Evaluation of Carotid–Femoral Pulse Wave Velocity

Influence of Timing Algorithm and Heart Rate

Sandrine C. Millasseau, Andrew D. Stewart, Sundip J. Patel, Simon R. Redwood, Philip J. Chowienczyk

Abstract—Carotid–femoral pulse wave velocity (PWV), a measure of arterial stiffness, is determined from the time taken for the arterial pulse to propagate from the carotid to the femoral artery. Propagation time is measured variously from the foot of the waveform or point of maximum upstroke. We investigated whether these methods give comparable values of PWV at rest, during β-adrenergic stimulation, and pacing-induced tachycardia. In subjects at rest (n = 43), values obtained using the foot-to-foot method (SphygmoCor system) were 1.7 ± 0.75 m/s (mean ± SD) greater than those obtained using the maximum slope (Complior system) at a mean value of 12 m/s. Isoprotenerol (0.5 to 1.5 μg/min; n = 10), and pacing (in subjects with permanent pacemakers; n = 11) increased heart rate but had differential effects on systolic blood pressure and pulse pressure. The increase in heart rate produced by isoprotenerol (18 ± 3 bpm) and pacing (40 bpm) was associated with an increase in PWV measured using both systems (increases of 0.7 ± 0.2 m/s and 0.9 ± 0.2 m/s for SphygmoCor and Complior, respectively, during isoprotenerol and increases of 2.1 ± 0.5 m/s and 1.1 ± 0.2 m/s for SphygmoCor and Complior, respectively, during pacing, each P < 0.001). Reanalysis of waveforms recorded from the Complior system using the foot-to-foot method produced similar values of PWV to those obtained with the SphygmoCor, confirming that the difference between these systems was attributable to the timing algorithm rather than other aspects of signal acquisition. Carotid–femoral PWV is critically dependent on the method used to determine propagation time, but this does not account for variation of PWV with heart rate. (Hypertension. 2005;45:222-226.)

Key Words: risk factors • compliance • pulse • heart rate

Stiffening of the aorta and large elastic arteries is a biophysical manifestation of vascular aging with important prognostic implications. It is elevated in conditions such as renal failure, diabetes, and hypertension, and in each of these conditions, it is predictive of subsequent cardiovascular events.1–6 Pulse wave velocity (PWV) is related to the intrinsic elasticity of the arterial wall and its anatomic dimensions by the Moens–Korteweg equation.7,8 It is recommended as one of the best methods for measuring stiffness9,10 and is the measure used in most large clinical studies.1–6 PWV is usually determined over the carotid–femoral region by measuring the propagation time of the pressure pulse from the carotid to femoral arteries. The 2 systems in common use, the SphygmoCor (AtCor) and Complior (Artech) differ with respect to their sensor technology and the algorithm used for calculating the pulse propagation time. The SphygmoCor device uses an arterial tonometer for recording pressure waveforms. Propagation time is measured from the foot of the carotid waveform to that of the femoral waveform using sequential recordings referenced to the ECG (Figure 1a). In the Complior system, carotid and femoral waveforms are recorded simultaneously using mechanotransducers, and timing is referenced to the point of maximum systolic upstroke (Figure 1b). The influence of the different methods for calculating pulse propagation time on values of PWV obtained using the 2 instruments is unknown, but it has been suggested that this might account for a variation of PWV with heart rate.11,12 In preliminary studies, we observed a marked difference between values of PWV obtained with the SphygmoCor and Complior devices. The purpose of the present study was to determine whether this is attributable to the method for measuring pulse propagation time and also to determine whether it might account for variation of PWV with heart rate. We compared measurements of PWV obtained with the 2 devices at rest and before and after an increase in heart rate induced by β-adrenergic stimulation and by pacing.

Methods

Measurements of carotid–femoral propagation time (transit time [TT]) and PWV obtained using the Complior and SphygmoCor systems were compared in subjects at rest (study 1), during intravenous infusion of isoprotenerol (study 2), and pacing (study 3). The studies were approved by the local research ethics committee, and all subjects gave written informed consent. Measurements obtained using the SphygmoCor system (TTsphy and PWVSphy) were determined with the SphygmoCor software using the intersecting tangent algorithm to identify the foot of the
waveform (Figure 1a). Those obtained with the Complior system (TT_{Comp} and PWV_{Comp}) were determined using the Complior software (timing referenced to the point of maximum systolic upstroke; Figure 1b). In addition, in-house software (MatLab; MathWorks) was used to calculate the propagation time from Complior waveforms using the intersecting tangent method (TT_{Comp*} and PWV_{Comp*}; Figure 1a). Care was taken to place the transducers over the same point of the arteries, and the same distance (sternal notch to femoral artery) was used to calculate PWV. A minimum of 3 readings using each device was obtained by the same operator with the different devices used in random order for alternate measurements.

Because of the influence of the timing algorithm could depend on the rate of change of the systolic upstroke of the pulse (dP/dt, calculated as the increment above diastolic pressure of the first systolic peak/shaok, divided by the time to this peak/shaok), this was computed from the carotid waveform obtained while measuring PWV_{Sphyg}. This waveform was also used to calculate carotid systolic blood pressure and carotid pulse pressure (which differ from brachial pressures as a result of peripheral amplification), assuming brachial and carotid mean and diastolic pressures are equal.16

**Study 1: Comparison of Resting Values of TT and PWV**

Study 1 was performed in 43 subjects with a range of risk factors for cardiovascular disease or established cardiovascular disease (Table 1) and included subjects who also participated in studies 2 and 3. After 15 minutes of rest supine, brachial blood pressure was measured using an oscillometric device (Omron 705CP; Omron), and measurements of TT and PWV were determined.

**Study 2: Comparison of PWV During Intravenous Infusion of Isoproterenol**

Study 2 was performed in 10 healthy volunteers (Table 1). After insertion of an intravenous cannula and after 15 minutes of rest supine, during which subjects received intravenous saline, baseline measurements of blood pressure and PWV were determined as described above. Subjects then received a stepped infusion of isoproterenol (0.5, 1, and 1.5 μg/min, each dose for 20 minutes). Blood pressure and PWV were determined during the last 15 minutes of each dose.

**Study 3: Comparison of PWV During Pacing-Induced Tachycardia**

This study was performed in 11 subjects with permanent pacemakers (Table 1). Eight subjects had dual-chamber pacemakers and 3 had single chamber pacemaker. The reasons for pacemaker insertion were complete heart block (n=8), sick sinus syndrome

<table>
<thead>
<tr>
<th>TABLE 1. Subject Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>resting PWV</td>
</tr>
<tr>
<td>n, male/female</td>
</tr>
<tr>
<td>Age, year</td>
</tr>
<tr>
<td>Height, cm</td>
</tr>
<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>CAD</td>
</tr>
</tbody>
</table>

Values are numbers or means±SD.

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, brachial pulse pressure; CAD, coronary artery disease.

(n=2), and vasovagal syncope (n=1). After 15 minutes of rest supine, the pacemaker was programmed to ventricular rates of 80, 100, and 120 bpm. After 5 minutes at each step, measurements of blood pressure and PWV were repeated over a 15-minute period.

**Statistical Analysis**

Subject characteristics are summarized as means±SD and results as means±SEM (except where otherwise stated). Repeatability was assessed by calculating within-subject coefficient of variation (WCV) for repeated measurements. Values of TT and PWV were compared using a Bland–Altman plot with calculation of the mean difference and SD of the difference. ANOVA for repeated measurements was used to test for changes in hemodynamic measurements during infusion of isoproterenol and pacing-induced tachycardia. The significance level was set at P<0.05.

**Results**

**Study 1: Comparison of Resting Values of TT and PWV**

For repeated measurements of TT, WCV was 5.6%, 6.8%, and 8.9%, for TT_{Sphyg}, TT_{Comp}, and TT_{Comp*}, respectively. For PWV, WCV obtained from the SphygmoCor and Complior devices were similar, irrespective of the timing algorithm used: WCV was 5.7%, 4.8%, and 5.5% for PWV_{Sphyg}, PWV_{Comp}, and PWV_{Comp*}, respectively. Values of TT_{Sphyg} were significantly lower than those of TT_{Comp} (mean difference±SD; 5.9±5.5 ms; P<0.001; Figure 2). Because of the reciprocal relationship between PWV and TT, this led to values of PWV_{Sphyg} significantly greater than those of PWV_{Comp} (mean difference±SD; 0.91±1.07 m/s; P<0.001), with the difference increasing with increasing PWV (Figure 3). At a mean PWV of 12 m/s, the difference was 1.7±0.75 m/s (mean±SD). However, when the intersecting tangent algorithm was implemented on waveforms recorded by the Complior device, values of PWV_{Sphyg} did not differ significantly from those of PWV_{Comp*} (Figures 2 and 3).
Study 2: Comparison of PWV During Intravenous Infusion of Isoprotenerol

During infusion of isoprotenerol, heart rate, brachial and carotid systolic blood pressure, pulse pressure, and dP/dt increased significantly (Table 2). There was a small but significant increase in mean arterial pressure (4 ± 1 mm Hg at the highest dose; \( P < 0.01 \)). As in study 1, mean values of PWV_{Sphyg} were greater than those of PWV_{Comp} at rest and remained greater during infusion of isoprotenerol (\( P < 0.001 \)). Both PWV_{Sphyg} and PWV_{Comp} increased significantly (by 0.7 ± 0.2 m/s and 0.9 ± 0.2 m/s, respectively, at the highest dose; each \( P < 0.001 \)). Application of the intersecting tangent algorithm to waveforms obtained using the Complior resulted in similar values of PWV to those obtained by the SphygmoCor (Figure 4).

Study 3: Comparison of PWV During Pacing Induced Tachycardia

Brachial and carotid systolic blood pressure and dP/dt did not change significantly during pacing from 80 to 120 bpm (Table 3). Diastolic blood pressure increased by 7 ± 1 mm Hg (\( P < 0.001 \)), with a corresponding increase in mean arterial pressure of 5 ± 1 mm Hg (\( P < 0.01 \)). Mean values of PWV_{Sphyg} were consistently higher than values of PWV_{Comp} throughout the paced heart rate range (Figure 4; \( P < 0.001 \)). PWV_{Sphyg} and PWV_{Comp} increased by 2.1 ± 0.5 m/s and 1.1 ± 0.2 m/s, respectively (each \( P < 0.001 \)). Mean values of PWV_{Comp} obtained by applying the intersecting tangent algorithm to Complior waveforms did not differ significantly from those of PWV_{Sphyg} (Figure 4).

Discussion

The first major finding of the present study is a substantial difference between values of PWV obtained using the SphygmoCor and Complior systems attributable to a systematic difference in TT. Because of the reciprocal relationship between PWV and TT, values of PWV obtained using the SphygmoCor system are greater than those obtained with the Complior and the difference increases in proportion to the mean value of PWV. At a mean value of 12 m/s, the difference between the 2 devices is 1.7 m/s. Using the coefficient relating PWV to age obtained in a healthy European population,\(^1\) this difference represents 27 years of vascular aging. Such a difference could, in principle, arise from the different transducers used in the 2 devices, difference between simultaneous (Complior) or sequential/ECG-referenced (SphygmoCor) recordings, or the different algorithms used to measure propagation time. When the intersecting tangent algorithm was used to calculate TT from waveforms recorded using the Complior, PWV values obtained from the 2 devices were in agreement. This suggests that computation of PWV is critically dependent on the algorithm used to determine TT and that the contribution of other sources of variation is relatively

Figure 2. a, Scatter plot showing TT determined by the Complior (TT_{Comp} and TT_{Comp*}) and SphygmoCor systems (TT_{Sphyg}). TT_{Comp} was calculated using the in-built Complior maximum upslope algorithm and TT_{Comp*} calculated using the intersecting tangent algorithm (as in the SphygmoCor). The dotted line is the line of identity, the broken line the regression line for TT_{Comp} vs TT_{Sphyg}, and the solid line the regression line for TT_{Comp*} vs TT_{Sphyg}. b, Bland–Altman plot showing the difference (\( \Delta \)TT) between TT_{Comp} and TT_{Sphyg} plotted vs the mean of TT_{Comp} and TT_{Sphyg}. The solid line represents the mean value of \( \Delta \)TT and the dotted lines mean ±2 SD. c, Bland–Altman plot showing the difference (\( \Delta \)TT) between TT_{Comp} and TT_{Sphyg} plotted vs the mean of TT_{Comp} and TT_{Sphyg}.
PWV determined using the SphygmoCor system (intersecting tangent algorithm, PWV_{Sphyg}; ○), the Complior system (maximum upslope, PWV_{Comp}; △) and from Complior traces with the same intersecting tangent algorithm as used in the SphygmoCor system (PWV_{Comp}; △) during intravenous infusion of isoproterenol (top) and during pacing (bottom). P<0.001 for the increase in PWV in each case.

**TABLE 2. Hemodynamic Measurements During Intravenous Isoproterenol**

<table>
<thead>
<tr>
<th>Hemodynamic Measure</th>
<th>Saline</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, bpm</td>
<td>60±2</td>
<td>69±2</td>
<td>73±2</td>
<td>79±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brachial SBP, mm Hg</td>
<td>115±3</td>
<td>125±3</td>
<td>130±3</td>
<td>137±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brachial DBP, mm Hg</td>
<td>69±2</td>
<td>62±2</td>
<td>65±2</td>
<td>64±2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Brachial PP, mm Hg</td>
<td>46±3</td>
<td>63±3</td>
<td>65±2</td>
<td>73±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>85±3</td>
<td>83±2</td>
<td>86±2</td>
<td>88±2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Carotid SBP, mm Hg</td>
<td>105±4</td>
<td>119±6</td>
<td>123±5</td>
<td>130±5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carotid PP, mm Hg</td>
<td>36±3</td>
<td>57±6</td>
<td>58±4</td>
<td>67±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>dP/dt, mm Hg/s</td>
<td>315±28</td>
<td>635±81</td>
<td>651±48</td>
<td>828±54</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means±SE. P-values refer to change from baseline by repeated measures ANOVA.

HR indicates heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; dP/dt, slope of upstroke of carotid pressure.

PWV determined using the SphygmoCor system (PWV_{Sphyg}; ○), the Complior system (maximum upslope, PWV_{Comp}; △) and from Complior traces with the same intersecting tangent algorithm as used in the SphygmoCor system (PWV_{Comp}; △) during intravenous infusion of isoproterenol (top) and during pacing (bottom). P<0.001 for the increase in PWV in each case.

**TABLE 3. Hemodynamic Measurements During Pacing**

<table>
<thead>
<tr>
<th>Hemodynamic Measure</th>
<th>80</th>
<th>100</th>
<th>120</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td>HR, bpm</td>
<td>60±2</td>
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<td>73±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brachial SBP, mm Hg</td>
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</tr>
<tr>
<td>Brachial DBP, mm Hg</td>
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<td>65±2</td>
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<td>828±54</td>
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</table>

Values are means±SE. P-values refer to change from initial value by repeated measures ANOVA.

HR indicates heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; dP/dt, slope of upstroke of carotid pressure.

Minor. Furthermore, within-subject variability was similar for PWV_{Sphyg} and PWV_{Comp}, suggesting that sequential acquisition of waveforms (SphygmoCor) does not contribute significantly to random variation when hemodynamic conditions are stable. Our study does not determine which of the 2 methods for measuring propagation time is “correct.” A comparison with a definitive method would be ideal, but there is no consensus as to what constitutes the definitive method. However, there are theoretical reasons to prefer using the foot of the pressure wave as identified by the intersecting tangent method. The foot of the wave is least likely to be influenced by distortion of the pressure waveform during its forward propagation through the arterial tree attributable, for example, to pressure wave reflections.

The impact of using the foot of the pressure wave (identified by the intersecting tangent algorithm) versus the maximum upslope might be expected to depend on the initial rate of change of the pulse waveform and hence on heart rate or ejection time. It has been suggested that the variation of PWV with heart rate that has been observed in studies using the Complior system but not in studies using the foot-to-foot method is an artifact related to the algorithm used to measure propagation time. To examine this, we studied the effects of intravenous isoproterenol and pacing-induced tachycardia. The only consistent hemodynamic changes common to both interventions were a marked increase in heart rate and a small (≈5 mm Hg) increase in mean arterial blood pressure. For both interventions, the increase in heart rate was associated with an increase in PWV irrespective of the device or algorithm used. Thus, although the use of different timing algorithms produces different values of PWV, it is unlikely to account for variation of PWV with heart rate.

Comparison with previous studies in which we have produced acute changes in blood pressure in the absence of changes in heart rate suggest that the increase in mean arterial pressure was too small to account for the observed change in PWV. Furthermore, an increase in PWV with heart rate, in the absence of changes in arterial pressure, suggests that the increase in PWV is due to a decrease in the rate of change of pulse wave velocity with heart rate. Finally, an increase in PWV with heart rate has been observed in studies using the Complior system but not in studies using the foot-to-foot method. The increase in PWV with heart rate is likely to be due to changes in pulse wave velocity with heart rate.
of any change in mean arterial blood pressure, has been observed in other studies.\(^\text{19,21}\) Therefore, the results of the present study in combination with these other studies are consistent with a true increase in arterial PWV associated with an increase in heart rate. However, it is likely that the size of the effect varies according to age, gender, and degree of aortic stiffening.\(^\text{22}\) The possible mechanism underlying such an increase in PWV with heart rate remains poorly understood. Visco-elastic properties of the arterial wall have been invoked to explain variation of PWV with heart rate,\(^\text{21}\) but O’Rourke et al have argued that this explanation is unlikely.\(^\text{11,12}\) They point out that at the high frequencies that determine the foot of the wave, visco-elastic properties of the arterial wall vary little with heart rate.\(^\text{23–25}\) However, these experiments on visco-elastic properties of the arterial wall were performed in canine arteries, and we are not aware of any data in the human aorta. The positive correlation between PWV and heart rate observed in cross-sectional studies\(^\text{22,26,27}\) could be attributable to a similar effect to that observed in this study or to a chronic effect leading, for example, to increased PWV secondary to tissue fatigue.

It is important to note the limitations of this study relating to the interpretation of the changes in PWV seen during \(\beta\)-adrenergic stimulation and pacing. Because changes in heart rate were also accompanied by changes in mean arterial pressure or pulse pressure, we cannot be certain that heart rate is the primary determinant of such changes. However, change in blood pressure would not be expected to influence the difference in PWV attributable to the timing algorithm. Thus, the fact that changes in heart rate were accompanied by changes in PWV calculated using different algorithms suggests that the influence of heart rate on PWV described in previous studies is unlikely to be explained by the timing algorithms used.

Perspectives

There are substantial differences between values of PWV obtained using the SphygmoCor and Complior systems, the 2 commercially available devices described in the recent task force recommendation on measuring arterial stiffness using PWV.\(^\text{9}\) The size of the difference is clinically significant, being equivalent to \(>2\) decades of vascular aging for subjects with a moderate degree of aortic stiffening (PWV \(>12\) m/s). Values obtained from the 2 devices cannot be used interchangeably, and the system used to measure PWV must be considered when estimating cardiovascular risk from measurements of PWV. The difference between the 2 systems is attributable to the algorithm used to calculate TT. However, the use of different algorithms does not explain variation of PWV with increases in heart rate produced by \(\beta\)-adrenergic stimulation or pacing. Further studies to determine the mechanism underlying variation of PWV with heart rate are required.

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