-based approach was 99 ± 22 ms and for the tonometer-based approach was 67 ± 14 ms, a mean difference of 32 ± 12 ms (P < 0.001). The mean transit time for the adjusted cuff-based approach was 67 ± 13 ms, the mean difference from the tonometer-based approach being 1 ± 6 ms (P = 0.10). The application of the adjustment for the femoral segment to the cuff-based approach increased the correlation to the tonometer-based system (cuff-based approach R = 0.87, cuff-based approach-adjusted R = 0.92, Fig. 2a,b, Table 2), with a decrease in slope from 1.28 ± 0.08 to 0.82 ± 0.04, and intercept from 13 ± 5 to 11 ± 3 ms, the difference in these regressions being significant (ANCOVA, P < 0.001). There was also an interaction with increasing values of transit time (P < 0.001), indicating a divergence in the two techniques with greater values of transit time.

The mean cfPWV for the cuff-based approach was 6.11 ± 1.27 m/s and for the tonometer-based approach was 7.02 ± 1.88 m/s, the mean difference being 0.91 ± 0.84 m/s (P < 0.001). According to the ARTERY Society guidelines, the accuracy of the adjusted cuff-based approach was ‘acceptable’ (mean difference less than 1.0 m/s, SD of difference less than 1.5 m/s). After applying the adjustment for the femoral segment to the cuff-based approach, the mean cfPWV was 7.04 ± 1.72 m/s, with an average difference from the tonometer-based approach of 0.01 ± 0.71 m/s (P = 0.86). According to the ARTERY Society guidelines, the accuracy of the adjusted cuff-based approach was ‘excellent’ (mean difference less than 0.5 m/s, SD of difference less than 0.8 m/s). The application of the adjustment for the femoral segment to the cuff-based

TABLE 1. Individual demographics across the three age ranges

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All</th>
<th>18–30 years</th>
<th>30–60 years</th>
<th>&gt;60 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>88</td>
<td>31</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46 ± 20</td>
<td>26 ± 2</td>
<td>44 ± 10</td>
<td>72 ± 7</td>
</tr>
<tr>
<td>Age (min/max, years)</td>
<td>22/83</td>
<td>22/29</td>
<td>30/60</td>
<td>61/83</td>
</tr>
<tr>
<td>Male</td>
<td>45 (51%)</td>
<td>14 (45%)</td>
<td>18 (58%)</td>
<td>13 (50%)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68 ± 12</td>
<td>67 ± 12</td>
<td>68 ± 12</td>
<td>69 ± 10</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23 ± 3</td>
<td>23 ± 2</td>
<td>23 ± 3</td>
<td>25 ± 3</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>126 ± 19</td>
<td>119 ± 12</td>
<td>126 ± 21</td>
<td>135 ± 19</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73 ± 10</td>
<td>70 ± 9</td>
<td>76 ± 12</td>
<td>73 ± 8</td>
</tr>
</tbody>
</table>

SBP and DBP were measured using an oscillometric brachial cuff device with individuals in the supine position.
FIGURE 2 Comparison of cuff-based results (gray) and cuff-based results adjusted for the additional femoral segment (black) compared with the tonometer-based method for both transit time (left panels) and cfPWV (right panels). Linear regression statistics are presented in Table 2. Fitted second-order polynomials have been applied by least squares regression to capture the movement of the cfPWV measurement away from linearity with increasing cfPWV. \( PWV_C = -0.03 \times PWV_T^2 + 1.11 \times PWV_T - 0.07 \text{m/s} \) (\( R = 0.94, P < 0.001 \)); \( PWV_{CA} = -0.04 \times PWV_T^2 + 1.48 \times PWV_T - 1.26 \text{m/s} \) (\( R = 0.93, P < 0.001 \)).

| TABLE 2. Results for fitting of a linear relationship by least squares regression to each of the datasets displayed in transit time (t) and carotid-femoral pulse wave velocity (Fig. 2) data for the cuff-based (C) and the adjusted cuff-based approach (CA), including regression for the between-device differences (\( \Delta t, \Delta PWV \)) |
|---|---|---|---|---|---|---|
| Slope | Intercept | Intercept 95% confidence interval | \( R \) | RMSE | \( P \) |
| Tonometer-based transit time against: | | | | | |
| \( t_c \) | 1.28 ± 0.08 | 13 ± 5 | 3–23 | 0.87 | 10 | < 0.001 |
| \( t_{CA} \) | 0.82 ± 0.04 | 11 ± 3 | 5–17 | 0.92 | 5 | < 0.001 |
| Tonometer-based cfPWV against: | | | | | |
| \( PWV_C \) | 0.63 ± 0.03 | 1.70 ± 0.19 | 1.33–2.07 | 0.93 | 0.46 | < 0.001 |
| \( PWV_{CA} \) | 0.85 ± 0.04 | 1.08 ± 0.27 | –0.45–0.61 | 0.93 | 0.64 | < 0.001 |
| Device mean transit time against: | | | | | |
| \( \Delta t_c \) | 0.40 ± 0.05 | –1 ± 5 | –11–9 | 0.62 | 9 | < 0.001 |
| \( \Delta t_{CA} \) | –0.12 ± 0.04 | 7 ± 3 | 1–13 | –0.27 | 6 | 0.01 |
| Device mean PWV against: | | | | | |
| \( \Delta PWV_C \) | –0.40 ± 0.04 | 1.72 ± 0.27 | 1.19–2.25 | –0.74 | 0.56 | < 0.001 |
| \( \Delta PWV_{CA} \) | –0.09 ± 0.04 | 0.66 ± 0.30 | 0.07–1.25 | –0.23 | 0.69 | 0.03 |

Data are presented as mean ± standard error with intercept, intercept confidence intervals and RMSE values given in ms for transit time measurements, and m/s for cfPWV measurements. The sample 95% confidence interval was calculated as the mean ±1.96 times the standard error. cfPWV, carotid-femoral pulse wave velocity; PWV, pulse wave velocity; RMSE, root mean square error.
approach did not alter the correlation with the tonometer-based system \((R = 0.93)\) in both cases, Fig. 2c,d, Table 2). However, the slope of regression moved closer to linearity \((0.65 \pm 0.03–0.85 \pm 0.04)\) coupled with a decrease in the intercept \((1.70 \pm 0.19–1.08 \pm 0.27 \text{ m/s})\), the difference in these regressions being significant \((\text{ANCOVA, } P < 0.001)\). There was also an interaction with increasing values of cfPWV \((P < 0.001)\), indicating a divergence in the two techniques with greater values of cfPWV.

There was a significant effect of age on PWV \((P < 0.001)\), a PWV method related effect \((P < 0.001)\), and an interaction effect between age and the method of PWV analysis chosen \((P = 0.01, \text{ Fig. 3})\). This was evident for the cuff-based approach compared with the tonometer-based approach for both the method \((P < 0.001)\), and the method interaction with age \((P = 0.004)\), when compared with the tonometer-based approach. However, this was not evident for the adjusted cuff-based approach for either the method \((P = 0.94)\) or the method interaction with age \((P = 0.46)\) when compared with the tonometer-based approach. The age/cfPWV relationship was well fitted by linear regression (Fig. 3), similar to other studies of similar size \([6,10]\) but not showing the second-order relationship seen in larger populations studies \([2]\).

**DISCUSSION**

This study aimed to validate a method of adjustment of cuff-based cfPWV assessment that accounts for the effect of the additional femoral segment measured. Tonometer-based cfPWV was chosen as the standard for comparison, as the majority of population data to date \([1–3]\) have been collected using a tonometer-based approach, and equivalence to these data is a necessary requirement in order for cuff-based cfPWV measurements to be meaningful and useful in risk assessment. The correlation between cfPWV, in general, and aortic PWV was not addressed in this study, but has been quantified in purpose-designed studies employing phase-contrast MRI \([10]\) or invasive aortic pressure measurement \([11]\). As advised by the ARTERY Society guidelines \([7]\), tonometer-based assessment of cfPWV was chosen as the standard of reference, as it is this parameter, not aortic stiffness per se, that has been used in large population studies and in the clinic.

Using a volume displacement cuff around the thigh for recording of the femoral pulse resulted in an underestimation of cfPWV compared with the use of a tonometer to detect the femoral pulse, especially at higher values of cfPWV (Fig. 2c,d, Table 2). This underestimation, also found in other cuff-based cfPWV measurement systems \([6]\), could originate from either a difference in the algorithm that detects the waveform foot, critical differences in waveform shape or transmission due to the use of a cuff instead of a tonometer, or anatomical differences due to the change in site at which the femoral pulse is detected.

In a validation study conducted by Millasseau et al. \([12]\) investigating the Complior device, the foot detection algorithm was shown to be the cause of a comparative bias in the measurement of cfPWV. However, the current study used the same algorithm for both the tonometer-based and cuff-based cfPWV assessment, eliminating this as a source of the difference in cfPWV.

The waveform shape of the pulse measured by the cuff is significantly different from the waveform measured using the tonometer. This is in part not only due to the measurement of the pulse at a different site but also due to the inherent damping characteristics of the volume displacement method of pulse acquisition. However, the late diastolic and early systolic components of the waveform are not vastly different between the two techniques (Fig. 4) and did not drastically alter the detected position of the foot.

The adjustment technique used a constant \((k_2)\) femoral PWV, derived from 15 individuals, of the order of existing published femoral PWV values \([13]\). This adjustment technique assumes the same femoral PWV for all individuals, independent of sex, age and blood pressure. A previous

![Figure 3](https://example.com/figure3.png)

**FIGURE 3** Carotid-femoral pulse wave velocity, as measured by the three methods, plotted against age. ANCOVA confirmed that the cuff-based method was offset from the tonometer-based method \((P < 0.001)\) with an interaction with age \((P = 0.004)\), whereas the adjusted cuff-based method showed a similar result to the tonometer-based method \((P = 0.94)\) with no interaction with age \((P = 0.46)\). Regression and ANCOVA was conducted on the individual data, not age-averaged points as plotted.

![Figure 4](https://example.com/figure4.png)

**FIGURE 4** The foot of the femoral pulse as recorded by volume displacement with a thigh cuff (solid line) and by applanation tonometry (dashed line, time shifted to align the diastolic feet of the waves), highlighting the similarity in the shape of the waveform foot. Waveforms shown are from individuals in each of the three nominal age groups: (a) 79-year-old man, BMI 20 kg/m², cfPWV 10.2 m/s; (b) a 45-year-old man, BMI 17 kg/m², cfPWV 7.6 m/s; (c) a 26-year-old woman, BMI 25 kg/m², cfPWV 5.2 m/s.

Cuff-based pulse wave velocity measurement

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study showed that PWV in the leg changes little with age, on average increasing 0.06 m/s per year [13], the same trend being confirmed in other peripheral arterial beds such as the arm [13,14]. However, it is known that there are ethnic and disease-related differences in the arteries of the leg [15]. A population-based look-up table, or measurement of individual femoral PWV, could improve correlation of the adjusted cuff-based methods to tonometric results and may be important for results in different ethnic groups or disease subtypes. Femoral PWV is also dependent upon the distending pressure, and this aspect too could be individualized.

This is the first study to use the only guidelines to date for the validation of devices that measure cPFV. The ARTERY Society guidelines [7] recommend the use of simultaneous tonometric recording of carotid and femoral pulses as the standard for comparison. However, in this study, the secondary reference cited by the guidelines, tonometry using ECG gating, was used. The secondary reference was used, as it enabled the study to be carried out in a multicentre fashion, all centres holding the same cPFV tonometer device (SphygmoCor; AtCor Medical). Individuals with a BMI greater than 30 kg/m² were excluded from the analysis, as recommended by the guidelines. The inclusion of these 10 individuals did not significantly alter any results (analysis not shown). However, further studies are required to ascertain whether the same results hold true within such subpopulations.

The accuracy of measurement of arterial distances has not been addressed in this study, as it has been in other studies [11,16–18]. However, distances for both techniques were measured in the same manner to avoid this confounding factor. Inflation of the thigh cuff above the diastolic pressure alters the pressure waveform during the diastolic period by occlusion of the artery when the cuff pressure exceeds the instantaneous arterial pressure. So as to avoid the diastolic portion of the wave being altered in some individuals, as would be the case if a constant cuff pressure was applied to all individuals, the cuff pressure was individualized below the measured brachial diastolic pressure. This assumed that brachial and femoral diastolic pressures were approximately equal.

Although there is no statistical difference between cPFV measured by tonometry and the adjusted cuff-based method, the relationship between the two devices has a slope less than unity. On average, the value of cuff-based cPFV is lower than tonometry-based assessment for cPFV greater than 7.2 m/s, and greater at values less than 7.2 m/s. For example, an individual with a tonometry-based cPFV assessment of 12 m/s will have an average-adjusted cuff-based technique cPFV reading of 11.28 m/s. Although the adjusted cuff-based results are within the ARTERY Society guideline 'excellent' category, the impact of this difference in an individual measurement is dependent upon treatment guidelines, and upon whether changes to patient treatment are implemented using this value.

The effect in population-based studies is highlighted in Fig. 3. Without any adjustment, the cuff-based approach underestimated cPFV compared with the conventional, tonometer-based approach, and this effect was statistically greater at higher cPFV and thus also with greater age. However, applying an adjustment correcting for the additional femoral segment gives results similar to that obtained using the tonometric-based approach.

cPFV is accepted as a powerful predictor of cardiovascular disease and has traditionally been measured using tonometry. However, the sequential measurement used in tonometric measurement and the intrusive nature of taking the femoral pulse limit the use in clinical settings. Use of cuff-based acquisition of the femoral pulse permits assessment of cPFV in a shorter time with less intrusion. However, the values are different than those when assessed using the tonometric approach. Adjustment of the cuff-based measured cPFV for the additional femoral segment measured gives results similar to those of the tonometric approach. Therefore, the cuff-based approach, when adjusted, provides a practical arterial stiffness assessment tool for clinical use and screening, with cPFV values able to be compared with existing population data.

ACKNOWLEDGEMENTS

None.

Conflicts of interest

All sites, other than Cambridge University, received funding from AtCor Medical, Australia, for the collection of cPFV data using the SphygmoCor 'classic' and SphygmoCor XCEL devices. No restrictions were placed on the publication of results. The values of the constants used in the algorithm for adjustment of cPFV could not be published, as they form part of an integrated proprietary algorithm that is the subject of a patent pending (AtCor Medical). A.Q. is an employee of AtCor Medical, Australia, and a Visiting Fellow at Macquarie University.

REFERENCES


**Reviewers’ Summary Evaluations**

**Reviewer 1**
This is a clear and straightforward methodological study on the – successful – validation of the new version of the Sphygmocor system for carotid-femoral pulse wave velocity measurements (using a tonometer on the carotid and cuff for the femoral signal). The study is conducted in compliance with guidelines that were provided by the Artery Society and is exemplary for this type of studies. The only – albeit minor – limitation is the fact that not all methodological details (values of some parameters) can be disclosed for commercial reasons.

**Reviewer 2**
The strengths of this paper relate to the excellent design and methodology to examine tonometer-based versus thigh cuff-based methods for determining carotid-femoral pulse wave velocity. The authors convincingly validate the adjustment algorithm for cuff-based methods against the universally accepted tonometric methods. There are no apparent weaknesses.