

Assessment of arterial stiffness in hypertension: comparison of oscillometric (Arteriograph), piezoelectronic (Complior) and tonometric (SphygmoCor) techniques*

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Background Arterial stiffness, measured as aortic pulse wave velocity (PWV), and wave reflection, measured as augmentation index (AIx), are independent predictors for total and cardiovascular morbidity and mortality. The aim of this study was to compare a new device, based on oscillometric pressure curves (Arteriograph), which simultaneously measures PWV and AIx, with standard techniques for measuring PWV (Complior) and AIx (SphygmoCor) in untreated hypertensive patients.

Methods We compared PWV and AIx measured using the Arteriograph with corresponding Complior and SphygmoCor measurements in 254 untreated hypertensive patients, age 48 ± 14 years (mean \pm SD, range 17–85 years).

Results Arteriograph PWV and AIx were closely related with Complior ($r = 0.60$, $P < 0.001$) and SphygmoCor ($r = 0.89$, $P < 0.001$), respectively. Using stepwise regression analysis, the independent determinants of Arteriograph PWV were age, mean arterial pressure, heart rate and sex ($r^2 = 0.44$, $P < 0.0001$) and for AIx were age, weight, mean arterial pressure, heart rate and sex ($r^2 = 0.65$, $P < 0.0001$). The bias between the different techniques was determined by age and sex for PWV and age, body weight, sex, heart rate and mean arterial pressure for AIx. Bland–Altman plots showed

that although the techniques were closely related, the limits of agreement were wide.

Conclusion Although Arteriograph values and the determinants of PWV and AIx are in close agreement with corresponding parameters obtained by Complior and SphygmoCor, respectively, the techniques are not interchangeable. *J Hypertens* 27:2186–2191 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: arterial stiffness, arteriograph, augmentation index, hypertension, pulse wave velocity

Abbreviations: AIx, augmentation index; BP, blood pressure; CAD, coronary artery disease; CI, confidence interval; ESH, European Society of Hypertension; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity

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Introduction

Arterial stiffness is now regarded as an important marker of cardiovascular risk [1] and measured as pulse wave velocity (PWV) has been shown to be a strong independent predictor of cardiovascular morbidity in hypertension [2], type II diabetes [3] and of all-cause mortality in patients with hypertension [2] end-stage renal disease [4], and in the general population [5] and is recommended in current European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines for risk assessment in hypertension [6]. Wave reflection as an augmentation index (AIx), a composite of PWV, arterial wave reflection and left ventricular ejection is an independent factor associated with poor survival in end-stage renal disease [7] and the extent of angiographic coronary artery disease (CAD) in men of less than 60 years of age [8].

Currently, two systems are in common use: Complior system (Artech Medical, Pantin, France) simultaneously

records pressure waves in the carotid and femoral arteries by using a piezoelectronic device, and the PWV is calculated by dividing the distance between the two sites by the transit time between waves. The SphygmoCor (version 8.1; AtCor Medical, Inc., Sydney, Australia) utilizes radial applanation tonometry and the application of a generalized transfer function to measure wave reflection as AIx and aortic pressures noninvasively. The Arteriograph (TensioMed Ltd., Budapest, Hungary) is a recently developed computerized device using an oscillometric method to determine PWV and AIx. Oscillometric pressure curves (pulsatile pressure changes in the brachial artery) registered in the upper arm are detected by plethysmography. Fluctuations in pulsatile pressure in the artery beneath an inflated pressure cuff induce periodic pressure changes in the inflated cuff. These periodic pressure oscillations provide an indirect measure for the pulsatile pressure changes in the artery beneath [9]. The Arteriograph, which yields a simultaneous measure of brachial blood pressure (BP), PWV and AIx, has recently been validated against the

* This paper is dedicated to Professor John Feely.

Complior and SphygmoCor largely in a healthy population [9] and for PWV in 64 patients with longstanding hypertension [10]. We compared the PWV and AIx measures obtained using the Arteriograph with those generated by the Complior and SphygmoCor and explored the determinants of these measures using the respective techniques in a large population of untreated patients referred for assessment of high BP. In addition, we used a statistical method for assessing agreement between two methods of clinical measurement as described by Bland and Altman [11].

Material and methods

Patients

We studied 254 untreated hypertensive patients with elevated BP ($\geq 140/90$ mm Hg) on three occasions and confirmed by ambulatory BP recording (daytime $>135/85$ mmHg). Patients' age was 48 ± 14 (mean \pm SD, range 17–85 years) and 44% were women (Table 1). None of the patients were on antihypertensive medication or other vasoactive agents, including statins, oral contraceptives, steroids or hormone replacement therapy. None of the patients had secondary hypertension, peripheral vascular disease, cerebrovascular disease and CAD, valvular heart disorders, dysarrhythmias, diabetes, heart failure or other significant medical conditions.

All measurements were made in the same temperature-controlled room (22°C). Body weight, height, waist and hip measurements were recorded in each patient and BMI was calculated (kg/m^2). Patients gave informed consent, and the study had institutional ethics committee permission.

Reproducibility and repeatability for PWV and AIx measured using the Arteriograph were performed in 40 untreated hypertensive patients. Two measurements were performed at the same session by the same operator, and the measurements were repeated 1 week later.

Table 1 Clinical characteristics of untreated hypertensive patients ($n = 254$, mean \pm SD)

Variable	Untreated hypertensive patients
Age (years)	48 ± 14
Sex (male/female, %)	56:44
Height (cm)	170 ± 11
Weight (kg)	84 ± 18
BMI (kg/m^2)	29 ± 7
Nonsmoker/exsmoker/smoker (%)	50/27/23
HR (/min)	69 ± 13
SBP (mmHg)	146 ± 20
DBP (mmHg)	90 ± 10
PP (mmHg)	56 ± 46
MAP (mmHg)	109 ± 13
PWV (m/s) (Arteriograph)	9.7 ± 2
PWV (m/s) (Complior)	10.5 ± 2
AIx (%) (Arteriograph)	-0.65 ± 31
AIx (%) (SphygmoCor)	27.3 ± 14

AIx, augmentation index; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity.

Blood pressure measurements

Patients rested in a supine position for 5 min in a quiet room at 22°C before the baseline haemodynamic measurements were obtained. Brachial BP and heart rate (HR) were measured in the right arm with an automated digital oscillometric sphygmomanometer (Omron, Model HEM 705-CP; Omron Corporation, Shimogyo-ku, Kyoto, Japan). Three readings separated by 1-min intervals were taken, and the mean was used for the analysis.

Measures of pulse wave velocity and wave reflection

The carotid–femoral PWV was measured with an automated system Complior (Artech Medical) using the foot-to-foot method. The carotid and femoral waveforms were acquired simultaneously with two pressure-sensitive transducers. The distance between the two arterial sites was measured on the body using a tape measure, and PWV was calculated as the distance divided by time (m/s). Aortic pressure waveform was derived from radial applanation tonometry using a previously validated transfer function relating radial to aortic pressure waveform within the system software of the SphygmoCor (SphygmoCor, version 8.1; AtCor Medical, Inc.) by a single operator. Ascending aortic pressures and the AIx were derived from the aortic pressure waveform, as described previously [12].

Arteriograph

After Complior and SphygmoCor measurements, the Arteriograph cuff was applied on the left arm for measurement of BP, PWV (m/s) and AIx (%) with the computerized portable device, Arteriograph (TensioMed Ltd.).

The Arteriograph determines PWV and AIx by analysis of the oscillometric pressure curves registered on the upper arm. It initially measures the BP in the upper arm oscillometrically and afterwards produces a cuff pressure over the brachial artery that is 35 mmHg in excess of the SBP 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. The difference in time between the beginning of the first wave and the beginning of the second (reflected wave) is related to the measured distance from the jugulum to the symphysis, resulting in the PWV in m/s. The software of Arteriograph decomposes the early, late systolic and diastolic waves and also determines the onset and peaks of the waves. For PWV analysis, the onsets of the waves are determined by using first and second derivatives. 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 supra-SBP of 35 mmHg has been attained.

The AIx corresponds to the pressure difference (amplitude difference; $P_1 - P_2$) 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 [9].

Statistical analysis

All data were analysed using JMP software (version 7.0, SAS for Windows; SAS Institute Inc., Cary, North Carolina, USA). Results were expressed as mean and standard deviation (mean \pm SD) and confidence intervals (CIs) for continuous and percentages for categorical data. A *P* value of less than 0.05 was considered significant. The difference observed between the average values of PWV (Arteriograph vs. Complior) according to Bland–Altman [11] and the relationship between the values of AIx (Arteriograph vs. SphygmoCor) in scatter plot were likewise calculated (MedCalc version 9.3.9.0; MedCalc Software bvba, Mariakerke, Belgium) as an estimate of measurement error for the repeat measurements between the two methods. For AIx, we normalized the data to the SD, as values for Arteriograph are largely negative, whereas those for SphygmoCor were positive. The relationship between parameters was analysed using correlation (Spearman ρ). Regression analysis of PWV and corrected AIx were analysed separately by using the following determinants: age, body height and weight, sex, HR and mean arterial pressure (MAP, forward stepwise regression). In addition, the differences between the standard and studied technique were calculated and regression analysis applied to obtain the determinants (as above) of any discrepant bias. Regression coefficients and 95% CIs are presented.

Results

The characteristics of the untreated hypertensive patients are shown in Table 1.

The correlation coefficients between two consecutive measurements using the Arteriograph on the same day by same operator were: SBP ($r=0.92$), DBP ($r=0.95$), PP ($r=0.88$), MAP ($r=0.96$), PWV ($r=0.95$) and AIx ($r=0.99$) (all $P < 0.0001$). The correlation coefficients for two measurements performed a week apart were: SBP ($r=0.89$), DBP ($r=0.75$), PP ($r=0.83$), MAP ($r=0.85$), PWV ($r=0.97$) and AIx ($r=0.96$) (all $P < 0.0001$). The coefficients of variation of two measurements of PWV and AIx performed on the same day were 0.08 m/s and 0.55% and 0.1 m/s and 0.77% performed a week later.

The values of BP measurements by Arteriograph and digital oscillometric sphygmomanometer (Omron, Model HEM 705-CP; Omron Corporation) were correlated for SBP ($r=0.81$, $P < 0.001$), DBP ($r=0.79$, $P < 0.001$) and PP ($r=0.67$, $P < 0.001$). The difference observed between the average values of SBP and DBP (mmHg) for both methods (Arteriograph and sphygmomanometer) using Bland–Altman analysis is presented in Fig. 1a and b.

Difference observed between the average values of PWV using both methods with Bland–Altman analysis is presented in Fig. 1c. PWV measured by Complior and Arteriograph was positively correlated ($r=0.60$, $P < 0.0001$) as shown in Fig. 2a. PWV measured by Arteriograph and Complior was significantly correlated with age ($r=0.56$ vs. 0.50 , $P < 0.001$), height ($r=-0.32$ vs. -0.19 , $P < 0.01$), HR ($r=0.21$ vs. 0.19 , $P < 0.05$), SBP ($r=0.40$ vs. 0.45 , $P < 0.001$), DBP ($r=0.33$ vs. 0.31 , $P < 0.001$) and MAP ($r=0.45$ vs. 0.44 , $P < 0.001$), and in the case of Arteriograph, body weight was also significant ($r=-0.14$, $P < 0.05$). In stepwise regression analysis of PWV (Arteriograph), the independent determinants were age, sex, HR and MAP ($r^2=0.44$, $P < 0.0001$), and for PWV (Complior), age, HR and MAP ($r^2=0.37$, $P < 0.0001$), although sex was not significant (Table 2).

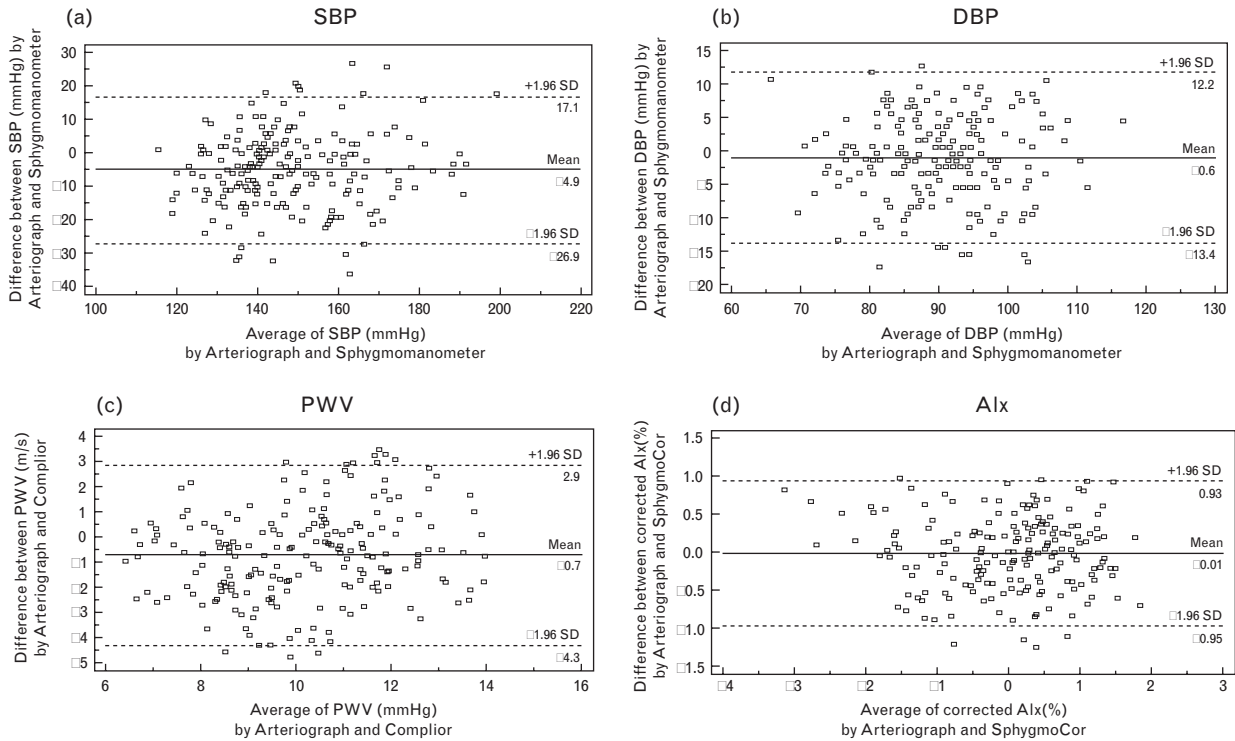
Differences observed between the average values of AIx (%) of both methods using Bland–Altman analysis are presented in Fig. 1d. The two methods of measuring AIx (SphygmoCor as compared with Arteriograph) correlated significantly with each other ($r=0.89$, $P < 0.001$), as shown in Fig. 2b. The AIx measured by Arteriograph and SphygmoCor was significantly correlated with age ($r=0.60$ vs. 0.58 , $P < 0.001$), height ($r=-0.45$ vs. -0.44 , $P < 0.01$), body weight ($r=-0.45$ vs. -0.41 , $P < 0.001$), HR ($r=-0.15$ vs. -0.19 , $P < 0.05$), SBP ($r=0.35$ vs. 0.29 , $P < 0.001$), DBP ($r=0.32$ vs. 0.32 , $P < 0.001$) and MAP ($r=0.44$ vs. 0.44 , $P < 0.001$). In stepwise regression analysis, the independent determinants of AIx measured by Arteriograph were: age, body weight, MAP, HR and sex ($r^2=0.65$, $P < 0.0001$) (Table 3), and by SphygmoCor were: age, body weight, MAP, HR, height and sex ($r^2=0.54$, $P < 0.0001$) (Table 3). A regression model was constructed to analyse the determinants of the residual difference between the different techniques: Arteriograph vs. Complior for PWV and Arteriograph vs. SphygmoCor for corrected AIx (Table 4). For PWV, the bias between PWV measured with the Arteriograph and the Complior increased in young male patients. For AIx, the difference between the Arteriograph and SphygmoCor measurements was determined by age, body weight, sex, HR and MAP (Table 4); the bias decreased with body weight and HR and increased with age, female sex and MAP.

Discussion

The aim of this study was to compare the indices of arterial stiffness measured by Arteriograph with those measured by Complior and SphygmoCor in an untreated hypertensive population to study whether the determinants of PWV and AIx were similar with the different techniques and finally to explore the determinants of the discrepancies observed between the different techniques.

The present study shows that PWV and AIx measurements obtained with the Arteriograph were significantly

Fig. 1



Bland–Altman analysis of the difference in values obtained by comparative techniques vs. average of the techniques. (a) SBP and (b) DBP by Arteriograph and Omron Sphygmomanometer, (c) pulse wave velocity by Arteriograph and Complior, (d) augmentation index by Arteriograph and SphygmoCor. AIx, augmentation index; PWV, pulse wave velocity.

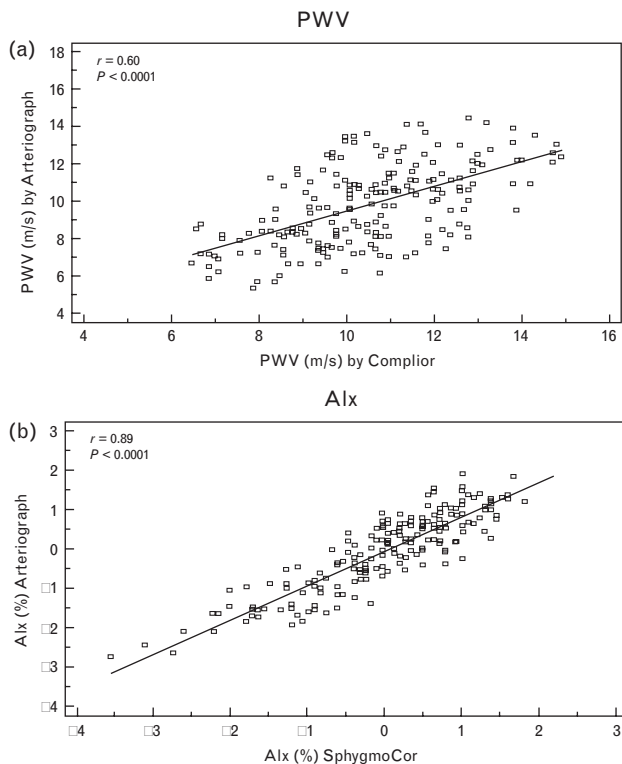
correlated with piezoelectronic PWV (Complior, $r = 0.60$) and tonometric AIx (SphygmoCor, $r = 0.89$) and extends similar observations by Baulmann *et al.* [9] in a largely normotensive or treated hypertensive population with correlations of 0.69 and 0.92, respectively, and by Rajzer *et al.* [10] for PWV by Arteriograph and Complior ($r = 0.36$) in 64 patients with longstanding hypertension. The lower correlation coefficient for measurements observed in the present study may in part be expected as one moves from a normotensive to a hypertensive population with a wider age and BP range. Similarly, our study examined a wider range of values for PWV, 5.4–14.5 compared with 5.8–11.3 m/s in the study by Baulmann *et al.* [9] but similar to that of Rajzer *et al.* [10]. Covering a wider range of values is of importance as the major purpose of such measurements in clinical practice is to stratify risk in patients with medical conditions, such as hypertension, renal failure and so on, in which PWV values of more than 12 m/s are used to influence therapy and determine prognosis. Both Baulmann *et al.* [9] and Rajzer *et al.* [10] reported a similar divergence for PWV determined by Arteriograph and Complior and indeed also with the SphygmoCor.

Although the strength of relationship between values by Arteriograph and SphygmoCor/Complior is reassuring,

the correlation coefficient does not measure agreement and is misleading when comparing two techniques [11]. A more appropriate statistical approach is required to estimate the 95% CI for the ability of one method to predict another. By applying Bland–Altman analysis (Fig. 2), it is clear that the extent of variation for all parameters is greater than one would accept and is outside the published reproducibility of the individual techniques employed and greater than the SD of both PWV and AIx in our population. For PWV, a value obtained by one technique may vary by ± 3.6 m/s and by $\pm 17\%$ for AIx to that determined by the other technique. The former is similar to that seen in the studies by Baulmann *et al.* [9] and Rajzer *et al.* [10], although such data were not reported for AIx. Such a magnitude of difference implies that studies using one technique cannot utilize the others for follow-up.

A second objective of our study was to compare the determinants of PWV and AIx as recorded by the different techniques, although our findings relate only to a cohort of untreated hypertensive patients. A number of physiological factors influence AIx and PWV, including age [13], body height [14], HR [15], SBP and DBP [16], MAP [17] and PP [18]. The present study shows that age, MAP and HR are the main determinants of PWV

Fig. 2



Correlation analysis of pulse wave velocity (m/s) obtained with Arteriograph and Complior (a) and corrected augmentation index (%) obtained with Arteriograph and SphygmoCor (b). Alx, augmentation index; PWV, pulse wave velocity.

regardless of which technique is employed, with sex only a significant determinant for PWV measured using the Arteriograph. For Alx, age, body weight, sex, HR and MAP were independent determinants with both techniques, with body height only significant for the SphygmoCor. Exploring the determinants of the differences between the different techniques showed that for PWV, the bias between Arteriograph and the Complior increased with young age and male sex. For Alx, age, female sex and BP increased, whereas body weight and

Table 2 Stepwise regression analysis of using pulse wave velocity (m/s) by Arteriograph and Complior as the dependent variable (n = 254)

Variables	r ²	β	SE	P
Model for PWV (Arteriograph, m/s) r ² = 0.44, P < 0.0001				
Age (years)	0.32	0.04	0.004	<0.0001
Sex (female)	0.05	0.22	0.054	<0.0001
HR (/min)	0.01	0.01	0.004	0.04
MAP (mmHg)	0.07	0.02	0.005	<0.0001
Model for PWV (Complior, m/s) r ² = 0.37, P < 0.0001				
Age (years)	0.25	0.03	0.004	<0.0001
Sex (female)	0	0.08	0.056	0.15
HR (/min)	0.017	0.01	0.005	0.025
MAP (mmHg)	0.10	0.024	0.005	0.0001

HR, heart rate; MAP, mean arterial pressure; PWV, pulse wave velocity.

Table 3 Stepwise regression analysis using corrected augmentation index (%) by Arteriograph and SphygmoCor as the dependent variable (n = 254)

Variables	r ²	β	SE	P
Model for Alx (%) r ² = 0.65, P < 0.0001 (Arteriograph)				
Age (years)	0.36	0.033	0.0029	<0.0001
Weight (kg)	0.14	-0.02	0.0026	<0.0001
Height (cm)	0.005	-0.009	0.0046	0.06
Sex (female)	0.034	0.21	0.049	<0.0001
HR (/min)	0.077	-0.024	0.0033	<0.0001
MAP (mmHg)	0.038	0.025	0.0035	<0.0001
Model for Alx (%) r ² = 0.54, P < 0.0001 (SphygmoCor)				
Age (years)	0.34	0.032	0.003	<0.0001
Weight (kg)	0.11	-0.014	0.005	0.047
Height (cm)	0.04	-0.015	0.005	0.0057
Sex (female)	0.01	0.11	0.057	0.047
HR (/min)	0.02	-0.017	0.004	<0.0001
MAP (mmHg)	0.03	0.017	0.004	<0.0001

Alx, augmentation index; HR, heart rate; MAP, mean arterial pressure; PWV, pulse wave velocity.

HR decreased the discrepancy between the two techniques. For PWV, the greater bias in young men may reflect the high prevalence of abdominal obesity in these patients, which may influence the distance measured to calculate PWV; however, more studies are needed to investigate this observation. The greater bias observed between Alx measured with the Arteriograph and SphygmoCor with older age, female sex and higher BP may suggest differences in identification of the inflection point at high levels of Alx; how higher body weight and HR may improve bias is not entirely clear. More studies are needed to explore these interesting data in different populations as our results apply only to hypertensive patients.

In conclusion, in comparative terms, the Arteriograph is easier to apply as it measures BP, PWV and Alx simultaneously. The precise placement of the brachial cuff is less critical in contrast to the placing of sensors over the carotid and femoral artery or tonometers over the radial

Table 4 Stepwise regression analysis showing the determinants of the residuals in pulse wave velocity (m/s, top) and augmentation index (% , bottom) measured by Arteriograph, Complior and SphygmoCor (n = 254)

Variables	r ²	β	SE	P
Residual of PWV (m/s) measured by Arteriograph and Complior (r ² = 0.07, P < 0.001)				
Age (years)	0.024	-0.02	0.009	0.02
Sex (female)	0.038	-0.34	0.13	0.008
HR (/min)	0.004	-0.009	0.01	0.37
MAP (mmHg)	0.0002	0.002	0.01	0.86
Residual of Alx measured by Arteriograph and SphygmoCor (r ² = 0.58, P < 0.0001)				
Age (years)	0.29	0.56	0.064	<0.0001
Weight (kg)	0.12	-0.30	0.06	<0.0001
Height (cm)	0.0008	-0.065	0.10	0.51
Sex (female)	0.058	4.92	1.07	<0.0001
HR (/min)	0.073	-0.54	0.07	<0.0001
MAP (mmHg)	0.039	0.54	0.08	<0.0001*

Alx, augmentation index; HR, heart rate; MAP, mean arterial pressure; PWV, pulse wave velocity.

(or carotid) artery. The low correlation observed between the BP values measured using a standard sphygmomanometer and the Arteriograph, however, suggests that the latter cannot be used to reliably measure BP on its own. It has less variation and similar reproducibility as the other two techniques, and the determinants for both AIx and PWV are generally similar for the different methods. As there is a poor agreement between PWV and AIx measured with the different devices, these techniques cannot be used interchangeably. Furthermore, as the Complior method for measuring PWV has been validated against the gold standard manual method [19], a poor agreement with the Arteriograph method suggests that the latter is not a suitable method for assessing PWV in clinical practice.

To conclude, the Arteriograph is an operator-independent, reproducible oscillometric method for the estimation of arterial stiffness and wave reflection in hypertensive patients and, as shown previously, in normotensive populations. Although the Arteriograph, SphygmoCor and Complior are not interchangeable, the Arteriograph cannot be considered the 'gold standard' technique pending prospective outcome studies.

Acknowledgement

There are no conflicts of interest.

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