Determination of Aortic Pulse Wave Velocity From Waveform Decomposition of the Central Aortic Pressure Pulse

Ahmed Qasem, Alberto Avolio

Abstract—Aortic pulse wave velocity (PWV), calculated from pulse transit time (PTT) using 2 separate pulse recordings over a known distance, is a significant biomarker of cardiovascular risk. This study evaluates a novel method of determining PTT from waveform decomposition of central aortic pressure using a single pulse measurement. Aortic pressure was estimated from a transformed radial pulse and decomposed into forward and backward waves using a triangular flow wave. Pulse transit time was determined from cross-correlation of forward and backward waves. Pulse transit time, representing twice the PTT between 2 specific sites, was compared with independent measurements of carotid-femoral PTT in a cohort of 46 subjects (23 females; age 57±14 years). Linear regression between measured PTT (y; milliseconds) and calculated PTT (x; milliseconds) was y=1.05x−2.1 (r=0.67; P<0.001). This model was tested in a separate group of 44 subjects (21 females; age 55±14 years) by comparing measured carotid-femoral PWV (y; meters per second) and PWV calculated using the estimated value of PTT (eTR/2) and carotid femoral distance (x; meters per second; y=1.21x−2.5; r=0.82; P<0.001). Findings indicate that the time lag between the forward and backward waves obtained from the decomposition of aortic pressure wave can be used to determine PWV along the aortic trunk and shows good agreement with carotid-femoral PWV. This technique can be used as a noninvasive and nonintrusive method for measurement of aortic PWV using a single pressure recording. (Hypertension. 2008;51:188-195.)

Key Words: pulse ■ aorta ■ arterial pressure ■ digital signal processing ■ blood flow

Pulse wave velocity (PWV) has become a well-accepted surrogate measure of arterial stiffness1–5 and has been shown to be a significant predictor of cardiovascular risk in diseased2,4 and older healthy populations.6 Aortic PWV is determined noninvasively by measuring the pulse transit time (PTT) over a known distance of the aortic trunk. Although in some studies the arterial pulse has been detected using Doppler ultrasound probes in the aortic arch or subclavian artery and the femoral artery,7,8 the general convention is to register the pressure pulse using some form of mechanical transducer.9 The carotid and femoral pulses are either recorded simultaneously (as in the Complior device, Artech Medical10,11) or recorded sequentially using a single probe and the carotid-femoral PTT determined with reference to the R wave of the ECG signal (as in the SphygmoCor device, AtCor Medical11–13). Both methods have been shown to be comparable in detecting similar relative changes in PTT with interventions.11 Although these methods are useful in research and clinical laboratories, there is increasing interest in attempts at simplifying the procedure for routine clinical measurements in terms of eliminating the necessary intrusion of recording the femoral pulse or when a reliable femoral recording cannot be readily obtained, as can often occur in obese subjects or those with excessive abdominal adipose tissue. Attempts at providing a less intrusive methodology have resulted in determination of parameters related to PTT from recording of a single pulse trace, such as the use of the second derivative of the finger photoplethysmogram.14 Although of limited use, this method has not shown a strong association with PWV.14,15

In this present study, we propose a novel noninvasive and less intrusive method to assess arterial stiffness from a single peripheral pulse waveform. This method determines carotid-to-femoral PTT from the radial pressure waveform, which is transformed to derive the central aortic pressure waveform via a validated transfer function.12,16–18 The central aortic pressure waveform is decomposed into forward and reflected waves using an uncalibrated triangular aortic flow waveform, as shown in a recent study validating the proof of concept.19 PTT is then estimated from the time difference between the derived forward and reflected waves after a signal processing procedure based on waveform constraints criteria. Calculated PTT was evaluated against transit time measurements determined from independent recordings of carotid and femoral...
pulses in 2 groups of subjects. A regression model relating measured carotid-femoral transit time and estimated time from wave decomposition was obtained in 1 group and then tested with independent measurements in the other group.

**Materials and Methods**

**Analytical Treatment**

The measured time-varying pressure wave, \( P_m(t) \), can be expressed as a sum of forward \( P_f(t) \) and backward \( P_b(t) \) waves:

\[
P_m(t) = P_f(t) + P_b(t)
\]

Because reflected waves increase pressure but decrease flow, similarly, measured flow \( Q_m(t) \) is the algebraic sum of forward \( Q_f(t) \) and backward \( Q_b(t) \) flow:

\[
Q_m(t) = Q_f(t) - Q_b(t)
\]

From transmission line analysis, \( P_f(t) \) and \( P_b(t) \) can be obtained from \( P_m(t) \) and \( Q_m(t) \) and characteristic impedance, \( Z_c \), as follows:

\[
P_f(t) = 0.5[P_m(t) + Z_cQ_m(t)]
\]

\[
P_b(t) = 0.5[P_m(t) - Z_cQ_m(t)]
\]

Whereas \( P_m(t) \) is obtained from the transformed radial pressure wave using a transfer function for the brachial artery, the flow waveform, \( Q_m(t) \), is assumed to have a triangular shape, with the peak occurring at the time of the first systolic inflection (\( T_1 \)) and the base with a measured ejection duration (\( ED \)); Figure 1). Both \( T_1 \) and \( ED \) are obtained from the measured radial pulse and the derived aortic pressure wave. \( T_1 \) is obtained from the time index of the digital values of the vector containing the derivatives of the ascending aortic pressure wave. It is calculated from the first negative 0 crossing (ie, in the direction from positive to negative) of the first derivative. If a 0 crossing is not present before the peak of the pressure wave, \( T_1 \) is then determined from the positive (ie, direction of negative to positive) 0 crossing of the second derivative. In all of the data analyzed, this algorithm was able to determine a value for \( T_1 \) in all of the waves. The triangular approximation is consistent with the general aortic flow envelope obtained from Doppler ultrasound or electromagnetic flow measurements. Furthermore, the timing of peak flow corresponds with the time of early systolic inflection in the aortic pressure wave. Input impedance (\( Z_{in} \)) is calculated as a function of frequency from Fourier decomposition of \( P_m(t) \) and \( Q_m(t) \) shown in Figure 1, and \( Z_c \) is estimated from the average of the \( Z_{in} \) modulus between harmonics 4 and 7. Because \( Z_{in} \) is a ratio of pressure and flow quantities, the product \( Z_cQ_m(t) \) in equations 3 and 4 is always in units of pressure; hence, an absolute flow calibration is not required. Thus, a flow scale is assumed of 0 to 100 arbitrary units. Application of equations 3 and 4 results in calculated \( P_f(t) \) and \( P_b(t) \) as shown in Figure 2. \( P_f(t) \) and \( P_b(t) \) indicate the “initial” calculated forward and backward waves, respectively.

The pure triangular flow wave shape produces sharp inflections in the derived pressure waveforms (Figure 2). To preserve the relationship between measured and derived pressure waves, the following criteria were applied.

First, a constant value is maintained for the reflected wave between the start of ejection and peak flow such that there is no change in pressure value during this interval:

\[
\frac{d[P_b(t)]}{dt} = 0, \quad 0 \leq t \leq T_1
\]

Second, because the initial ventricular ejection causes the forward-going wave, there should be a decrease in the forward wave, whereas the flow is decelerating between peak flow and end of ejection:

\[
\frac{d[P_f(t)]}{dt} < 0, \quad T_1 < t \leq ED
\]

Third, the sum of both forward and backward waveforms should always be equal to the original measured waveform \( P_m(t) \). The above criteria (first and second parts) result in a \( P_f(t) \) and \( P_b(t) \) modified to \( P_f'(t) \) and \( P_b'(t) \) (Figure 3A).

\[
P_m(t) = P_f'(t) + P_b'(t) = P_f(t) + P_b'(t)
\]
A modified flow waveform, $Q'_{m}(t)$, was then calculated from $P_{m}(t)$ and $P\prime_{f}(t)$ as follows:

$$Q'_{m}(t) = \frac{[2 \cdot P\prime_{f}(t) - P_{m}(t)]}{Z_c}$$

The original $[Q_{m}(t)]$ and modified $[Q'_{m}(t)]$ flow waveforms are shown in Figure 3B. From the pressure recordings and analysis described above, TPT was obtained from the value of the maximum lag (TR2) determined from the cross-correlation\(^{29}\) of the modified waves $P'_{f}(t)$ and $P'_{b}(t)$ normalized to the same amplitude (Figure 4). TR2/2 was compared with the measured carotid-femoral transit time (CF-PTT). The normalization process was made so as to avoid inconsistencies because of different magnitudes of relative scales of the forward and backward waves. This procedure ensured that all of the pairs of waves were analyzed in an identical manner. Because of the algebraic relationship between flow and pressure components following equations 1 to 4, and because flow is 0 during diastole, the values of forward and backward waves during diastole are identical, as seen in Figure 2 and 3. The normalization procedure would have the effect of increasing the relative contribution of the rising part of the waves in early systole.

**Experimental Validation**

Measurements were performed on a cohort of 90 healthy volunteers divided into 2 groups (group 1: $n=46$; group 2: $n=44$; Table 1). Group 1 was used to determine the regression model for TR2 calculated from waveform decomposition and tested with independent measurements in group 2. Informed consent and institutional ethics approval were obtained for all of the subjects. All of the measurements were conducted in the supine position. The radial pulse wave was measured noninvasively using applanation tonometry and central pressure waveforms calculated using the pulse wave analysis mode in the SphygmoCor device. This device uses a general transfer function representing the upper limb large arteries and validated in conditions of steady state,\(^{12}\) Valsalva maneuver,\(^{16}\) and exercise.\(^{18}\) CF-PTT was measured using the PWV mode in SphygmoCor during the same session a short time apart (≈1 minute). Measurements on the same subject where heart rate varied >5 bpm were excluded so as to avoid any confounding effects of heart rate on PWV,\(^{30}\) as well as ensuring that the pressure pulse waveform did not change from the pulse wave analysis to the PWV measurement. All of the recordings were sampled at 128 Hz. Reproducibility for the CF-PTT in aortic PWV measurements using carotid and femoral
Tonometry was determined in previous studies and was found to be within 4%. For the calculated PTT using the methodology described in this present study, reproducibility was assessed in a subgroup of 39 subjects with repeated measures (3 to 4 measurements) and was found to be 3.3%.

The SphygmoCor PWV mode determines PTT by obtaining the wave foot-to-foot time delay between the CF-PTT using the R wave of the ECG signal as a reference. PWV is then calculated by using the superficial distance CF-DIST, where CF-DIST is the distance between the suprasternal notch and the femoral site minus the distance between the suprasternal notch and the carotid site (CF-PWV = CF-DIST/CF-PTT).

Results

The PTT calculated from the aortic waveform decomposition (TR2/2) was compared with the measured aortic PTT from the CF-PTT in group 1. From these measurements, a linear regression model was obtained between CF-PTT (y; milliseconds) and TR2/2 (x; milliseconds; Figure 5A) The regression equation (r = 0.67; P = 0.001) was as follows:

\[ y = 1.05x - 2.1 \]

The Bland-Altman plot (Figure 5B) showed a mean difference of -3.8 ms. This model was tested in group 2 by estimating the value of PTT from equation 9, where y (in milliseconds) is TR2/2, as obtained from waveform decomposition, and x (milliseconds) is the estimated PTT value (eTR2/2). This is shown in Figure 6A with the regression line of y = 1.32x - 22 (r = 0.80; P < 0.001). The Bland-Altman plot (Figure 6B) showed a mean difference of -3.1 ms. The measured value of PWV and that estimated from the model were compared by calculating the estimated CF-PWV by using the path length (CF-DIST) divided by eTR2/2. This is shown in Figure 7A with the regression equation between measured (CF-PWV; y; meters per second) and calculated PWV (CF-DIST/eTR2/2; x; meters per second) being y = 1.21x - 2.5 (r = 0.82; P < 0.001). The Bland-Altman plot (Figure 7B) showed a mean difference of 0.6 m/s.

The comparison for the calculated and measured transit times was made assuming a factor of 2 for the time delay (TR2) between the forward and backward wave and the aortic PTT between carotid and femoral arteries. This suggests a constant value for the effective distance between the effective reflecting sites. To test this assumption across the wide age range, the data for the whole cohort were divided into tertiles. Table 2 shows that, for the whole cohort, the mean value is very close to 2 (1.97 ± 0.31). A mild age dependency is also seen with the lower age tertile having a ratio lower than 2 and the higher tertile a ratio slightly higher than 2, and the difference between the first (Tert1) and third (Tert3) tertile being statistically significant (P < 0.05). To take into account this age dependency in the comparison of the measured and

**Table 1. Subjects Characteristics**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Total</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (females)</td>
<td>46 (23)</td>
<td>44 (20)</td>
<td>90 (43)</td>
<td>NS</td>
</tr>
<tr>
<td>Age, y</td>
<td>57 ± 14 (26 to 74)</td>
<td>55 ± 14 (29 to 74)</td>
<td>56 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>170 ± 10 (146 to 189)</td>
<td>169 ± 11 (150 to 195)</td>
<td>170 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>75 ± 14 (39 to 100)</td>
<td>74 ± 15 (42 to 102)</td>
<td>74 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68 ± 10 (41 to 87)</td>
<td>68 ± 10 (48 to 88)</td>
<td>68 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>SP, mm Hg</td>
<td>133 ± 14 (109 to 163)</td>
<td>126 ± 16 (89 to 171)</td>
<td>129 ± 16</td>
<td>0.03</td>
</tr>
<tr>
<td>DP, mm Hg</td>
<td>81 ± 7 (63 to 97)</td>
<td>77 ± 11 (58 to 111)</td>
<td>79 ± 9</td>
<td>0.04</td>
</tr>
<tr>
<td>MP, mm Hg</td>
<td>99 ± 9 (80 to 123)</td>
<td>94 ± 12 (69 to 129)</td>
<td>97 ± 11</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Values are mean ± SD or mean ± SD (range), unless otherwise specified. SP indicates systolic pressure; DP, diastolic pressure; MP, mean pressure; NS, not significant.

*P values are for differences between groups 1 and 2, P = 0.05.

![Figure 5. A, Scatter plot of the calculated PTT (TR2/2) vs measured carotid to femoral transit time (C-F PTT) with regression line in group 1. B, Bland Altman plot of TR2/2 vs C-F PTT in group 1. Solid line is the mean difference, and the dashed lines are ±2 SD of the difference.](http://hyper.ahajournals.org/DownloadedFrom/hyper.ahajournals.org)
calculated PTTs, the values were corrected for age using the values in Table 2. Figure 8 shows that correcting for age brings the slope closer to unity (1.09), improves the correlation \( r = 0.83 \), and reduces the mean difference close to 0 (0.06 m/s). There is also a reduction of overall bias as seen from the scatter of the differences (Figures 7B and 8B). In general, the differences are not large, and, so, to a first approximation, this suggests a reasonable justification for the use of a factor of 2 to compare the transit time estimated from a single pressure pulse (TR2) with independent measurements of aortic PTT from 2 separate sites.

**Discussion**

The recent studies described by Westerhof et al.\(^{19} \) and supported by an editorial communication by Mitchell\(^ {32} \) have demonstrated the proof of concept that parameters of wave reflection can be estimated from the measurement of a single pressure pulse and assuming a triangular flow pulse for ventricular ejection. They showed that wave reflection could be quantified by comparing amplitudes of forward and backward waves from wave separation of the measured pressure pulse. This present study extends this concept by estimating time delay between the forward and backward waves to obtain an effective measure of arterial PWV, a well-established surrogate measure of arterial stiffness.\(^ {1-6} \)

We have shown that, in addition to magnitude measures,\(^ {19} \) time delay estimates can provide a noninvasive and noninvasive estimate of PWV from a single peripheral pressure measurement.

In the method proposed in this study, the significance of T1 and ED (Figure 1) is in the correspondence of the time of peak flow and the cessation of flow respectively, because they are the only parameters required to construct a triangular flow wave. The study by Mitchell et al.\(^ {28} \) of measurement of both aortic flow and carotid pressure wave, which was used as a surrogate for aortic pressure, found a close correspondence between time of the first systolic shoulder of the

<table>
<thead>
<tr>
<th>Tertile</th>
<th>Age, mean ± SD, y</th>
<th>Range, y</th>
<th>Transit Time Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tert1 (n=30)</td>
<td>38 ± 5</td>
<td>26 to 46</td>
<td>1.88 ± 0.32</td>
</tr>
<tr>
<td>Tert2 (n=30)</td>
<td>60 ± 7</td>
<td>47 to 66</td>
<td>1.93 ± 0.38*</td>
</tr>
<tr>
<td>Tert3 (n=30)</td>
<td>70 ± 3</td>
<td>66 to 74</td>
<td>2.10 ± 0.31††</td>
</tr>
<tr>
<td>Total (n=90)</td>
<td>56 ± 14</td>
<td>26 to 74</td>
<td>1.97 ± 0.31</td>
</tr>
</tbody>
</table>

*Compared with Tert1 (not significant; ††P < 0.05). ††Compared with Tert2 (not significant).
A possible source of error could arise from the variation in the estimation of T1 from the derived central aortic waveform because of the variation in waveform morphology. An estimate of the error was determined by applying a 30% variation in T1, such that the initial estimate of T1 was reduced in graded steps by 15% and then increased in graded steps by 15%. Results shown in Table 3 are for calculations performed in 44 subjects. The 30.0% range of variation produced a maximum percentage error magnitude between 8.4% and 10.3% in the final estimate of the transit time (eTR2/2). A 30% variation range would seem quite large, and it is expected that the more likely variation range of 10.0% to 20.0% would result in probable error magnitudes in the final transit time estimate of between 3.6% and 8.0%. This is well within the tolerances expected for any clinical measurement.

In formulating the criteria for processing the initial estimates of the forward and backward waves, P_f(t) and P_b(t), it was assumed that reflected pressure is constant from the beginning of ejection until the time of peak flow, ignoring the delay time between forward and backward waves (T fb1; Figure 2), the foot-to-foot delay between final estimates of forward and backward waves (T fb2; Figure 3), and the lag obtained from the processed waveforms (TR2; Figure 3). For the whole cohort of subjects, the cross-correlation method gave a much higher correlation coefficient (r) in relation to the measured carotid-femoral PTT (T1; r = 0.37; T fb1: r = 0.57; T fb2: r = 0.58; TR2: r = 0.73). The cross-correlation technique is limited to a delay of 1 sample point. For a sampling rate of 128 Hz, as has been used in this analysis, this corresponds with 8 milliseconds. Because delays of the order of 110 milliseconds were obtained, the accuracy is of the order of 7% and well within experimental error.

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independent measurement of PTT over the aortic trunk is close to 2 (Table 2).

In this study, the method of waveform decomposition was applied to the central aortic pressure waveform estimated from the noninvasive measurement of the radial artery pressure waveform using a general transfer function. The transformation has been shown to provide reliable estimates of central aortic systolic, diastolic, and pulse pressure under conditions of steady state (to within a mean value of 1 mm Hg), severe interventions such as change of intrathoracic pressures during Valsalva maneuver, and exercise. Although there may be some larger variation on the time point estimated from the first systolic inflection because of higher-frequency components of the transfer function, this was shown to produce small effects in the final calculation of reflection factors in term of pulse amplitude and also in this present study involving time factors (Figure 6). In addition, the strength of the agreement found between the measured (CF-PTT) and calculated PTT parameters in this study is in the fact that they were obtained from independent measurements. That is, the waveforms used for calculation of the PTT (ie, TR2) were not the same as those for the measurement of CF-PTT. The high agreement, therefore, indicates that the transformed radial artery pulse to estimate the central aortic pressure wave contains sufficient information that, in combination with an estimated aortic flow wave based on pressure waveform features and ED, can be used to estimate pulse transmission times in the aorta that can then be used to calculate aortic PWV.

There have been other attempts at obtaining stiffness indices from waveform analysis of single peripheral pulses. Millasseau et al report a technique where features are extracted from the digital volume pulse that provide markers for time points related to pulse wave transmission. By use of higher-order differentials, the time difference is obtained between time to peak and time to late systolic inflection or early diastolic peak. This time interval (Δt) is assumed to be related to aortic wave transmission, and a stiffness index (equivalent to a PWV parameter) is obtained by the ratio of height and Δt. Although a significant correlation was found between calculated stiffness index and measured aortic PWV, there are potential problems associated with the digital volume pulse related to external influences on the peripheral microvasculature because of vasomotor tone. In this study, we have applied a similar analysis to the radial pulse to ascertain whether any association exists between the radial waveform features and the measured CF-PTT. Although a significant relationship was found between radial Δt (y) and PTT (y = 0.77x + 244.2), the correlation (r = 0.34) was significantly lower than that for TR2 and CF-PTT (r = 0.73) for the whole cohort of subjects (n = 90).

Findings of this study have shown that decomposition of the central aortic pressure wave can be used for aortic PWV estimates. Although it has been shown to be applicable to derived central aortic pressure, it is expected that it is also applicable to other measures of aortic pressure, such as direct measurement, or indirect measurement, such as the use of the carotid pressure or diameter waveform as a surrogate measure of the aortic pressure pulse.

Conclusions
A new noninvasive method to determine the aortic PTT from a single pulse recording has been proposed and validated with independent noninvasive measurements of CF-PTT. The method can be used as an alternative means for aortic PWV, especially as a noninvasive method not requiring femoral artery recordings.

Perspectives
This study has shown that decomposition of the central aortic pressure wave derived from the radial pulse can be used to estimate PTT over the aortic trunk. Furthermore, it has been shown that the estimated transit time corresponds very closely with independent measurements of transit time between carotid and femoral sites. The important implication of these findings is that aortic PWV can be estimated from a single pressure pulse recording, hence eliminating the intrusive procedure of obtaining a femoral pulse recording. The technique has been evaluated in supine resting subjects. Further studies would be required to evaluate the influence of change in physiological parameters, such as heart rate, on the estimated values. Although the method has been shown to be applicable to derived central aortic pressure, it is expected that it is also applicable to other measures of aortic pressure, such as direct measurement, or indirect measurement, such as the use of the carotid pressure or diameter waveform as a surrogate measure of the aortic pressure pulse.

Acknowledgments
We are grateful to Drs Ian Wilkinson and Carmel McEniery from the University of Cambridge and Prof John Cockcroft from the University of Cardiff for the pulse wave velocity data on the cohort of subjects used to validate the analytical technique proposed in this study.

Disclosures
A.Q. is a visiting fellow in the Graduate School of Biomedical Engineering, University of New South Wales. The remaining authors report no conflicts.

References


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In the Hypertension article by Qasem and Avolio (Qasem A, Avolio A. Determination of aortic pulse wave velocity from waveform decomposition of the central aortic pressure pulse. Hypertension. 2008;51:188–195) Equation 3 is incorrect. The correct equation is

\[
P_f(t) = 0.5[P_m(t) + Z_c Q_m(t)]
\]

The authors regret the error.