Noninvasive Assessment of Local Pulse Pressure
Importance of Brachial-to-Radial Pressure Amplification

Francis Verbeke, Patrick Segers, Steven Heireman, Raymond Vanholder, Pascal Verdonck, Luc M. Van Bortel

Abstract—The advocated SphygmoCor procedure uses a radial-to-aorta transfer function with calibration on brachial instead of radial artery pressure to assess the central pulse pressure. We compared these values with carotid artery pulse pressures obtained from a validated calibration method, assuming mean minus diastolic blood pressure constant throughout the large artery tree. From 44 healthy subjects (21 males; 22 to 68 years) pressure waves were obtained at the radial, brachial, and carotid artery with applanation tonometry. Using the calibration method, radial and carotid artery pressures were assessed from brachial artery waves and pressures. The effect of brachial-to-radial pulse pressure amplification, brachial pulse pressure, mean pressure, age, gender, height, body mass index, and smoking on differences between the 2 methods was assessed. Brachial artery pressure was $118 \pm 12/72 \pm 10$ mm Hg. SphygmoCor central pulse pressure was $9.7 \pm 4.6$ mm Hg lower ($P<0.001$) than the carotid artery pulse pressure ($33.0 \pm 6.8$ versus $42.7 \pm 8.9$ mm Hg). The difference between the 2 methods strongly depended ($P<0.001$) on brachial-to-radial artery pulse pressure amplification ($5.8 \pm 5.1$ mm Hg; $12 \pm 11\%$) and less on brachial artery pulse pressure ($P=0.005$). After calibration of the radial pressure wave with radial instead of brachial artery pressures, the difference between SphygmoCor central pulse pressure and carotid pulse pressure decreased with 4 mm Hg. The advocated SphygmoCor procedure systematically underestimates the central pulse pressure with brachial-to-radial pulse pressure amplification as important determinant. Therefore, calibration of radial artery pressure waves on brachial artery pressures should be avoided. The underestimation of central aortic pulse pressure caused by the radial-to-aorta transfer function itself is much less than previously reported. (Hypertension. 2005;46:1-5.)

Key Words: pulse ■ blood pressure ■ blood pressure determination ■ arterial pressure

Brachial artery (BA) pulse pressure (PP) is a strong and independent predictor of cardiovascular morbidity and mortality in the general population,1 patients with hypertension,2 coronary heart disease,3 and end-stage renal disease.4 Although this peripheral PP is of great clinical value, from a pathophysiological point of view it seems more logical to presume that the left ventricle is merely affected by the central aortic pressure opposing the left ventricular ejection.5,6 Because PP is not constant throughout the large artery tree, BA PP may not be a good surrogate for central aortic PP.7,8 Methods have been developed to measure central blood pressure. One method has been proposed by Kelly and Fitchett.9 It makes use of calibration on pressure waveforms obtained at superficial arteries with applanation tonometry. This method assumes that mean arterial pressure (MAP) minus diastolic blood pressure is constant throughout the large artery tree9 and has been found accurate.10 Alternatively, radial-to-aorta pressure transfer can be used to mathematically transform radial artery (RA) waveforms into central aorta waveforms. A population-based radial-to-aorta transfer function is used in the SphygmoCor device (AtCor Medical Pty Ltd, Sydney, Australia). The advantage of this technique is the ease to perform applanation tonometry at the RA. Although this transfer function has been validated,11 the accuracy of central aortic PP obtained with the SphygmoCor has been largely debated.12–19 The debate focused mainly on the validity of the transfer function but ignored a second possible source of error in the advocated SphygmoCor procedure: calibration of the RA wave with brachial instead of radial blood pressure values.

We hypothesize that both the generalized transfer function and the use of BA blood pressure values as surrogate of RA blood pressure contribute to the presumed erroneous assessment of central PP by SphygmoCor. The present study investigates this hypothesis as well as the relative contribution of the 2 procedures. The validated calibration method proposed by Kelly and Fitchett is used as reference method.
Subjects and Study Design
Healthy subjects aged 18 to 70 years were eligible. Smoking was not allowed for 3 hours before the study. Measurements were performed while subjects were in a quiet environment after at least 10 minutes of supine rest. Local blood pressures were in random order consecutively assessed with the calibration method (CAL) and the SphygmoCor (Figure 1). Assessment of local pressures was preceded and followed by conventional measurement of the ipsilateral BA blood pressure with a sphygmomanometer. The mean of arm blood pressure values was used to calibrate the 2 methods. The calibration method was used to calculate the PP at the radial (PP_{RA Calif}) and carotid artery (CA) (PP_{CA Calif}). The SphygmoCor was used to calculate the aortic PP from RA waveforms applying a radial-to-aorta transfer function (PP_{RTF RA}) and from CA waveforms applying a carotid-to-aorta transfer function (PP_{RTF CA}). All reported data are mean values of 3 consecutive high-quality recordings. The study was approved by the local ethics committee and written informed consent was obtained from all subjects.

Materials and Methods

Measurements and Derived Parameters
BA blood pressure was measured with a validated oscillometric device (Omron HEM-705CP; Omron Healthcare Europe), and the mean of the 3 stable (coefficient of variation <5%) consecutive measurements was subsequently used. MAP was estimated from the numeric integral of the BA pressure wave over time measured with applanation tonometry, calibrated with the systolic and diastolic BA blood pressure. PP (PP_{BA}) was defined as the difference between systolic and diastolic blood pressure.

Arterial pressure waves were recorded at the BA, RA, and common CA using applanation tonometry. For both the calibration method and the SphygmoCor, the same applanation tonometer was used (Millar SPT-301B probe, Millar Instruments, Houston, Tex). For the calibration method, a dedicated homemade data acquisition system was used consisting of a hardware set-up (NI SC 2345; National Instruments, Houston, Tex) connected to a personal computer and post-processing software written in Matlab 6.0 (The Mathworks). This device allowed to calculate an average waveform over a defined time period (Figure 2).

Aortic PP was assessed in several ways: (1) PP_{RTF RA} was calculated according to the advocated SphygmoCor procedure, using a population based generalized radial-to-aorta transfer function with RA waveform calibration on BA blood pressure; (2) PP_{RTF RA} was also used the radial-to-aorta transfer function, but RA waveform calibration was performed on RA pressures; and (3) PP_{RTF CA} was obtained from CA waveforms, calibrated on the carotid pressures obtained with the calibration method, and using the carotid-to-aorta transfer function in the SphygmoCor. PP_{CA Calif} was used as primary estimate of aortic pressure (reference method) and PP_{RTF CA} as secondary estimate.

PP amplification between different arterial sites was expressed as the absolute difference between PPs at each site and in percent amplification. For example, PP amplification from brachial-to-RA (PP_{RA-RA}) was calculated as follows: absolute PP_{RA-RA} = PP_{RA Calif} - PP_{RA} and in percent PP_{RA-RA} = (PP_{RA Calif} - PP_{RA})/PP_{RA} x 100.

Statistics
Demographic data are presented as numbers or means±SD. Bland–Altman plots were used to evaluate the agreement between estimates of the same parameter: the mean difference between estimates reflects systematic bias and the SD of the differences [between estimates reflects], the level of agreement. Reproducibility was assessed by calculating the coefficients of variation. Differences in PP were examined by paired-samples t tests or Wilcoxon signed ranks tests for normal or not normal distributed variables, respectively. The effect of age, gender, height, body mass index, smoking status, PP_{BA}, and MAP. The carotid-to-BA PP amplification was 3.1±5.4 mm Hg (7±13%) and was smaller than the brachial-to-radial PP amplification of 5.8±5.1 mm Hg (12±11%) (P=0.002). Brachial-to-radial PP amplification was only dependent on gender (women less than men; P=0.006), not on age, height, body mass index, smoking, BA PP, and MAP.

Results
Forty-four subjects entered the study. Subject characteristics are shown in Table 1. Peripheral and central PP according to different methods are given in Table 2. Reproducibility of the MAP, radial, and carotid systolic pressure obtained with the calibration method was high with a coefficient of variation of 0.9%, 1.6%, and 0.9%, respectively. The carotid-to-BA PP amplification was 3.1±5.4 mm Hg (7±13%) and was smaller than the brachial-to-radial PP amplification of 5.8±5.1 mm Hg (12±11%) (P=0.002). Brachial-to-radial PP amplification was only dependent on gender (women less than men; P=0.006), not on age, height, body mass index, smoking, BA PP, and MAP.

TABLE 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males/females, n</td>
<td>21/23</td>
</tr>
<tr>
<td>Smokers, n</td>
<td>11</td>
</tr>
<tr>
<td>Age, y</td>
<td>46±12</td>
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<tr>
<td>Height, cm</td>
<td>170±11</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>24±3</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>118±12</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>72±10</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>63±13</td>
</tr>
</tbody>
</table>

Data are numbers (n) or mean±SD. BP indicates blood pressure.
TABLE 2. Peripheral and Central Pulse Pressures

<table>
<thead>
<tr>
<th>Peripheral Pulse Pressures Method</th>
<th>PP</th>
<th>Mean±SD, mm Hg</th>
<th>Central PP Method</th>
<th>PP</th>
<th>Mean±SD, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibration</td>
<td>PP&lt;sub&gt;CA-CAL&lt;/sub&gt;</td>
<td>42.7±8.9</td>
<td>SphygmoCor</td>
<td>PP&lt;sub&gt;AD-RTF&lt;/sub&gt;</td>
<td>33.0±6.8</td>
</tr>
<tr>
<td>Omron</td>
<td>PP&lt;sub&gt;RA&lt;/sub&gt;</td>
<td>45.8±7.8</td>
<td>SphygmoCor</td>
<td>PP&lt;sub&gt;AD-RTFIMP&lt;/sub&gt;</td>
<td>37.1±8.2</td>
</tr>
<tr>
<td>Calibration</td>
<td>PP&lt;sub&gt;RA-CAL&lt;/sub&gt;</td>
<td>51.6±10.8</td>
<td>SphygmoCor</td>
<td>PP&lt;sub&gt;AD-CTF&lt;/sub&gt;</td>
<td>40.2±8.6</td>
</tr>
</tbody>
</table>

Aortic Pulse Pressures, Differences Between Test and Reference Method

<table>
<thead>
<tr>
<th>PP Difference</th>
<th>Mean±SD, mm Hg</th>
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</thead>
<tbody>
<tr>
<td>PP&lt;sub&gt;AD-RTF&lt;/sub&gt;−PP&lt;sub&gt;CA-CAL&lt;/sub&gt;</td>
<td>−9.7±4.6*</td>
</tr>
<tr>
<td>PP&lt;sub&gt;AD-RTF&lt;/sub&gt;−PP&lt;sub&gt;AD-CTF&lt;/sub&gt;</td>
<td>−7.1±3.6*</td>
</tr>
<tr>
<td>PP&lt;sub&gt;AD-RTFIMP&lt;/sub&gt;−PP&lt;sub&gt;CA-CAL&lt;/sub&gt;</td>
<td>−5.7±2.8*</td>
</tr>
<tr>
<td>PP&lt;sub&gt;AD-RTFIMP&lt;/sub&gt;−PP&lt;sub&gt;AD-CTF&lt;/sub&gt;</td>
<td>−3.1±2.3*</td>
</tr>
</tbody>
</table>

PP indicates pulse pressure.
*P<0.001.

PP<sub>AO-RTF</sub> was always lower than the aortic PP obtained with any of the 2 candidate reference methods (PP<sub>CA-CAL</sub>, PP<sub>AD-CTF</sub>). The difference with PP<sub>CA-CAL</sub> is shown in Figure 3a. The use of brachial instead of RA pressures to calibrate the radial pulse pressure wave resulted in an underestimation of mean arterial pressure by 3.2±1.8 mm Hg. Calibration of the RA wave with RA pressures instead of BA pressures resulted in an increase of estimated central PP from 33.0±6.8 mm Hg (PP<sub>AO-RTF</sub>) to 37.1±8.2 mm Hg (PP<sub>AO-RTFIMP</sub>). At the same time, the difference with the candidate reference methods decreased with 4 mm Hg (9.7 to −5.7 mm Hg when compared with PP<sub>CA-CAL</sub>; −7.1 to −3.1 mm Hg when compared with PP<sub>AD-CTF</sub>) but remained statistically significant (Table 2). The difference with PP<sub>CA-CAL</sub> is shown in Figure 3b.

In multiple linear regression analysis, the difference between PP<sub>AO-RTF</sub> and PP<sub>CA-CAL</sub> appeared to be strongly dependent on PP<sub>Pamp<sub>BA</sub>-RA</sub> and brachial PP but not on MAP, age, gender, smoking status, height, or body mass index (Table 3). PP<sub>Pamp<sub>BA</sub>-RA</sub> and brachial PP together explained 69% of the variation (63% for PP<sub>Pamp<sub>BA</sub>-RA</sub>) between the 2 methods (adjusted R<sup>2</sup>=0.69, P<0.001).

Discussion

Estimation of central aortic hemodynamic parameters such as PP and augmentation index from the radial pulse using a transfer function has become common practice. Several validation studies confirmed the accuracy of the transfer function for estimation of both aortic PP and aortic augmentation index. In a majority of these studies, the pressure curve was calibrated using invasive blood pressure measurements. When noninvasive calibration was performed, conforming to the noninvasive nature of the technique, a considerable bias in the estimation of the central PP was observed. However, as in these studies, aortic pressures obtained from invasive measurements were compared with the SphygmoCor procedure calibrated on noninvasively obtained arm blood pressure, it was not clear whether the observed difference between methods was caused by the SphygmoCor procedure, the deviation of sphygmomanometer blood pressures from invasive pressures, or both. To eliminate this potential source of bias, in the present study, both SphygmoCor and calibration method were calibrated on the same blood pressure values obtained noninvasively with a validated device (Omron HEM 705 CP).

In the present study, we identified inadequate calibration caused by centrifugal PP amplification and transfer function.

TABLE 3. Determinants of Difference Between PP<sub>CA-CAL</sub> and PP<sub>AD-RTF</sub>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficients</th>
<th>Normalized</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td></td>
<td>0.376</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>−0.188</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>−0.005</td>
<td>0.974</td>
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</tr>
<tr>
<td>Height, cm</td>
<td>−0.170</td>
<td>0.259</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>−0.078</td>
<td>0.425</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>0.013</td>
<td>0.882</td>
<td></td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>0.134</td>
<td>0.158</td>
<td></td>
</tr>
<tr>
<td>PP&lt;sub&gt;BA&lt;/sub&gt;, mm Hg</td>
<td>0.288</td>
<td>0.005*</td>
<td></td>
</tr>
<tr>
<td>PP&lt;sub&gt;Pamp&lt;sub&gt;BA&lt;/sub&gt;-RA&lt;/sub&gt; %</td>
<td>0.768</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
</tbody>
</table>

*Variables remaining statistically significant in stepwise linear regression. BMI indicates body mass index; MAP, mean arterial pressure.
effects as major source of bias in the estimation of the central PP using the SphygmoCor when compared with PPAO, a validated calibration method. Because the primary objective was to verify the accuracy of the SphygmoCor procedure as advocated by the manufacturer, we initially compared the PPAO with the PPAO, which yielded a systematic underestimation of 9.7 ± 4.6 mm Hg by PPAO. This systematic bias is lower than the 19.0 to 24.8 mm Hg observed in studies comparing the PPAO with invasively measured central PP, and supports the view of O'Rourke et al that a large part of the difference found in these studies was caused by the difference between sphygmomanometer and invasive blood pressure values.

The present study identified a substantial PP amplification between brachial and RA pressure, and also that the carotid-to-brachial PP amplification. Because the SphygmoCor procedure advocates the use of brachial instead of RA pressure to calibrate the radial pressure wave, a substantial error is introduced accounting for a 4 mm Hg underestimate. Because PP amplification may vary considerably, the degree of underestimation by using brachial pressure values as a surrogate for RA pressure is unpredictable. The brachial-to-radial PP amplification largely determined the underestimation of aortic PP estimated by the SphygmoCor procedure (PPAO). The level of PP was only additional but less important determinant of this underestimation.

After calibration of the RA pressure wave with RA pressure obtained with the calibration method (PPAO), the difference between PPAO and PPAO decreased to 5.7 mm Hg. The question remains whether this residual difference can be attributed to the transfer function itself. We used the PP at the CA obtained with the calibration method (PPAO) as surrogate for RA pressure in the ascending aorta. The important question is whether PPAO is a valid surrogate for aortic PP. Although some authors have shown that the PP in the common CA and in the ascending aorta is identical. Other studies indicate a small difference. In a validation study of the calibration method, CA PP was found on average 1.8 ± 5.2 mm Hg higher than ascending aortic PP. Another way of obtaining surrogate aortic PP is to calculate aortic pressure from carotid waveforms via a carotid-to-aorta transfer function (PPAO), presuming that the carotid-to-aorta transfer function is valid. This method shows aortic PP to be 2.6 mm Hg lower than at the CA and reduces the residual underestimation of the aortic pressure to 3.1 mm Hg. Thus, depending on the candidate estimate of aortic PP, the residual underestimation is between 3.1 and 5.7 mm Hg. This residual underestimation of aortic pressure may be caused by the generalized population-based transfer function itself, but is larger than the 0.7 ± 4.2 mm Hg found by Pauca et al in an invasive study in anesthetized patients.

The present study shows that depending on the candidate estimate of aortic PP used, the average error from the CA PP as surrogate for aortic PP (ranging between 0 and +2.6 mm Hg) is smaller than the average error (ranging between −3.1 and −5.7 mm Hg) from the improved SphygmoCor procedure using RA pressures. This supports the idea that CA pressure can be used as surrogate for central aortic pressure. A drawback of the calibration method and the improved SphygmoCor method is the need for an additional tonometry at the BA as long as reliable RA pressures from noninvasive devices are not available.

This study had some limitations. First, we did not have invasive blood pressure measurements in the present study. However, simultaneous comparison of invasive pressures at different arterial sites, like in the present study, might pose ethical problems, especially in a healthy population. In addition, the reference method had previously been validated against invasive measurements. Second, the calibration and SphygmoCor methods were performed consecutively and during this time blood pressure could have changed. To limit this bias, CAL and SphygmoCor procedures were performed in random order and both procedures were calibrated on the same BA blood pressure values. This procedure is presumed to limit systematic bias but cannot avoid variation between methods.

Perspectives

The use of BA pressure as surrogate for RA pressure in the advocated SphygmoCor procedure is an important source of error and should be avoided. This means a real need for an easy and reliable method to measure RA blood pressure noninvasively. Although oscillometric wrist sphygmomanometers have been developed, they do not provide RA pressures, because they have been calibrated on BA pressures. As long as direct accurate noninvasive measurement of RA pressure is not available, the more complex calibration method by Kelly and Fitchett remains advocated. The underestimation of central aortic PP caused by the radial-to-aorta population-based transfer function itself is much less than previously reported by some authors. However, its validity in different situations has not been fully established. Future research should further validate this and other transfer functions. Progress could be made by automation of the calibration method proposed by Kelly and Fitchett and by developing alternative methods for handheld applanation tonometers to obtain arterial pressure waves at different arterial sites.

References

7. Kelly RP, Gibbs HH, O’Rourke MF, Daley JE, Mang K, Morgan JJ, Avolio AP. Nitroglycerin has more favourable effects on left ventricular
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