A novel device for measuring arterial stiffness using finger-toe pulse wave velocity: Validation study of the pOpmètre®

Maureen Alivon a, Thao Vo-Duc Phuong a, Virginie Vignon a, Erwan Bozec b, Hakim Khettab a, Olivier Hanon c, Marie Briet a, Jean-Michel Halimi d, Magid Hallab e,*, Matthieu Plichart c, Kamel Mohammedi f, Michel Marre f, Pierre Boutouyrie a, Stéphane Laurent a

a Inserm U970, HEGP, AP–HP, Université Paris-Descartes, Paris, France
b CIC-Inserm, Hôpital Vandoeuvre-lès-Nancy, Nancy, France
c Hôpital Broca, AP–HP, Université Paris-Descartes, Paris, France
d Nephrology Department, François-Rabelais University, Tours, France
e Gerontology Department, Nantes University, 1, place Alexis-Ricordeau, 44000 Nantes, France
f Service d’Endocrinologie Diabétologie et Nutrition, Hôpital Bichat, AP–HP, Paris, France

Received 22 June 2014; received in revised form 24 September 2014; accepted 5 December 2014
Available online 11 February 2015

KEYWORDS
Arterial stiffness; Pulse wave velocity; Finger-to-toe transit time

Summary
Background. — The finger-toe pathway could be a good alternative for assessing arterial stiffness conveniently.
Aim. — To evaluate the accuracy of the pOpmètre® — a new device that measures finger-toe pulse wave velocity (ft-PWV).

Abbreviations: cf-PWV, Carotid-femoral pulse wave velocity; cf-TT, Carotid-to-femoral transit time; ft-TT, finger-to-toe transit time; ft-PWV, Finger-to-toe pulse wave velocity; ft-TT, Finger-to-toe transit time; PWV, Pulse wave velocity.

* Corresponding author.
E-mail address: magid.hallab@popmetre.com (M. Hallab).

http://dx.doi.org/10.1016/j.acvd.2014.12.003
1875-2136/© 2015 Elsevier Masson SAS. All rights reserved.
Background

Aortic pulse wave velocity (PWV) is the ‘gold standard’ of large artery stiffness. It is one of the best predictors of cardiovascular morbidity and mortality, independent of traditional risk factors, in a large number of populations [1–4]; this has been established with carotid-femoral PWV (cf-PWV), a direct measurement of aortic stiffness [5,6]. Although cf-PWV is robust, reproducible and relatively simple to use, it may be inconvenient for routine use in clinics because the measurement requires time and training. Additionally, access to the femoral artery might be difficult for cultural or clinical reasons. Other pathways have therefore been investigated, such as brachial-ankle PWV, which provides interesting prognostic data [7,8]. The pOpmètre® (Axelife SAS, Saint Nicolas de Redon, France) is an original...
Methodology, taking advantage of easy recording of the pulse wave at the finger and the toe using two photodiodes sensors, and deriving finger-toe PWV (ft-PWV). This very simple technique may be a good alternative for the measurement of arterial stiffness evaluation in outpatient and epidemiological settings. The pOpmètre has already been studied in the general population: ft-PWV correlates with ageing [9] and is linked with carotid plaques in metabolic syndrome [10]. However, ft-PWV has not yet been validated against reference techniques. Moreover, the extent to which ft-PWV reflects central or peripheral arterial stiffness is unknown.

Accordingly, the aims of the present study were: to compare ft-PWV obtained with the pOpmètre with the gold standard cf-PWV (Study 1); then to determine whether ft-PWV is altered similarly to cf-PWV during acute sympathetic stimulation (Study 2); and, finally, to study the repeatability of the pOpmètre PWV measurement (Study 3).

Methods

Study 1

A total of 86 subjects were included: 69 patients and 17 healthy normotensives (42 men; mean age 53±20 years; mean systolic blood pressure 130±18 mmHg) from Georges Pompidou European Hospital and Broca Hospital. Patients were either well-controlled hypertensive patients (n=49) or patients with cognitive impairment (n=20). In each subject, ft-PWV and cf-PWV were measured in a random order with the pOpmètre and the SphygmoCor® (AtCor Medical, Sydney, Australia). Measurements were performed according to the recent expert consensus [6].

Additionally, carotid-radial PWV and femoral-post-tibial PWV were obtained in 30 subjects using the SphygmoCor. Blood pressure and heart rate were recorded by an automatic device (Colin BP-880; Colin Medical, TX, USA) every 3 minutes to calculate the mean blood pressure value.

Study 2

The ‘cold pressor test’ was chosen as a sympathetic stimulation [11–13]; it was performed by immersing the right hand into an ice water container (4–5°C) for 1 minute. Ten healthy subjects (4 men; mean age 30±8.5 years; systolic blood pressure 118±14.3 mmHg) were measured, and three sequences of measurements were performed: at baseline (every minute during 4 minutes), during the test (at 0, 30 and 60 seconds) and during recovery (at 30, 60, 90, 120 and 180 seconds). Blood pressures were recorded continuously with the oscillometric device during the test. We used the Complior® system (Alam Medical, Vincennes, France) for cf-PWV measurement, to obtain simultaneous measurement of cf-PWV and ft-PWV during these dynamic conditions.

Study 3

The ft-PWV was measured in 45 patients in the nephrology clinic of Tours Hospital; 38 patients with various patholo-

gies and 7 healthy subjects were measured according to the guidelines [6] after 10 minutes of supine resting. Measurements were done every 5 minutes. If the two first measures differed by more than 0.5 m/s, then a third was performed and the median retained; the two closest measures were kept and the third discarded. All patients gave informed consent.

The study designs were approved by the ethics committee of the Georges Pompidou European Hospital, Paris, France.

Pulse wave velocity measurements

The pOpmètre was developed based on similar assumptions as those for brachial-ankle devices [14–16]. The pOpmètre takes advantage of two photodiodes sensors, similar to pulse oximeters [17] (see Fig. 1). The photodiodes are positioned on the finger and the toe, so that the pulpar arteries are in the scope of the infrared ray. The pOpmètre measures the transit time between the foot of the pulse waves of the finger and the toe, approximating the aortic pulse transit time if the timings in the upper and lower limbs are similar; it measures continuously for 20 seconds and simultaneously on the same pulse wave. Two indices are computed: difference in pulse wave transit time between toe and finger (ft-TT; in ms); and ft-PWV [in m/s; ft-PWV=k×subject’s height/ft-TT], using a chart based on the height of 187 individuals measured in occupational medicine (personal data), where k is dependent on height. The use of the height chart relates to the fact that the aortic valves correspond to an anatomical stable landmark [18].

For cf-PWV measurements, the SphygmoCor records carotid and femoral pulses successively and then, related to the R wave of the electrocardiogram, calculates the transit time.

The Complior measures the arterial pulse wave at the carotid and femoral sites simultaneously. The travelled distance is the direct distance between the carotid and femoral sites of measurement multiplied by 0.8, according to the consensus for the travelled distance measurement [6].

Statistical analysis

Data are expressed as means±standard deviations. A value of P<0.05 was considered significant. The statistical analysis was performed using NCSS 2007 (NCSS LLC, Kaysville, UT, USA).

The correlation between measurement values was investigated using Pearson regression coefficient. The Bland-Altman plot [19] was used to analyse the agreement between the two methods. The relative differences between each pair of measurements were plotted against their mean. The discrepancy between two methods was studied using multivariable correlation analyses between the relative differences and other variables.

For Study 2, ft-PWV and cf-PWV were analysed by mixed models to demonstrate the evolution of blood pressure, heart rate and PWV in the same time frame. We also determined the correlation between changes in ft-PWV and changes in cf-PWV during the test and recovery period.

In Study 3, we used the Bland-Altman method for graphic representation, and we calculated the coefficient of variation as the standard deviation divided by the mean.
**Figure 1.** Pulse wave velocity (travelled distance/time of travel). $A = k \times$ height; $B = k' \times$ height. The artery qualities in the upper and lower limb are similar (muscular arteries) and have quite similar transit times. The distance $B-A$ is approximately equal to the aortic path. The transit time $B-A = \Delta t$ and reflects the aortic transit time; this measurement reflects the aortic pulse wave velocity. In the top left corner: infrared (IR) source and receptor around the pulp arterioles.

**Results**

**Study 1**

Table 1 shows the descriptive variables for the main population of studies 1 and 2, and those of the study 3. As shown in Fig. 2, ft-PWV correlated with cf-PWV ($R^2 = 0.43; P < 0.0001$) and the plot of the transit time of the two methods showed a better correlation ($R^2 = 0.61; P < 0.0001$). Table 2 shows the mean values and comparisons of the PWVs, transit times and distances measured by the two methods. Table 3 shows the detailed data for controls and patients.

In Fig. 3, the Bland-Altman plots show individual relative differences (i.e. $[\text{SphygmoCor—pOpmètre}] / \text{mean}$, expressed as a percentage) observed between PWVs, and transit time values obtained by the two methods, according to the mean level, calculated as $\frac{[\text{SphygmoCor}+\text{pOpmètre}]}{2}$.

---

**Table 1** Descriptive variables for the main population of Studies 1 and 2, and for the population of Study 3.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Studies 1 and 2 (n = 86; 42 men)</th>
<th>Study 3 (n = 45; 28 men)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>$53.2 \pm 20.0$ [22.0–87.0]</td>
<td>$49.7 \pm 17.5$ [19.1–78.9]</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>$167 \pm 11$ [147–198]</td>
<td>$168 \pm 8$ [151–187]</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>$66 \pm 16$ [52–116]</td>
<td>$67 \pm 12$ [40–103]</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>$23.1 \pm 5.1$ [16.8–32.5]</td>
<td>$23.5 \pm 4.1$ [17–34.4]</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>$130 \pm 18$ [98–192]</td>
<td>$137 \pm 8$ [96–174]</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>$92 \pm 13$ [65–139]</td>
<td>$109 \pm 68$ [43–100]</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>$72 \pm 12$ [52–113]</td>
<td>$79 \pm 11$ [51–98]</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>$67 \pm 12$ [45–121]</td>
<td>$58 \pm 16$ [26–98]</td>
</tr>
<tr>
<td>cf-PWV (m/s)</td>
<td>$8.74 \pm 2.15$ [5.52–16.24]</td>
<td>–</td>
</tr>
<tr>
<td>cf-TT (ms)</td>
<td>$59 \pm 14$ [32–91]</td>
<td>–</td>
</tr>
<tr>
<td>ft-PWV (m/s)</td>
<td>$8.52 \pm 3.26$ [3.58–22.53]</td>
<td>$11.25 \pm 3.94$ [5.03–28.20]</td>
</tr>
<tr>
<td>ft-TT (ms)</td>
<td>$76 \pm 27$ [23–150]</td>
<td>$66 \pm 18$ [16–127]</td>
</tr>
<tr>
<td>Normalized ft-PWV</td>
<td>$8.77 \pm 2.36$ [4.48–14.79]</td>
<td>–</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation [range]. BMI: body mass index; cf-PWV: carotid-femoral pulse wave velocity; cf-TT: carotid-to-femoral transit time; DBP: diastolic blood pressure; ft-PWV: finger-toe pulse wave velocity; ft-TT: finger-to-toe transit time; MBP: mean blood pressure; PP: pulse pressure; SBP: systolic blood pressure.
Figure 2. Left chart: relationship between carotid-femoral pulse wave velocity (cf-PWV) (m/s) and finger-toe pulse wave velocity (ft-PWV) (m/s) ($R^2 = 0.43$; ft-PWV = $-0.16 + 0.79 \times$ cf-PWV). Right chart: relationship between the difference in pulse wave transit time at toe and finger (ft-TT) (pOpmètre) and carotid-to-femoral transit time (cf-TT) ($R^2 = 0.61$ finger-to-toe transit time [ft-TT] = $-12 + 1.48 \times$ cf-TT).

Table 2  Pulse wave velocities, transit times and differences between two methods.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Difference SphygmoCor–pOpmètre</th>
<th>Percentage difference (%)</th>
<th>$R^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>cf-PWV (m/s)</td>
<td>8.7 ± 2.2</td>
<td>0.22 ± 2.46</td>
<td>6.1 ± 24.5</td>
<td>0.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ft-PWV (m/s)</td>
<td>8.5 ± 3.3</td>
<td>0.22 ± 2.46</td>
<td>6.1 ± 24.5</td>
<td>0.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>cf-TT (ms)</td>
<td>59.4 ± 14.4</td>
<td>-17.5 ± 19.7</td>
<td>-20.3 ± 25.2</td>
<td>0.60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ft-TT (ms)</td>
<td>75.9 ± 27.6</td>
<td>-8.8 ± 4.9</td>
<td>-13.3 ± 10.1</td>
<td>0.21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SphygmoCor distance (cm)</td>
<td>49.4 ± 5.4</td>
<td>-6.8 ± 4.9</td>
<td>-13.3 ± 10.1</td>
<td>0.21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>pOpmètre distance (cm)</td>
<td>56.2 ± 3.6</td>
<td>-6.8 ± 4.9</td>
<td>-13.3 ± 10.1</td>
<td>0.21</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 3  Detailed descriptive values for the three populations.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Healthy controls</th>
<th>Patients with cognitive impairment</th>
<th>Hypertensive patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 17; 29% women)</td>
<td>(n = 20; 55% women)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>28.6 ± 4.2</td>
<td>74.2 ± 13.1</td>
<td>53.2 ± 15.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171 ± 12</td>
<td>161 ± 10</td>
<td>168 ± 10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64 ± 15</td>
<td>67 ± 12</td>
<td>67 ± 17</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.5 ± 2.6</td>
<td>24.3 ± 6.9</td>
<td>23.2 ± 4.9</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>115.8 ± 9.5</td>
<td>134.4 ± 17.6</td>
<td>132.4 ± 18.4</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>81.1 ± 6.8</td>
<td>95.1 ± 10.5</td>
<td>93.9 ± 14.2</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>66.2 ± 10.0</td>
<td>70.4 ± 14.7</td>
<td>65.9 ± 11.9</td>
</tr>
<tr>
<td>cf-PWV (m/s)</td>
<td>6.73 ± 0.54</td>
<td>10.60 ± 2.35</td>
<td>8.68 ± 1.75</td>
</tr>
<tr>
<td>cf-TT (ms)</td>
<td>73 ± 10</td>
<td>48 ± 11</td>
<td>60 ± 13</td>
</tr>
<tr>
<td>ft-TT (ms)</td>
<td>102 ± 16</td>
<td>55 ± 24</td>
<td>75 ± 24</td>
</tr>
<tr>
<td>cf-PWV–ft-PWV (m/s)</td>
<td>5.76 ± 0.93</td>
<td>11.04 ± 3.54</td>
<td>8.46 ± 2.86</td>
</tr>
<tr>
<td>Difference in TT (ms)</td>
<td>-29.6 ± 14.7</td>
<td>-7.6 ± 6.8</td>
<td>-17.4 ± 20.3</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation [range]. BMI: body mass index; bpm: beats per minute; cf-PWV: carotid-femoral pulse wave velocity; cf-TT: carotid-to-femoral transit time; DBP: diastolic blood pressure; ft-PWV: finger-toe pulse wave velocity; ft-TT: finger-to-toe transit time; HR: heart rate; MBP: mean blood pressure; SBP: systolic blood pressure.
Additionally, the ft-TT correlated with the transit time between the femoral artery and the post-tibial artery (lower limbs artery) \( (R^2 = 0.16; P = 0.03) \), but not with the transit time between the carotid artery and the radial artery (upper limbs artery). The relative difference between the transit time obtained by the two methods correlated with age \( (R^2 = 0.41; P = 0.0001) \) (Fig. 4), but not with other clinical variables.

**Study 2**

The cold pressor test led to significant increases in blood pressure and PWV followed by decreases during the recovery period. The changes in heart rate were not significant. Both cf-PWV and ft-PWV gave similar patterns (Fig. 5). However, the correlation between the change in ft-PWV and the change in cf-PWV was weak \( (R^2 = 0.07; P = 0.02) \).

**Study 3**

The repeatability in the intra-session variability study was very good: three measurements were made with the pOpmètre in the same session, involving 38 patients (12 women, 26 men; mean age 53.8 ± 15 years) and seven controls (six women, one man; mean age 27 ± 10 years). In this group, ft-PWV was 11.25 ± 3.94 m/s (range 5.03–28.2 m/s). The coefficient of variation was 4.52%, with a mean difference of 0.02 ± 0.50 m/s.
Sensitivity analysis

Because we could see that the discrepancy between ft-PWV and cf-PWV was mainly caused by inadequacy of distance estimation, we normalized ft-PWV by using the direct cf-distance measured for the SphygmoCor, and applied a correction factor to the transit time, calculated by using the Z-score ([value—mean]/standard deviation). By doing this, the regression line of cf-PWV and ft-PWV came close to the identity line, with no residual bias and mean difference = 0. The correlation coefficient $R^2$ was equal to 0.54 (see Fig. 6).

No side effects were reported during the study, especially while using the pOpmètre.

Discussion

In this present study, we were able to compare ft-PWV measured by the pOpmètre with cf-PWV measured by accepted devices (SphygmoCor, Complior). We found that the agreement between the pOpmètre and the reference techniques was good, especially when dealing with transit time, whereas when transit times were translated into velocities, the agreement decreased. Agreement for the transit time with $R^2$ in the range of 0.6 and coefficients of variation of 20%, in the presence of perfect distance measurements, would lead to the good category according to the guidelines for validation of non-invasive haemodynamic measurement devices [20]. This bias could be corrected by adequate calibration as a function of age, but this new calibration would need further validation on a separate sample, ideally using magnetic resonance imaging, as this technique can truly measure distance [6,21]. This reflects that the transit time from finger to toe is an acceptable proxy for the carotid-to-femoral transit time (cf-TT), whereas the distance estimation initially proposed induces significant bias. Distance measurement is problematic even for the carotid-to-femoral pathway [6,21,22]. Here, the distance estimation is complicated by the fact that it is impossible to use the anatomical landmarks of pulse measurements. When distance was estimated via the carotid-to-femoral direct distance, obtained from the SphygmoCor measurement, after adequate calibration of the distance measurement using fixed coefficients from Z-score analysis, the quality of the agreement of the transit time was translated into the ft-PWV. This new estimation of distance needs to be validated in a separate patient sample.

The fact that age is related to transit time bias (with overestimation of ft-TT at younger age compared with cf-TT) indicates that ft-TT captures some additional information related to the ageing process, compared with cf-PWV. This feature has been noted previously by investigators using brachial-ankle PWV, which is often more sensitive to metabolic risk factors than cf-PWV. Whether this particularity confers additional information or whether it is detrimental remains to be studied.

It was important to show that cf-PWV and ft-PWV could vary in the same direction during acute changes in blood pressure. We have shown that this is indeed the case, the two techniques providing similar patterns that follow changes in blood pressure. It must be noted that cf-PWV is more sensitive, and its differences versus baseline were significant at 0, 30 and 60 seconds during the cold pressor test, whereas ft-PWV was significant only at the end of the cold exposure. This could be interpreted in two ways. Either ft-PWV is less robust than cf-PWV or it really is less sensitive to the time of measurement of blood pressure effect. Despite this lesser reactivity to the pressor test, we should take into account that the pOpmètre is a really easy-to-use measurement device, totally investigator independent, whereas measurements with the Complior are demanding and require two investigators.

The measurement repeatability with the pOpmètre was very good, especially as repeatability was obtained over a wide range of PWVs.

The fact that this measure is operator independent and highly acceptable to patients helps to limit perturbations during the measurement session and facilitates good repeatability. Further, the absence of manipulation of the carotid bifurcations makes involuntary activation of the baroreflex unlikely, and the absence of groin palpation limits patient stress and subsequent variations in blood pressure and heart rate.

Study limitations

This study has several limitations. The number of patients included complied with the recommendations [20], but was relatively small ($n = 86$) and may have led to overoptimistic results. The physical principles also need to be studied more in depth, through precise modelling of the arterial tree, to explain this level of agreement between ft-PWV and cf-PWV. The small number of subjects also limits interpretation of Study 2.
Conclusions

In conclusion, the results of this study indicate that the ft-PWV is a promising means of assessing arterial stiffness. The greatest advantages of ft-PWV are probably simplicity, rapidity, feasibility, patient acceptability and correct agreement with the reference technique. The good repeatability may lead to its use being considered in arterial stiffness monitoring in long-term follow-up of patients. This technique is also affected by age-dependent bias in arterial stiffness assessment. Further studies are needed to adjust the bias concerning peripheral stiffness and age, and to validate the pOpmètre in a larger population.

Disclosure of interest

Dr Magid Hallab is the owner of a patent. The other authors declare that they have no conflicts of interest concerning this article.

References