

A new oscillometric method for assessment of arterial stiffness: comparison with tonometric and piezo-electronic methods

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Introduction Pulse wave velocity (PWV) and augmentation index (AIx) are parameters of arterial stiffness and wave reflection. PWV and AIx are strong indicators for cardiovascular risk and are used increasingly in clinical practice. Previous systems for assessment of PWV and AIx are investigator dependent and time consuming. The aim of this study was to validate the new oscillometric method (Arteriograph) for determining PWV and AIx by comparing it to two clinically validated, broadly accepted tonometric and piezo-electronic systems (SphygmoCor and Complior).

Design and method PWV and AIx were measured up to five times in 51 patients with the SphygmoCor, Complior and Arteriograph. In 35 patients, the measurements were repeated after 1 week in a second session using the same protocol.

Results The correlations of the PWV as assessed with the Arteriograph with the values obtained using the SphygmoCor ($r=0.67$, $P<0.001$) and the Complior ($r=0.69$, $P<0.001$) were highly significant. Variability and reproducibility for PWV were best for the Arteriograph, followed by Complior and SphygmoCor. AIx (SphygmoCor

versus Arteriograph) were very closely correlated ($r=0.92$, $P<0.001$).

Perspectives The Arteriograph is a new, easy-to-use and time-effective method for assessing arterial stiffness and wave reflection. *J Hypertens* 26:523–528 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: arterial stiffness, Arteriograph, augmentation index, Complior, oscillometry, pulse wave velocity, SphygmoCor, tonometry, validation

Abbreviations: PWV, Pulse Wave Velocity; AIx, Augmentation Index; NYHA, New York Heart Association; PP, Pulse Pressure; BHS, British Hypertension Society; AAMI, Association for the Advancement of Medical Instrumentation

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Introduction

Scientific interest has focused increasingly on arterial stiffness in consequence of its pre-eminent cardiovascular significance. Pulse wave velocity (PWV) is widely recognized as a direct marker of arterial stiffness [1,2]. Augmentation and the augmentation index (AIx) are being used ever more often in studies as parameters of wave reflection [3]. PWV is correlated with very diverse familiar cardiovascular risk factors, e.g. age, systolic blood pressure, pulse pressure, left ventricular hypertrophy and coronary heart disease [4]. It has been proved that PWV is a strong vascular risk factor for prediction of mortality in the elderly [5] and in patients with end-stage renal disease [6], diabetes mellitus [7] or hypertension [8] and in the general population [9].

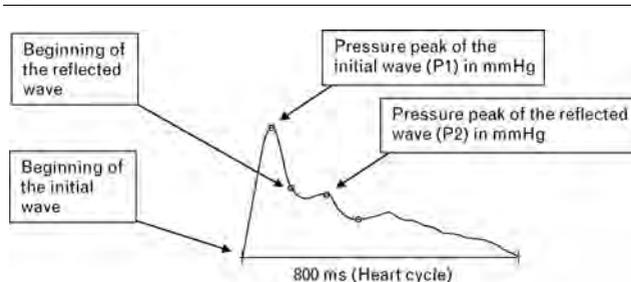
The AIx is regarded as an indirect marker for arterial stiffness and a direct measure of wave reflection. The aortic pulse wave comprises the initial pressure wave from the left ventricle and a later reflected wave [10]. The effect of wave reflection on the aortic systolic pressure peak can be described as augmentation. Accordingly, augmentation is a measure of the additional pressure caused by pulse-wave reflection that is 'seen' by the

left ventricle [11]. Dividing the augmentation pressure by the pulse pressure gives the AIx. In principle, the AIx can be obtained by calculating the quotient of the pressure peak of the initial and the reflected wave (Fig. 1). It has also been shown that AIx is closely correlated with the cardiovascular risk; e.g. it is an independent predictor of mortality in patients with end-stage renal disease [12] and correlates with the left ventricular mass both in hypertensive and normotensive young men [13].

PWV and AIx increase in a somewhat different way in parallel to the ageing process, and convey different information on arterial vascular status [14,15]. Both PWV and augmentation provide extensive information on the arterial vascular system. The prognostic significance of arterial stiffness is very great. Measurement of arterial vascular stiffness and wave reflection (PWV and AIx) can stratify patients with a high risk of cardiac and cerebral events who might profit from more aggressive cardiovascular treatment [16].

Using the SphygmoCor, both PWV and AIx can be measured non-invasively. The Complior method records pulse waves via piezo-electronic pressure transducers

Fig. 1



Original measurement of an oscillometrically generated pulse wave. An oscillometrically derived pulse wave, representing one single heart cycle, is shown. To calculate the pulse wave velocity one multiplies the distance from jugulum to symphysis (in metres) by 2. The result is then divided by the difference in time between the beginning of the first wave and the beginning of the second (reflected wave), resulting in the pulse wave velocity (PWV) in m/s. Calculation of the augmentation index: $[(P2 - P1)/\text{pulse pressure}] \times 100$.

and determines the PWV from this, but is not able to measure the augmentation. A further simplification of arterial stiffness appraisal is potentially of great clinical importance.

The objective of the study was to validate a new investigator-independent oscillometric method for determining aortic pulse wave velocity and the augmentation index against the tonometric and piezo-electronic method that is clinically validated and widely accepted. In addition, we have compared the variance and the reproducibility of the methods in patients/test individuals with a broad spectrum of cardiovascular conditions.

Methods

Patients/test individuals

A total of 51 patients from the outpatient departments for cardiology, hypertension and angiology at the Medical Polyclinic, Bonn University Hospital, who were aged from 24 to 75 years were included in the study. Exclusion criteria were atrial fibrillation, severe cardiac defects and heart failure [New York Heart Association (NYHA) criteria III–IV]. A declaration of consent was signed by all patients/test individuals investigated before the measurements were performed.

Technique

All vascular stiffness measurements were performed by the same investigator in accordance with the international guidelines [17]. The measurements were always made in the same room at a constant temperature (20°C) and were unaffected by external environmental influences.

Blood pressure was measured twice with an Omron HEM 750 and entered into the SphygmoCor system for calibration of the pulse waves. Afterwards, up to five measurements of PWV and augmentation were

made with the SphygmoCor (AtCor Medical, Sydney, Australia), Complior (Artech Medical, Pantin, France) and Arteriograph (TensioMed, Budapest, Hungary).

Measurements were repeated for 35 of the 51 patients during a second session with the same protocol, after an interval of 1 week, resulting in a total of more than 1000 measurements.

SphygmoCor

The pulse pressure curve was measured at the radial artery by means of applanation tonometry (SphygmoCor) and recorded at the same time. The pulse pressure level was calibrated against an oscillometrically measured upper-arm blood pressure (Omron HEM 750). The augmentation index (AIx) was then determined with the SphygmoCor software, initially by calculating the aortic pressures by means of a transfer function [18]. The SphygmoCor software then differentiated the initial and reflected wave, calculating the augmentation as well as the augmentation index as a quotient with the aortic pulse pressure.

To determine the pulse wave velocity, the pulse wave was recorded sequentially at the carotid artery and the femoral artery. With the SphygmoCor, the pulse wave transit time along the aorta was calculated in m/s by taking the R wave from simultaneously running ECG as a time frame and the time elapsed until the wave arrived at the carotid registration site or the femoral arterial registration site was then determined [19].

Complior

The Complior is a piezo-electronic method for determining the pulse wave velocity that is unable to effect a pulse wave analysis with determination of the augmentation. It is ECG-independent and functions by means of piezo-electronic pressure transducers, which in our case simultaneously recorded the pulse waves at the neck and at the groin.

For our measurements, the quality adjustment ‘optimum’ was chosen with a recording time of 15 s. In evaluating the pulse waves, the time interval between the carotid pulse wave and the femoral pulse wave was taken as the basis for the evaluation of the pulse waves: the point of maximum systolic upstroke served as the reference point. In relation to the distance measured, the pulse wave transit time was, likewise, calculated in m/s. Compared to the SphygmoCor, the Complior calculates the velocity of one and the same pulse wave on the basis of a simultaneous measurement technique.

Arteriograph

The Arteriograph uses an entirely novel method to determine PWV and AIx, by analysis of the oscillometric pressure curves registered on the upper arm.

The principle of the oscillometric method is based on plethysmography and registers pulsatile pressure changes in an artery. Since fluctuations in pulsatile pressure in the artery beneath the inflated pressure cuff induce periodic pressure changes in the inflated cuff, the oscillometric method measures these periodic pressure changes (oscillations) as an indirect measure for the pulsatile pressure changes in the artery beneath.

Consonant with this principle, the Arteriograph initially measures the blood pressure in the upper arm oscillometrically and afterwards produces a cuff pressure over the brachial artery that is 35 mmHg in excess of the systolic blood pressure measured. The pressure fluctuations in the brachial artery are now detected by the cuff. They are passed on to the computer and recorded and analysed as pulse waves (Fig. 1). The difference in time between the beginning of the first wave and the beginning of the second (reflected wave) is related to the distance from the jugulum to the symphysis, resulting in the PWV in m/s. The software of the Arteriograph decomposes the early, late systolic and diastolic waves and also determines the onset and the peaks of the waves. For PWV analysis, the onsets of the waves are determined by using first and second derivatives. In a technical stratagem, to intensify the signal and thus attain better differentiation of the initial wave from the reflective wave, the Arteriograph only records and analyses the pulse waves when a supra-systolic pressure of 35 mmHg has been attained.

The augmentation index corresponds to the pressure difference (amplitude difference; $P1 - P2$, Fig. 1) between the first and second wave in relation to the pulse pressure (PP). The Arteriograph calculates the AIx on the basis of the formula $AIx\% = [(P2 - P1)/PP] \times 100$ and thus provides the brachial AIx without applying a transfer function.

Statistics

All values are given as a mean and standard deviation. The correlation coefficient was defined as r according to Spearman. Differences between two groups were tested with the sample t -test or χ^2 -test. $P < 0.05$ was taken to be significant. The variance was calculated as an estimate of the measurement errors for the repeat measurements within one session according to Bland and Altman [20] in m^2/s^2 . The reproducibility was likewise calculated according to Bland and Altman as an estimate of the measurement errors for the repeat measurements between two sessions. The statistical calculations were carried out with SPSS 13.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Clinical and haemodynamic parameters of the study population

Altogether, measurements were performed in 51 patients, aged from 24 to 75 years, 32 men and 19 women (Table 1).

Table 1 Clinical parameters of the study population

	Min.	Max.	Mean	Standard deviation
Age (years)	24	75	46.3	16.7
Male	32 (62.7%)			
Smokers	10 (19.6%)			
Diabetes mellitus	4 (7.8%)			
Dyslipoproteinaemia	13 (25.5%)			
Coronary heart disease	3 (5.9%)			
Myocardial infarction	2 (3.9%)			

In 35 of these patients, measurements were repeated in a second session within 1 week. The clinical parameters are listed in Table 1 and the haemodynamic parameters in Table 2.

Comparison of the pulse wave velocity measurements

The PWV within one session and the mean values of up to five measurements per session per method were measured. Comparing the respective tonometric and piezo-electronic measurements obtained with the oscillometric method revealed highly significant correlations: Arteriograph as compared to SphygmoCor $r = 0.67$ and Arteriograph as compared to Complior $r = 0.69$, $P < 0.001$ in both instances (see Figs 2 and 3). The results obtained with the tonometric and the piezo-electronic method (SphygmoCor as compared to Complior) were likewise highly significantly correlated, with $r = 0.87$ ($P < 0.001$) according to Spearman.

Variance and reproducibility of the measurements of pulse wave velocity

As an estimate for the measurement errors for the repeat measurements, the variance within one session was lowest ($0.18 m^2/s^2$, $n = 219$) for the Arteriograph; for the Complior, it was $0.312 m^2/s^2$ ($n = 282$) and for the SphygmoCor, $0.363 m^2/s^2$ ($n = 296$). The reproducibility as an estimate for the measurement errors for the repeat measurements between two sessions was also lowest for the Arteriograph ($1.18 m^2/s^2$); as compared to Complior ($1.55 m^2/s^2$) and SphygmoCor ($1.67 m^2/s^2$).

Comparison of the augmentation index measurements

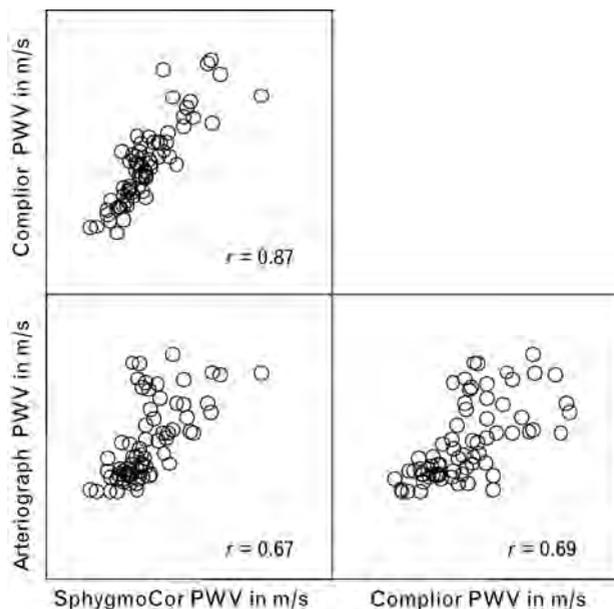
The augmentation indices were determined up to five times with the SphygmoCor and Arteriograph and the mean values were then compared in each instance. The two methods (SphygmoCor as compared to the

Table 2 Haemodynamic parameters of the study population

	N	Min.	Max.	Mean	Standard deviation
Systolic blood pressure	86	97	180	133	15
Diastolic blood pressure	86	57	104	76	10
Heart rate	86	46	93	66	8
SphygmoCor PWV	86	4	14	7.62	1.92
Complior PWV	78	4.88	12.70	8.08	1.84
Arteriograph PWV	77	5.80	11.34	7.82	1.55
SphygmoCor AIx	86	-13	51	15	16
Arteriograph AIx	77	-86	44	-29	34

AIx, augmentation index; PWV, pulse wave velocity.

Fig. 2



Comparison of the measurements of pulse wave velocity (PWV), correlation coefficient according to Spearman.

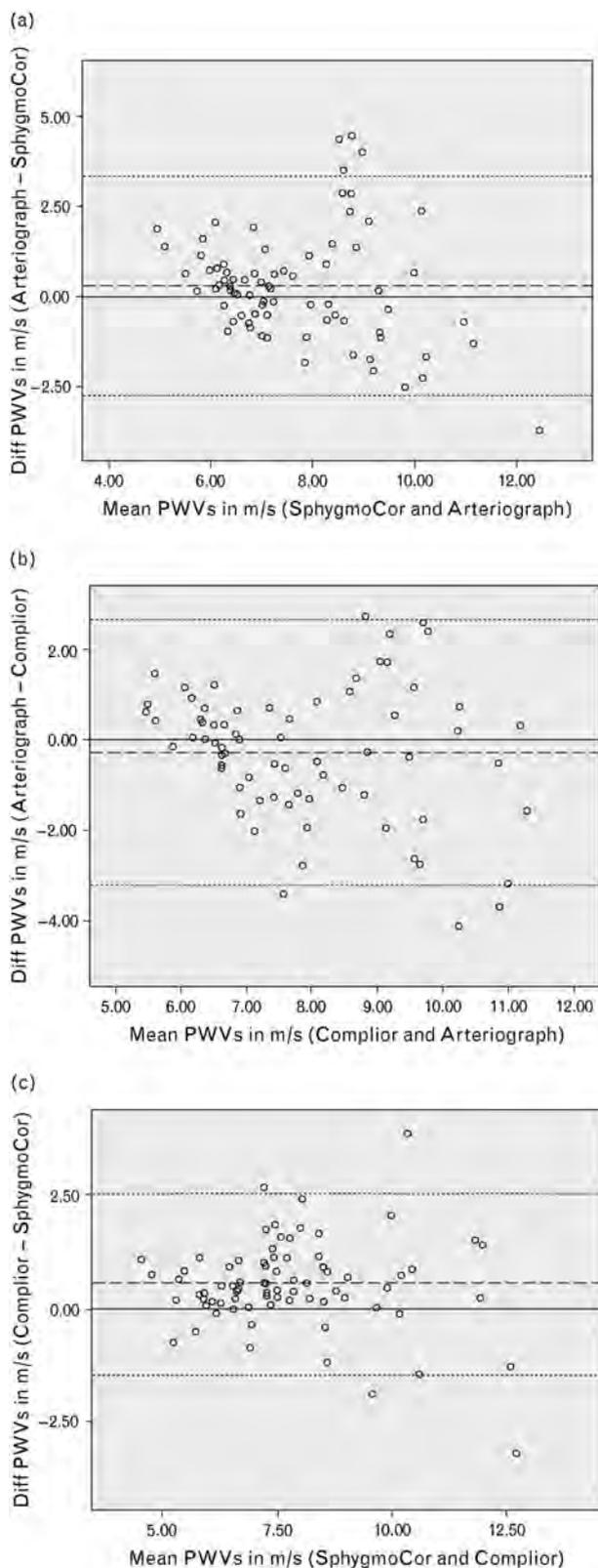
Arteriograph) correlated highly significantly with each other, with $r=0.92$ ($P < 0.001$, see Fig. 4) according to Spearman.

Discussion

The principal conclusion of this study is that the correlations of the new oscillometric measurements are highly significant compared to the tonometric and piezo-electronic appraisal of pulse wave velocity (PWV) and augmentation index (AIx). The new oscillometric instrument is therefore suitable to determine arterial stiffness and wave reflection.

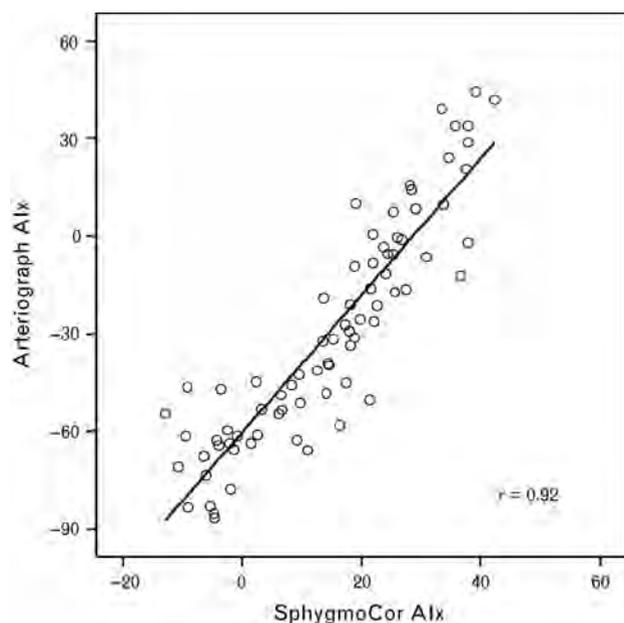
Whereas the determination of the augmentation index with the SphygmoCor is validated invasively [18], the determination of PWV is clinically validated, i.e. via indirect parameters and general consensus. Determination of PWV with the Complior is merely ‘validated’ manually against the pulse pressure curves obtained piezo-electronically [21]. The idea of tonometric PWV determination by recording the pulse wave over a specific time frame (PWV=distance covered by the pulse wave in metres divided by the time required in seconds) is widely recognized. Nevertheless, there has so far been no invasive and thus no direct validation either for SphygmoCor or for Complior. Besides the accepted concept of tonometric pulse wave determination coordinated in time, the clinical validation of the two reference methods used here is based on numerous studies which have impressively corroborated the high prognostic significance of PWV determination [16].

Fig. 3



Bland-Altman plots of different methods used to measure pulse wave velocity (PWV) in m/s: Arteriograph, SphygmoCor and Complior.

Fig. 4



Comparison of the augmentation index (AIx) measurements, Arteriograph (brachial augmentation index) versus SphygmoCor (aortic augmentation index); correlation coefficient according to Spearman.

Both established methods used here (SphygmoCor and Complior) are widely recognized for determination of PWV. Indeed, it has been shown in our study that the correlation of the PWV determined with SphygmoCor and Complior is very high ($r=0.87$); however, as these instruments have only been validated indirectly (see above), we decided to validate the new oscillometric method against these two generally accepted instruments.

The present study had the following sources of error. The SphygmoCor calculates the pulse wave transit time along the aorta by taking the R wave from the simultaneously recorded ECG as the time reference frame for the pulse wave. The time elapsing before the wave arrives at the carotid or femoral registration site is then determined. No deviations of the isovolumetric contraction time, which might result in systematic measurement variations, e.g. in the presence of heart failure, are considered. Moreover, the pulse wave is difficult to measure in some cases. Under certain circumstances (e.g. obesity), it may only be recorded with numerous artefacts at the femoral artery and additional breathing-dependent variations at the carotid artery. Nevertheless, the SphygmoCor is broadly accepted and is, at present, the most commonly used device for determining the direct and indirect vessel stiffness parameters PWV and AIx.

Distance measurement is also subject to pitfalls: in the case of the SphygmoCor between the jugulum and the carotid or the femoral measurement point, and in

the case of the Arteriograph between the jugular fossa and the symphysis. However, this possible source of error is likely to apply to a similar extent to all three instruments used.

The blood pressure measurement integrated into the Arteriograph is validated in accordance with the protocols of the British Hypertension Society (BHS) and the Association for the Advancement of Medical Instrumentation (AAMI) [22]. The SphygmoCor has first to be calibrated against a previous blood pressure measurement. In contrast to the Arteriograph, recording of blood pressure and the pulse wave within one cycle of measurement is not possible. In addition, determination of PWV within one cardiac cycle is not possible with the SphygmoCor for methodological reasons, but is entirely possible with the Complior and the Arteriograph.

A drawback of the Complior is that the distance actually traversed by the pulse wave can only be estimated. The pulse waves of the two sites of registration (carotid artery and femoral artery) are recorded simultaneously without determining the beginning of the pulse wave at the heart; however, since the pulse wave does not pass directly to the femoral artery from the carotid artery, the distance covered by the pulse wave from the heart to the carotid artery is contained in the time difference from the femoral artery, and thus cannot be determined exactly for methodological reasons. The extent of this systematic error has not been adequately investigated up to now. In several studies in which the PWV values obtained with the Complior were compared with those obtained using other methods, there was a tendency for higher values to be measured with the Complior; this may amount to up to 50% [23]. In the present study, the PWV measured with the Complior were likewise the highest, but the difference was only marginal. The mean values of all measurements for the Complior were 8.1 m/s, for the Arteriograph 7.8 m/s and for the SphygmoCor 7.6 m/s (Table 2).

The reason why we have found extremely strong correlations in the AIx between Arteriograph and SphygmoCor could be that the calculation of the AIx was based on the same formula in both devices, furthermore the physiological basis to calculate AIx (amplitude of the early and late systolic waves) was the same in both devices. Nevertheless, they produced numerically different results due to the fact that we compared the centrally derived AIx (SphygmoCor) to the brachial non-transferred AIx (Arteriograph).

We assume that the reason why we have found less powerful (although highly significant) correlations in the aortic PWV between Arteriograph versus SphygmoCor and Complior is that both SphygmoCor and Complior determine the aortic PWV by using the time difference in

the occurrence of the pulse wave between the measuring sites, namely the carotid and femoral arteries. For the PWV calculation the distance is measured in metres between the measuring sites; however, the wave propagation is opposite between the measuring sites, which makes the precise determination of the so-called 'true' aortic PWV theoretically impossible.

The Arteriograph determines the aortic PWV by measuring the time elapsed between the first wave ejected from the left ventricle to the aortic root, and its reflection from the bifurcation as the second systolic wave, consequently no opposite direction of the propagation modifies the measured value. The measured distance between the sternal notch and the upper edge of the pubic bone is anatomically roughly equal to the aortic root–bifurcation distance. Thus the Arteriograph-measured aortic PWV uses a different method, with a different theoretical and practical background, to determine PWV, and this could be the reason for the lower correlation power, as compared to the AIx.

There are specific limitations to the Arteriograph. The biggest limitation of the Arteriograph is the positioning of the cuff, which has to be very tightly wrapped around the arm. This is crucial in order to get exact measurements. Another limitation is that during measurements the arm of the person has to be absolutely motionless.

Compared to the variance and the reproducibility of the PWV measurements, the Arteriograph had the least variation, followed by the Complior and then by the SphygmoCor. The variances determined for the Complior and the SphygmoCor in our study were lower by a factor of 0.7 than those published previously [19,24]; however, the number of measurements taken in our study was very much greater than in the earlier comparative studies.

Our study shows that the new oscillometric determination of arterial stiffness and wave reflection (pulse wave velocity and augmentation index) correlates highly significantly with the results of conventional tonometric and piezo-electronic measurement techniques. The Arteriograph is a new investigator-independent oscillometric method for measuring vascular stiffness and wave reflection, with a high reproducibility. Further studies should investigate normal values of this new method. Additionally, the next step of validation of the Arteriograph PWV measurement could be the generation of clinical evidence that the Arteriograph does similarly, or better, in terms of prognostic value than the reference methods.

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