Short-Term Repeatability of Noninvasive Aortic Pulse Wave Velocity Assessment: Comparison Between Methods and Devices

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BACKGROUND
Aortic pulse wave velocity (PWV) is an indirect index of arterial stiffness and an independent cardiovascular risk factor. Consistency of PWV assessment over time is thus an essential feature for its clinical application. However, studies providing a comparative estimate of the reproducibility of PWV across different noninvasive devices are lacking, especially in the elderly and in individuals at high cardiovascular risk.

METHODS
Aimed at filling this gap, short-term repeatability of PWV, estimated with 6 different devices (Complior Analyse, PulsePen-ETT, PulsePen-ET, SphygmoCor Px/Vx, BPLab, and Mobil-O-Graph), was evaluated in 102 high cardiovascular risk patients hospitalized for suspected coronary artery disease (72 males, 65 ± 13 years). PWV was measured in a single session twice, at 15-minute interval, and its reproducibility was assessed though coefficient of variation (CV), coefficient of repeatability, and intraclass correlation coefficient.

RESULTS
The CV of PWV, measured with any of these devices, was <10%. Repeatability was higher with cuff-based methods (BPLab: CV = 5.5% and Mobil-O-Graph: CV = 3.4%) than with devices measuring carotid-femoral PWV (Complior: CV = 8.2%; PulsePen-TT: CV = 8.0%; PulsePen-ETT: CV = 5.8%; and SphygmoCor: CV = 9.5%). In the latter group, PWV repeatability was lower in subjects with higher carotid-femoral PWV. The differences in PWV between repeated measurements, except for the Mobil-O-Graph, did not depend on short-term variations of mean blood pressure or heart rate.

CONCLUSIONS
Our study shows that the short-term repeatability of PWV measures is good but not homogenous across different devices and at different PWV values. These findings, obtained in patients at high cardiovascular risk, may be relevant when evaluating the prognostic importance of PWV.

Keywords: aortic stiffness; arterial stiffness; blood pressure; coefficient of variation; coronary artery disease; hypertension; pulse wave velocity; repeatability.

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Aortic pulse wave velocity (PWV) is an indirect, well-established index of arterial stiffness[1,2] and a strong independent predictor for fatal and nonfatal cardiovascular events.[3–6] The 2013 Guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)[7] recognized the additive value of PWV above and beyond traditional risk factors and recommend its routine assessment in hypertensive patients as a marker of subclinical organ damage. More recently, a Scientific Statement from the American Heart Association[8] considered reasonable to measure arterial stiffness to provide incremental prognostic information beyond standard cardiovascular disease risk factors in the prediction of future cardiovascular disease events. At present, carotid-femoral PWV is the noninvasive "gold standard" method recommended for measuring aortic stiffness.[2,7,8] PWV is a simple, reproducible, achievable through noninvasive techniques, and clinically relevant index. Currently, several devices for its measurement, based on different theoretical and operating principles, are available on the market.[9–11] The most commonly

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used systems employ sensors such as tonometers or mechanotransducers, capable of acquiring the pressure waveforms simultaneously at the carotid and femoral level using 2 distinct sensors (like the Complior system and the PulsePen-ETT tonometer)[12,13] or, taking advantage of the ECG trace, making a sequential recording using the R wave as reference for synchronization (SphygmoCor Vx system and PulsePen-ET). Alongside these traditional appliances, new devices based on the oscillometric detection of the brachial pressure wave with a single cuff were conceived, free from the need to consider the operator expertise and aimed at simplifying the measuring procedures and reducing delays (as the BPLab and the Mobil-O-Graph).[14] Although all arm-cuff-based devices are considered an easy and reliable method for the assessment of PWV, very few underwent independent validation studies. Furthermore, comparative data on their repeatability are lacking. Every validation study assessing accuracy and precision of devices used for assessing PWV was carried out on heterogeneous populations, primarily on healthy subjects, young adults, and individuals with no evidence of cardiovascular risk factors. Almost all said studies evaluated individuals with preserved viscoelastic properties of the arterial wall, as evidenced by the low average values of PWV.[13,15–18] All these validation studies showed low coefficient of variation (CV) and a good repeatability of the measurements of PWV.

Nevertheless, the evaluation of PWV is usually performed also in elderly patients or subjects at higher risk of generalized arteriosclerosis, for a better estimation of their cardiovascular risk in daily clinical practice. Since the repeatability of PWV measurement is inversely related to arterial stiffness, its accurate assessment is essential to define the reliability and accuracy of PWV in a population at high cardiovascular risk or in the elderly.

The aim of the present study was to characterize the short-term repeatability of PWV in a population at high cardiovascular risk, using noninvasive measures obtained within a single session, in a controlled environment. The accurate appraisal of repeatability is mandatory for a correct interpretation of the noninvasive PWV measurements and to analyze the disagreements between several measurement techniques.

METHODS

All suitable consecutive patients hospitalized in the Cardiology Unit of the Monza Polyclinic (Monza, Italy) for suspected coronary artery disease were recruited in this study. The exclusion criteria were: an age <18 years; body mass index >35 kg/m^2; atrial fibrillation or paced rhythm; heart failure in unstable hemodynamic compensation; or emergency hospitalization. Enlistment was voluntary and all participants gave their written informed consent to study procedures. The protocol was approved by Istituto Auxologico Italiano IRCCS, Milan, Italy, and Monza-Brianza Ethics Committees and conducted in accordance with the Helsinki Declaration.

Study protocol

PWV measurements were obtained in a quiet environment, with soft lighting and controlled temperature (21.5 ± 0.5°C). Participants were asked to fast for 8 hours, refrain from tobacco, caffeinated beverages or vigorous physical activity in the morning of the visit, and bring all prescribed medications taken 2 weeks before the visit. After 15 minutes of rest, PWV was measured in each subject alternating 6 devices: BPLab, Complior Analyse, Mobil-O-Graph, PulsePen-ET, PulsePen-ETT, and SphygmoCor. For each patient, the 6 measurements were sequentially performed in random order. The overall sequence of measurements lasted roughly 15 minutes, and a second sequence was then performed, using the same order of the previous one. Seven skilled operators, familiar with the appliances performed all the measures. Two weeks training, prior to the study, was provided to all operators, and operators' ability to perform measurements and the between-observer repeatability was ascertained with all devices. During the acquisition, each patient was studied by 4 operators: 2 operators performed the measurements with cuff-based devices (BPLab and Mobil-O-Graph) on the left side of the patient; simultaneously, 2 operators were placed on the right side of the patients and drove the devices measuring carotid-femoral PWV (Complior, PulsePen, and SphygmoCor). The same distance (80% of direct carotid to femoral distance) was used for these latter devices. Before the procedure, a marker was placed at the widest pulsation point on the common carotid and femoral artery and all distance were measured using the marker points with an inelastic tape. To minimize the discomfort of the patients, the overall time of the measurements was limited to 30 minutes. In some cases, due to technical reasons, only a single acquisition was attained. All measurements were considered for analysis regardless of the possible presence of outliers.

Peripheral blood pressure (BP) and heart rate were measured throughout the PWV recording time by a validated oscillometer Omron 705IT (Omron Corporation, Kyoto, Japan),[19] with a repetitive measurement for each PWV assessment (total of 14 measurements). Mean BP for each measurement was then calculated by applying the form factor, with the formula: Mean BP = diastolic BP + (systolic BP − diastolic BP) × brachial form factor. Form factor was calculated on the pulse pressure curve measured at the brachial level by PulsePen tonometer, calibrated with contralateral systolic, and diastolic BP measured at brachial artery level by Omron 705IT, with the formula: form factor = [(mean BP − diastolic BP)/(systolic BP − diastolic BP)].[20]

Devices

Complior Analyse (Alam Medical, Vincennes, France) measures PWV employing two very sensitive piezoelectric sensors to simultaneously record carotid and femoral pressure waveforms.[15,21] Quality checks are automatically performed on each curve, discarding the poor ones from the evaluation. Complior Analyse measures pulse wave transit

time (PWTT) with the recommended foot-to-foot method, identifying the wave foot by intersecting tangent algorithm. Complior Analyse is characterized by a 1 kHz sampling rate (each signal every ms).

PulsePen (DiaTecne srl, Milan, Italy) is a pocket-size, high-fidelity tonometric sensors wirelessly connected to a laptop or tablet. PulsePen measures PWTT with the foot-to-foot method, identifying the wave foot by intersecting interpolating algorithm.[13,22] The software permits real-time quality checks by the operator, providing a "quality index" during the recording of 10 cardiac cycles. The PulsePen software allows the acquisition of pulse wave signals only if "quality index" is more than 85% (overlapping of pulse waves >85%). PulsePen is characterized by a 1 kHz sampling rate.

PulsePen is marketed in 2 versions: (i) the PulsePen-ETT, offered with 2 tonometric probes and a 2-lead ECG unit, capable of simultaneously recording the carotid and femoral curves and (ii) the PulsePen-ET, supplied with a single probe and ECG, offering a sequential recording of pulse waves.

SphygmoCor Px/Vx System (AtCor Medical Pty. Ltd., West Ride, Australia) is provided with a pencil-type high-fidelity Millar tonometer paired with a 3-lead ECG. Carotid and femoral pulse waves are sequentially acquired and gated with the ECG signal. The software calculates an "operator index" from electrocardiographic and tonometric data variability. Only carotid and femoral pulse waveforms with an operator index >85 were included in this study. SphygmoCor measures PWTT with the recommended foot-to-foot method, identifying the wave foot by intersecting tangent algorithm. Pulse wave and ECG signal are acquired with 128 Hz sampling rate (each signal every 7.8 ms).

BPLab (OOO Petr Telegin, Nizhny Novgorod, Russia) is a 24-hour BP monitoring system. This device also provides central BP, augmentation index, and aortic PWV thanks to a proprietary algorithm embedded in the Vasotens software. PWV is measured by analysis of the oscillometric pressure waves recorded on the upper arm, considering the delay between direct and reflected wave, the so-called reflected wave transit time.[9] The travelled path length is approximated by the distance between sternal notch and pubic symphysis.[23] If there are differences more than 10% between 2 sequential measures of PWV or reflected wave transit time, the manufacturer advises to considered the obtained PWV values unreliable. Thus, in this study only PWV measurements defined as reliable by Vasotens were included.

Mobil-O-Graph (IEM, Stolberg, Germany) is another 24-hour BP monitoring system. The inbuilt ARCSolver (Austrian Institute of Technology, Vienna, Austria) proprietary algorithm processes the upper arm oscillometric BP signals, verifies the accuracy and acceptability of the recorded signals and applies a general transfer function to obtain the aortic systolic pressure.[24] PWV values are derived from an algorithm which integrates age, central systolic blood pressure, and data derived from pulse wave analysis into a mathematical model.[10]

Comparative technical specifications of all devices used in this study are summarized in Table 1.

Statistical analysis

Data are reported as mean ± SD or confidence intervals (CI) where appropriate.

The correlations between 2 consecutive measurements were analyzed in 2 steps according to the analysis described by Bland and Altman.[25] In the first step, the correlation between measurement values (equation of the linear relationship, correlation coefficient, and P value) was investigated. Secondly, the relative differences within each pair of measurements were plotted against the mean of the pair.

The repeatability was expressed as coefficient of repeatability (1.96 SD of differences between 2 measurements)[25] and intraclass correlation coefficients (2,1). As strongly recommended by M.J. Bland,[26] the within-subject CV was calculated as the square root of the mean within-subject variance (σ_w^2)/subject mean squared (μ_s^2), as follow: $\sqrt{E\left[\frac{\sigma_w^2}{\mu_s^2}\right]}$, where $E[x]$ is the expected value of random variable x.

Table 1. Comparison between technical specifications and general features of tested devices

Device	Complior Analyse	PulsePen ETT	PulsePen ET	SphygmoCor	BPLab	Mobil-O-Graph
Aortic PWV assessment	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Carotid-femoral PWV	Cuff-based method	Cuff-based method
Probes	2 Piezoelectric sensors	2 Tonometers	1 Tonometer + ECG	1 Tonometer + ECG	Upper arm cuff	Upper arm cuff
Recording time	10 Cardiac cycles	10 Cardiac cycles	10 Cardiac cycles	10 seconds	4–8 Cardiac cycles	10 seconds
Method	Simultaneous carotid and femoral artery recordings. Foot-to-foot method; Intersecting tangent algorithm	Simultaneous carotid and femoral artery recordings. Foot-to-foot method; Intersecting interpolating algorithm	Sequential ECG-gated carotid and femoral artery recordings. Foot-to-foot method; Intersecting interpolating algorithm	Sequential ECG-gated carotid and femoral artery recordings. Foot-to-foot method; Intersecting tangent algorithm	Analysis of the oscillometric pressure waves deriving reflected wave transit time	Algorithm based on age, central systolic pressure, and data derived from pulse wave analysis
Sampling rate	1 kHz	1 kHz	1 kHz	128 Hz	100 Hz	100 Hz

RESULTS

One-hundred and two patients (30% female) with a mean age of 65 ± 13 years were included in this study. General characteristics of the sampled population are listed in the Supplementary data (Supplementary Table S1). Due to technical problems and protocol time exceeding 30 minutes, only 1 PWV value was occasionally recorded. Repeatability data were available for 85 patients with Complior, 89 patients with PulsePen-ETT, 93 patients with PulsePen-ET, 91 patients with SphygmoCor, 99 patients with Mobil-O-Graph. Mean characteristics of patients for each device were similar. The first 25 measurements with the BPLab were not included because of technical challenges due to a misunderstanding in the protocol. Thus, repeatability was studied in 67 patients with BPLab. Eighty percent of the subjects were older than 55 years and 40% older than 70 years. There was a high prevalence of hypertension, dyslipidemia, smoking, diabetes, and ischemic heart disease, with also many subjects taking antihypertensive treatment.

Mean values of the differences between repeated measurements in absolute values, coefficient of correlation, coefficient of repeatability, CV, and intraclass correlation coefficients (2,1) are reported in Table 2. Devices evaluating carotid-femoral PWV showed a good repeatability (CV for Complior: 8.16%; PulsePen-ETT: 8.03%; PulsePen-ET: 5.82%; SphygmoCor: 9.48%). Repeatability of PWV estimated by cuff-based devices was slightly higher (CV for BPLab: 5.52%; Mobil-O-Graph: 3.37%). Bland–Altman plots and coefficient of repeatability for each methodology are shown in Figure 1.

All devices evaluating carotid-femoral PWV (PulsePen, SphygmoCor, Complior) revealed higher variability for higher PWV values. Figure 2 shows the CV values subdividing the results in 2 groups: low PWV values (<10 m/s) and high PWV values (≥10 m/s). CV [confidence interval] for PWV more than 10 m/s was 9.72% [7.2–11.7] for Complior Analyse, 9.21% [6.5–11.3] for PulsePen-ETT, 6.54% [5.3–7.6] for PulsePen-ET, 10.29% [7.7–12.3] for SphygmoCor. On the other hand, no such differences were observed with cuff-based devices for PWV <10 m/s vs. PWV ≥10 m/s: BPLab 6.03% [3.6–7.7] vs. 5.14% [3.5–6.4], Mobil-O-Graph 3.52% [2.8–4.1] vs. 3.20% [2.6–3.7]. Differences in carotid-femoral PWTT analyzed with Bland–Altman plots and coefficient of repeatability are shown in Figure 3. The higher variability found in subjects with aortic stiffening (high PWV) disappears when the PWTT is considered. In fact, no upward trend in the variability with smaller transit times was shown.

Table 3 shows the relationship between change in PWV and changes in mean BP and heart rate between 1st and 2nd measurement. The univariate and multivariate analyses investigating the dependence of differences in PWV values from mean BP and heart rate are also shown. Short-term repeatability of PWV values was not influenced by BP or heart rate variations in all devices except for the Mobil-O-Graph. Changes in PWV values provided by Mobil-O-Graph are significantly ($P < 0.001$, $\beta = 0.418$) affected by mean arterial pressure variations.

DISCUSSION

In this study, for the first time, the short-term repeatability of aortic PWV measured with 6 different devices was systematically compared in elderly or high cardiovascular risk patients. Our data emphasize that all the assessed devices had a good repeatability for PWV assessment. The repeatability was higher with cuff-based devices (BPLab, Mobil-O-Graph) than with devices measuring carotid-femoral PWV (SphygmoCor, Complior, PulsePen). In the latter devices, the repeatability of PWV was lower in subjects with higher carotid-femoral PWV and the differences in PWV between repeated measurements did not depend on short-term variations of mean BP or heart rate.

Accuracy and precision define the reliability of a clinical measurement. In order to study the accuracy of a given measurement, it is very important to verify the repeatability of the provided values. Previous studies reported data on the repeatability of PWV measurements by different devices.[13,15,16,18,27,28] However, these studies were aimed at validating the tested devices, which was done in most case by recruiting younger and healthier individuals. Conversely, in our study most of the examined subjects were older cardiovascular patients, with multiple cardiovascular risk factors and high PWV values. Although not representative of the general population, these patients represent the type of population in which the PWV measurement devices are mostly applied in the daily clinical practice, for the prognostic stratification of cardiovascular diseases.

Table 2. Repeatability between consecutive pulse wave velocity measurements

Device	*N*	*r*	CV (%)	|*d*| (m/s)	CR (m/s)	ICC
Complior Analyse	85	0.92	8.2 [6.6–9.5]	0.99 ± 0.88	2.50	0.90 [0.85–0.92]
PulsePen-ETT	89	0.93	8.0 [6.2–9.5]	0.96 ± 1.11	2.88	0.90 [0.84 0.93]
PulsePen ET	93	0.95	5.8 [4.9–6.6]	0.75 ± 0.67	1.96	0.95 [0.93 0.97]
SphygmoCor Vx	91	0.85	9.5 [7.7–11.0]	1.10 ± 1.07	2.99	0.85 [0.78–0.90]
BPLab	67	0.89	5.5 [4.2–6.6]	0.59 ± 0.55	1.59	0.89 [0.83–0.93]
Mobil-O-Graph	99	0.98	3.4 [2.9–3.8]	0.38 ± 0.28	0.82	0.98 [0.96–0.99]

Abbreviations: CR, coefficient of repeatability; CV, coefficient of variation (square root of the mean) with the relative 95%-confidence interval; |*d*| absolute mean of differences ± SD; ICC, intraclass correlation coefficients with the relative 95%-confidence interval; *N*, number of subjects; *r*, coefficient of correlation.

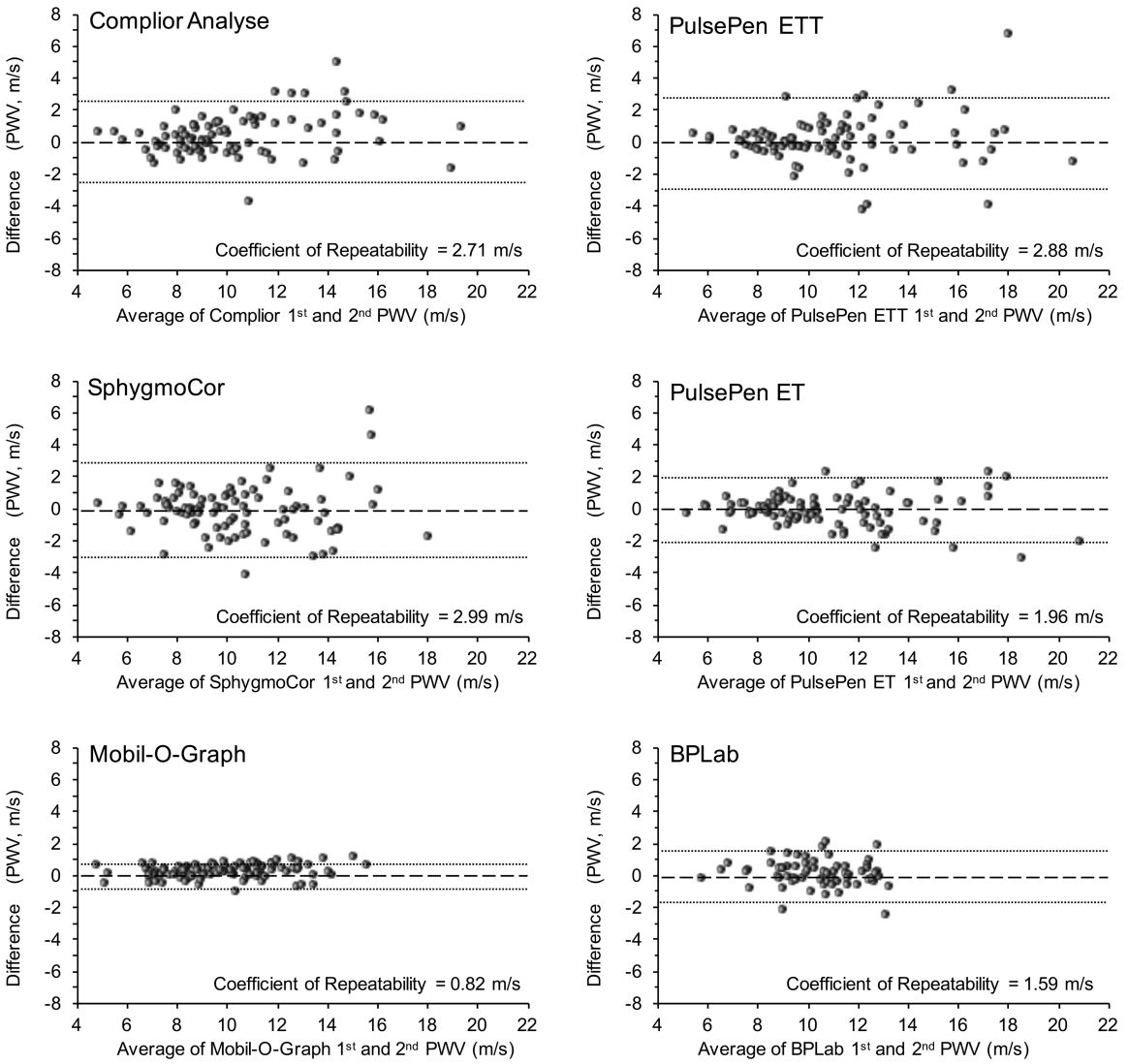

Figure 1. Bland–Altman analysis for repeated measurements of pulse wave velocity (PWV). The Bland–Altman analysis shows differences observed between 2 measurements of PWV according to the mean values. Coefficient of repeatability is 1.96 SD.

Compared to arm-cuff-based devices, higher values of CV were found in the devices assessing carotid-femoral PWV. CV values for carotid-femoral PWV found in our study are considerably higher than CV values shown in other published studies on a similar issue. In their study, comparing SphygmoCor and Complior devices, Stea *et al.*[15] found significantly different CV values: 5.25% for PWV measured by SphygmoCor and 3.4% for PWV measured by Complior Analyse. However, in that study, the mean age of recruited population was 47.2 ± 15.7 years (18 years younger than our population). What is more, only 25% of the study group had PWV value >10 m/s and a different method to calculate the CV was used. Likewise, the same results were presented for the SphygmoCor by Pirro *et al.*,[18] showing a CV of 5.1% in 50 healthy young volunteers and, more recently, by Reshetnik *et al.*,[29] showing CV values of 6.3 ± 4.33% in young adults (48.8 ± 19.1 years) with PWV mean values of 7.3 ± 1.7 m/s. The lower values of CV found in these studies are likely due to the type of individuals enrolled.

We observed that the variability of carotid-femoral PWV increased with increasing PWV levels: patients with higher arterial stiffness value had higher PWV variability. This is due to the fact that carotid-femoral PWV is related to the inverse of carotid-femoral PWTT. PWV is defined as the ratio between travelled distance and carotid-femoral PWTT. In our study, as the same travelled distances were used for all devices, the variability in PWV was thus due to variability in PWTT. In order to better understand this phenomenon, we can consider what happens at different PWV values, in the event of a little difference in PWTT of 4 ms between 2 measurements, supposing a fixed carotid-femoral distance value of 50 cm. In normal aortic distensibility conditions (PWV = 5 m/s) a difference of 4 ms in PWTT causes a very little change in PWV value: from 5.0 to 5.2 m/s (+0.2 m/s). In case of a PWV of 12 m/s, a PWTT difference of 4 ms causes

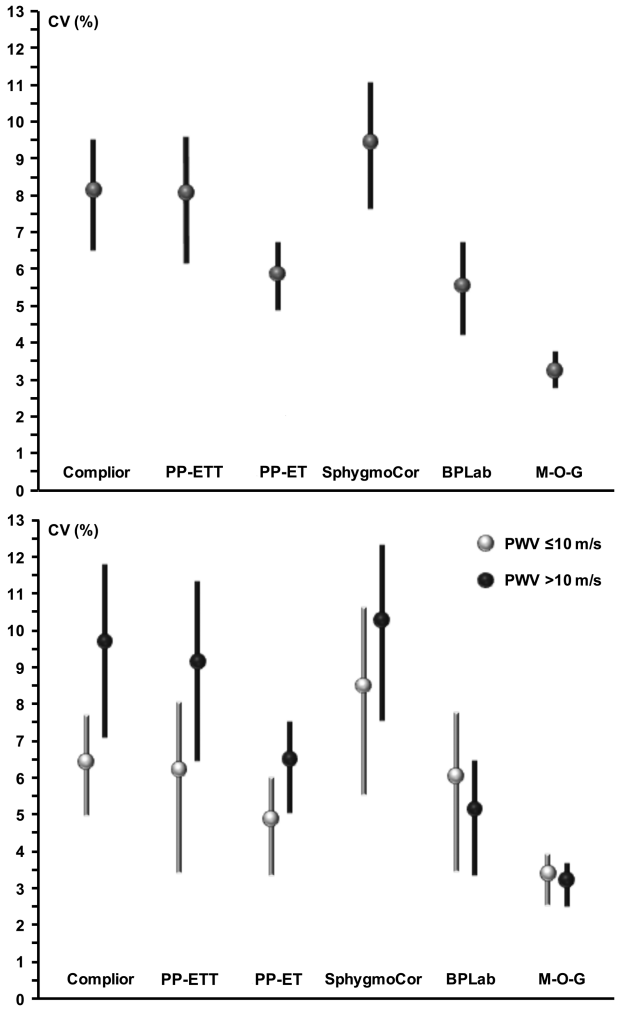

Figure 2. Coefficient of variation (CV, %) assessed for Complior Analyse, PulsePen-ETT (PP-ETT), PulsePen ET (PP-ET), SphygmoCor Vx, BPLab, and Mobil-O-Graph (M-O-G). Upper panel shows the CV for pooled measurements (dark gray). Lower panel shows CV values subdividing the results in 2 groups: PWV values <10 m/s (white) and PWV values ≥10 m/s. (black). Data are expressed as mean and 95% confidence intervals.

a change in PWV value from 12.0 to 13.2 m/s (+1.2 m/s). Finally, in a condition of severe arterial stiffness (PWV = 20 m/s), a difference in PWTT of 4 ms causes a very important change in PWV value: from 20.0 to 23.8 m/s (+3.8 m/s) (Supplementary Table S2).

For this reason, higher variability in PWV values are expected in patients at high cardiovascular risk, as they are usually characterized by arterial stiffening. Nevertheless, the studied devices assessing carotid-femoral PWV showed an acceptable repeatability in the PWV measurements with CV values <10% and intraclass correlation coefficients >0.8 for all the devices.

The higher PWV variability for high PWV values is an intrinsic characteristic of carotid-femoral PWV calculation as measure of arterial stiffness, and should be considered when applying carotid-femoral PWV in clinical and epidemiological studies. Even so, considered the proven efficacy in longitudinal studies of carotid-femoral PWV for the estimation of cardiovascular risk and the number and quality of clinical studies that validated its use, these findings should not be interpreted as a detraction from its clinical and prognostic value.

Differences in CV between the 4 devices measuring carotid-femoral PWV should be justified by the different approaches to measure PWV.

Unexpectedly, devices based on simultaneous recording of carotid and femoral pulse waves (Complior Analyse and PulsePen-ETT) provided PWV values which were not particularly less variable than PWV values obtained from devices based on ECG-gated measurements (PulsePen-ET and SphygmoCor Vx). In theory, one would expect that simultaneous recording would be more accurate, and thus characterized by lower variability. Yet, the identification of the R wave is immediate and unquestionable, whereas the identification of the foot of pressure waves is less precise. This may explain the difference in CV between the 2 models of PulsePen (ETT and ET).

It is also interesting to point out that 2 different algorithms to define the foot of the pulse waveform are employed. Complior Analyse and SphygmoCor both use the intersecting tangent algorithm in which the foot of the pressure waveform is identified by the intersection of the tangent to the maximum systolic upstroke with the horizontal line crossing the lowest point of the waveform.[27] PulsePen-ETT and ET use an intersection interpolating algorithm. With this algorithm, the foot of the pulse waveform is identified by the intersection of the line interpolant the early protosystolic phase of the pressure waveform, in a selected interval of its ascending slope, with the horizontal line crossing the lowest point of the waveform following the ECG complex[13] (Supplementary Figure S1). These different methods to detect the foot of the pulse waveform could partially explain the differences in repeatability between devices. Further studies are required to verify the accuracy and stability of these detection methods of the pulse wave foot, however.

Additionally, we should consider that different devices do not have the same sampling rate: Complior Analyse and PulsePen ETT and ET have a sampling rate of 1 kHz (1 point per millisecond), while SphygmoCor Vx signals are acquired at 128 Hz (1 point every 7.8 ms). The effect of the low sampling rate of SphygmoCor should be considered practically negligible at low PWV values but it may become progressively more important as aortic stiffness increases.

The 2 cuff-based devices tested in our study were characterized by lower PWV variability than devices using the carotid-femoral method. However, the good performance of the former devices can be easily explained. Indeed, PWV estimated by Mobil-O-Graph is calculated from an algorithm (ARCSolver), which includes several parameters such as age, central systolic BP values, and data derived from pulse wave analysis. As variables in the equation does not significantly change from one measurement to the other, PWV variability is expected to be low with this device. Our results agree with previous validation study involving Mobil-O-Graph, which reported a CV of 2.14% only.[10] Concerning BPLab, the quality control of PWV measurement is specifically based on the variability between 2 consecutive measurements. By definition, this approach will thus only provide high repeatability data.

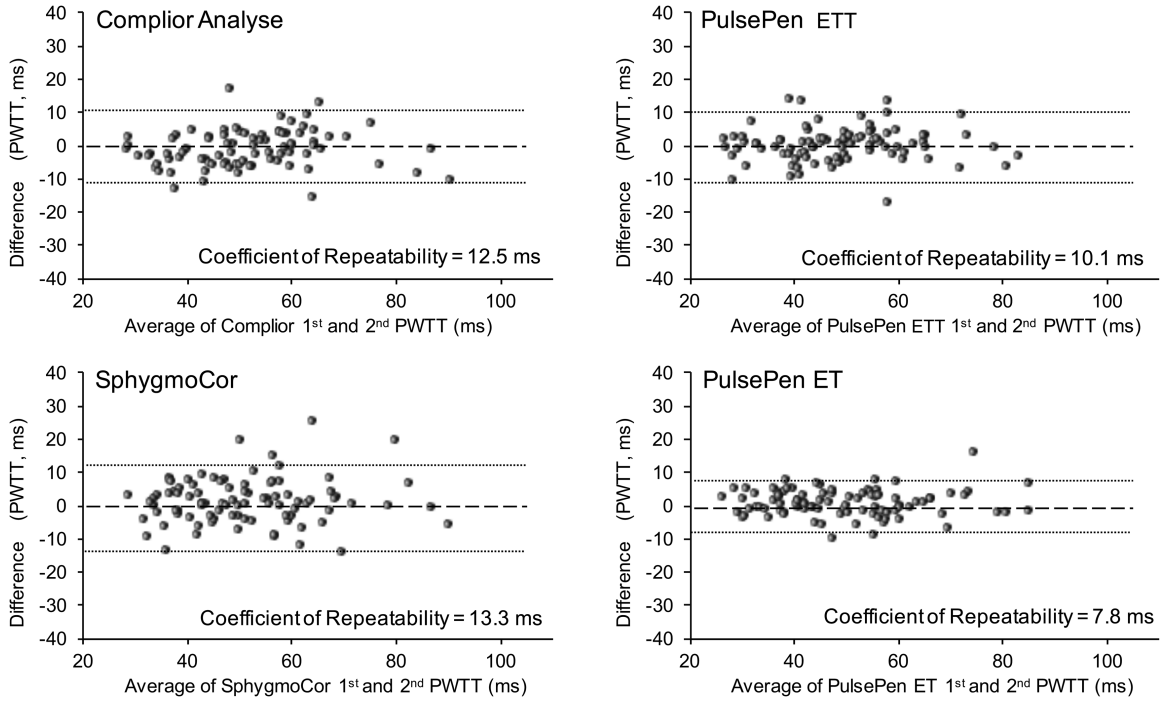

Figure 3. Bland–Altman analysis for repeated measurements of pulse wave transit time (PWTT). The Bland–Altman analysis shows differences observed between 2 measurements of PWTT according to the mean values. Coefficient of repeatability is 1.96 SD.

Since several studies[28,30–33] demonstrated a significant role of BP and heart rate in determining PWV, these 2 parameters should be expected to affect the short-term PWV variability. However, in our study, except for the Mobil-O-Graph, the differences in BP and heart rate between the 2 measurements were not significantly related to the corresponding differences in PWV. The absence of a documented correlation between the variability of the PWV and the changes in BP values does not exclude influence of BP on PWV. This must be assessed by exploring PWV variability in the medium and long-term, rather than by focusing on short-term repeatability. Only for the Mobil-O-Graph, a close link was found between the variation in PWV values and the changes in mean arterial pressure between the 2 sequential measurements, confirming that PWV values provided by Mobil-O-Graph depends on the variation of the parameters considered in the ARCSolver algorithm. Although a high repeatability is certainly an advantage for the estimation of PWV, estimating PWV from a model integrating age and BP values of the patient may carry some important limitations. First, this approach might not provide additional prognostic information beyond that already provided by the classical risk factors included in the ARCSolver algorithm used to compute PWV. Second, the estimation of PWV by such an algorithm could provide reliable values in the general population, but in individual subjects the estimate of PWV so obtained might be inaccurate as compared to values obtained through "gold standard" reference methods. Third, a BP-based algorithm for evaluation of PWV may be open to inaccuracies also when exploring changes in PWV induced by a variety of factors. As an example, using this algorithm-based approach to assess changes in PWV in response to exposure to environmental factors such as cold weather, physical activity, or assumption of food and drugs or during physical activity, might be misleading because the changes in PWV so computed might reflect changes in BP levels rather than changes in arterial distensibility. Thus, while waiting for additional evidence on the validity of this algorithm-based approach for PWV assessment, caution is needed in interpreting the results so obtained in population studies.

Even if not all the commercially available devices were represented in this study, the analyzed devices should be considered representative of the main methods used in research and in daily clinical practice. However, the results of this study are not passively exportable to other devices, only on the basis of methodological similarities.

Despite our findings were only related to the reproducibility, further data analysis from our study will assess the accuracy, i.e., the deviation of the noninvasively measured PWV values from the real PWV measured with invasive methodology. We hope that our findings will be helpful for a more accurate and thorough use of noninvasively determined PWV in clinical practice and research setting.

SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

Table 3. Relationship between differences in 1st and 2nd pulse wave velocity measurements and changes in mean arterial pressure and heart rate values for all tested devices

Device	Measurements		Univariate analysis		Multivariate analysis		
Parameters	1st	2nd	*r*	*P*	r^2 (model)	β	*P*
Complior Analyse					0.025		
PWV (m/s)	10.6 ± 3.2	10.2 ± 2.8					
MAP (mm Hg)	102.5 ± 12.2	101.1 ± 13.0	0.122	0.277		0.144	0.209
HR (bpm)	63.0 ± 10.9	62.3 ± 10.9	0.060	0.538		0.102	0.376
PulsePen-ETT					0.031		
PWV (m/s)	11.1 ± 3.3	11.0 ± 3.1					
MAP (mm Hg)	101.7 ± 13.3	99.9 ± 12.7	0.160	0.133		0.152	0.156
HR (bpm)	62.7 ± 10.2	62.1 ± 10.1	0.091	0.396		0.074	0.485
PulsePen ET					0.009		
PWV (m/s)	10.8 ± 3.1	11.0 ± 3.2					
MAP (mm Hg)	103.3 ± 13.5	101.1 ± 13.1	0.089	0.394		−0.093	0.383
HR (bpm)	63.8 ± 10.0	62.8 ± 10.5	0.016	0.882		0.027	0.796
SphygmoCor					0.038		
PWV (m/s)	10.4 ± 2.8	10.6 ± 2.8					
MAP (mm Hg)	102.2 ± 12.1	101.1 ± 12.8	0.081	0.446		0.052	0.622
HR (bpm)	63.4 ± 9.6	62.8 ± 10.4	0.188	0.075		0.179	0.094
BPLab					0.016		
PWV (m/s)	10.5 ± 1.7	10.4 ± 1.8					
MAP (mm Hg)	103.8 ± 13.6	103.6 ± 13.3	0.115	0.354		0.106	0.402
HR (bpm)	64.1 ± 9.7	63.6 ± 10.0	0.070	0.574		0.052	0.681
Mobil-O-Graph					0.172		
PWV (m/s)	10.0 ± 2.3	9.8 ± 2.3					
MAP (mm Hg)	108.1 ± 14.6	105.4 ± 14.3	0.413	<0.001		0.418	<0.001
HR (bpm)	65.2 ± 10.5	63.9 ± 9.8	0.002	0.986		−0.044	0.636

Left columns: mean values ± SD of PWV, MAP, and HR recorded during the first and second series of measurements. Middle column: results of univariate analysis. Coefficient of correlation (*r*) between ΔPWV vs. ΔMAP and ΔPWV vs. ΔHR. Right columns: multivariate analysis. ΔPWV as dependent variable and MAP and HR as independent variables. Abbreviations: HR, heart rate; MAP, mean arterial pressure; PWV, pulse wave velocity.

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DISCLOSURE

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