Comparison of aortic pulse wave velocity measured by three techniques: Complior, SphygmoCor and Arteriograph

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Background **New 2007 European Society of Hypertension guidelines recommend measuring arterial stiffness in patients with arterial hypertension, suggesting a carotid–femoral pulse wave velocity over 12 m/s as an estimate of subclinical organ damage. Considering this cutoff point, it is worth exploring whether or not there are significant differences in results obtained using various techniques for measuring aortic pulse wave velocity. The aim of the study was to compare aortic pulse wave velocity measurements using Complior, SphygmoCor, and Arteriograph devices, and to assess the effect of pulse wave transit time and traveled distance on pulse wave velocity values.**

Methods **Aortic pulse wave velocity was measured on a single visit, using these devices, in randomized order, in a group of 64 patients with grade 1 or 2 arterial hypertension.**

Results **Aortic pulse wave velocity measured using Complior (10.1 ± 1.7 m/s) was significantly higher than that obtained using SphygmoCor (8.1 ± 1.1 m/s) or Arteriograph (8.6 ± 1.3 m/s). No differences were noted between pulse wave velocity measurements using SphygmoCor and Arteriograph. Between-method comparison revealed that differences in traveled distance were significant: Complior versus Arteriograph [0.09 m, Confidence interval (CI): 0.08–0.12 m, *P*<0.05], Complior versus SphygmoCor (0.15 m, CI: 0.13–0.16 m, *P*<0.05), Arteriograph versus SphygmoCor (0.05 m, CI: 0.03–0.07 m, *P*<0.05). No between-method differences were found for transit times.**

Conclusion **Differences in pulse wave velocity obtained by compared devices resulted primarily from using various methods for measuring traveled distance. It appears reasonable to establish uniform principles for the measurement of traveled distance. Because a large number of prognosis/survival studies used direct distance between carotid and femoral sites of pulse wave recording, this distance should be mostly recommended. *J Hypertens* 26:2001–2007 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Keywords: carotid–femoral pulse wave velocity, pulse traveled distance, pulse wave transit time, Arteriograph, Complior, SphygmoCor

Abbreviations: ECG, electrocardiogram; PWV, pulse wave velocity; RT S35, return time at cuff pressure 35 mmHg over systolic pressure

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Introduction

Over the last years, measurement of large artery stiffness as a factor determining development of cardiovascular complications has become one of the most important issues in patients with arterial hypertension and other cardiovascular diseases. The 'Expert consensus document on arterial stiffness' [1] considers carotid–femoral (aortic) pulse wave velocity (PWV) as the gold standard for measurement of arterial stiffness.

New guidelines of the European Society of Hypertension (ESH) and European Society of Cardiology (ESC)-'2007 Guidelines for the Management of Arterial Hypertension' [2] not only recommend measurements of arterial stiffness in patients with arterial hypertension, but also a threshold of carotid–femoral PWV greater than 12 m/s has been suggested as an estimate of subclinical organ damage. Interest in measuring carotid–femoral PWV in patients with arterial hypertension is expected to grow in line with increasing availability of new measuring devices.

Currently available devices differ significantly with respect to measuring pulse transit time (TT). Each manufacturer recommends a device-specific arbitrary estimation of the distance traveled by the pulse wave (i.e., an indirect estimation of the distance on body surfaces). This distance (D) is another factor in the equation for calculating PWV (i.e., $PWV = D/TT$).

If carotid–femoral PWV is greater than 12 m/s it is to be considered the cutoff point for arterial stiffness and, consequently, used to stratify risk and prognosis, the question arises whether significant differences exist in

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the results obtained by the devices currently used to measure aortic PWV. Our institution has extensive experience in measuring carotid–femoral PWV using Complior and SphygmoCor, the most frequently used devices in PWV studies [3–8]. Arteriograph represents a slightly different approach for calculating aortic PWV [9].

The aim of this study was to compare aortic PWV measurements using Complior, SphygmoCor, and Arteriograph devices, and to assess the effect of pulse wave transit time and traveled distance on PWV values.

Material and methods

Carotid–femoral PWV was measured in a group of 64 patients (39 men and 25 women) with grade 1 or 2 arterial hypertension, diagnosed according to ESC/ESH guidelines [2]. Three devices, namely Complior, SphygmoCor and Arteriograph were used for aortic PWV measurement, at the same visit, in a random order, according to standards described in 2007 ESH/ESC guidelines [2]. Before calculating PWV, blood pressure (BP) and heart rate were measured three times, at 2 min intervals, on the nondominant arm, using an automatic oscillometric device (Omron Matsusaka Co., Ltd., Japan. EU Representative: Omron HEALTHCARE Europe B.V., The Netherlands M5-I) [10]. The mean value from these three measurements was used for further analysis. The study protocol was approved by the local ethics committee and informed consent was obtained from each study participant. Carotid–femoral PWV was measured using Complior (Colson, Garges les Genosse, France. Software version 2.1) according to Asmar *et al.* [11]. Complior has two TY-306 pressure transducers (Fukuda Denshi Co., Ltd.,Tokyo, Japan) for simultaneous recording of carotid and femoral pulse waves. When the operator observed a pulse waveform of sufficient quality, digitization was suspended and calculation of the time delay between the two pressure waveforms was initiated. On the computer display, two vertical lines indicate the positions of the maximal rate of change of the pressure waveforms. The delay between the two pulse waves in this device is determined by performing a correlation between the data of the two waveforms. Hence, waveform data are transferred into the correlation array from a point 100 ms before the first line position and up to 50 ms after the second line. This ensures that the correlation is performed on the initial rise of the pulse until just after the true pulse peak. The correlation algorithm is then performed, the distal pressure upstroke is time-shifted by subtracting one sample period, and the correlation coefficient is again calculated. The correlated waveforms are then displayed in their shifted positions, and the calculated pulse delay (transit time) is printed. PWV is then calculated using measurements of transit time and distance traveled by the pulse wave, between the two recording sites (i.e., $\Delta d/\Delta t$). As recommended by the manufacturer and similar to other investigations, distance traveled by the pulse wave was measured between two recording sites (i.e., carotid and femoral arteries) directly on the body surface [3–5].

SphygmoCor (AtCor Medical, Sydney, Australia. Model MM3. Software version 7.01 S) uses one tonometric Millar transducer. SphygmoCor offers the possibility of carotid–femoral PWV measurements in two steps. The first step is used to simultaneously record carotid pulse wave and ECG, the second step is the recording of femoral pulse wave and ECG. ECG recording during measurements is necessary for synchronization of carotid and femoral pulse wave times. Transit time between carotid and femoral pressure waves was calculated using the foot-to-foot method. Wave 'foots' are identified using intersecting tangent algorithms. Thus, using this method, PWV is calculated from measurements of pulse transit time and distance traveled by the pulse wave. However, distance traveled by the pulse wave is sometimes calculated differently when using SphygmoCor to measure carotid–femoral PWV. The most frequently used method involves measuring two distances on the body surface, that is, from sternal notch to the femoral location and from sternal notch to the carotid location of respective pulse wave recording. On entering data into the computer, traveled distance is calculated automatically as the difference between the two distances, that is, femoral location-sternal notch minus sternal notch-carotid location. In the present study, similar to most other studies measuring aortic (carotid–femoral) PWV using SphygmoCor, this latter method was used to calculate traveled distance [7,12–14].

For distance measurement in Complior and SphygmoCor methods we used the same scale calibrated in centimeters. Characteristic points of carotid and femoral pulse wave registration (the same for each method) and point of sternal notch were marked by a permanent marker. Each between-points distance was measured two times. Mean values were used for further calculations.

Arteriograph (TensioMed, Budapest, Hungary. Software Arterioraph for Windows 2000) does not measure propagation time from carotid–femoral waveform recordings or the distance between carotid and femoral arterial recording sites. The main principle of PWV estimation behind the Arteriograph device is to record oscillations detected on the upper-arm cuff by a special high fidelity sensor. Measurements are performed when cuff pressure exceeds systolic BP by 35–40 mmHg, with a completely occluded brachial artery [15]. This measurement is based on the fact that during systole, blood volume ejected into the aorta generates a pulse wave, the so-called 'early systolic peak'. As this pulse wave runs down, it reflects from the bifurcation of the aorta, creating a second wave, the 'late systolic peak'. It is recommended to refer to this method when measuring 'aortic PWV'.

Return time (S35) is calculated as the difference in milliseconds between the first and the reflected systolic wave, when cuff pressure is 35 mmHg over systolic BP. Aortic PWV (PWV S35) is calculated from (return time S35) as pulse transit time and the distance traveled by the pulse wave. The manufacturer's recommended technique, used in this study, is based on measuring the distance between the jugulum (sternal notch) and the symphsis pubica (pubic symphysis), two characteristic anatomical points. These points were marked by a permanent marker. Between-points distance was measured twice on the body surface using the same calibrated scale as used for Complior and SphygmoCor distance measurements. Mean value was used in further calculations.

Statistical analysis

SAS 8.1 (SAS Institute Inc., Cary, North Carolina, USA) and Statistical 8.0 (StatSoft Inc. Tulsa, Oklahoma, USA) were used for database management and statistical analysis. Central tendency and data spread are reported as the mean ± SD. Between-method comparison was performed using analysis of variance (ANOVA). In post-hoc analysis, means were compared by Tukey's multiple test. Pearson's correlations and Bland–Altman testing were also included in the panel of statistical methods for comparison of pulse wave velocity across the three techniques.

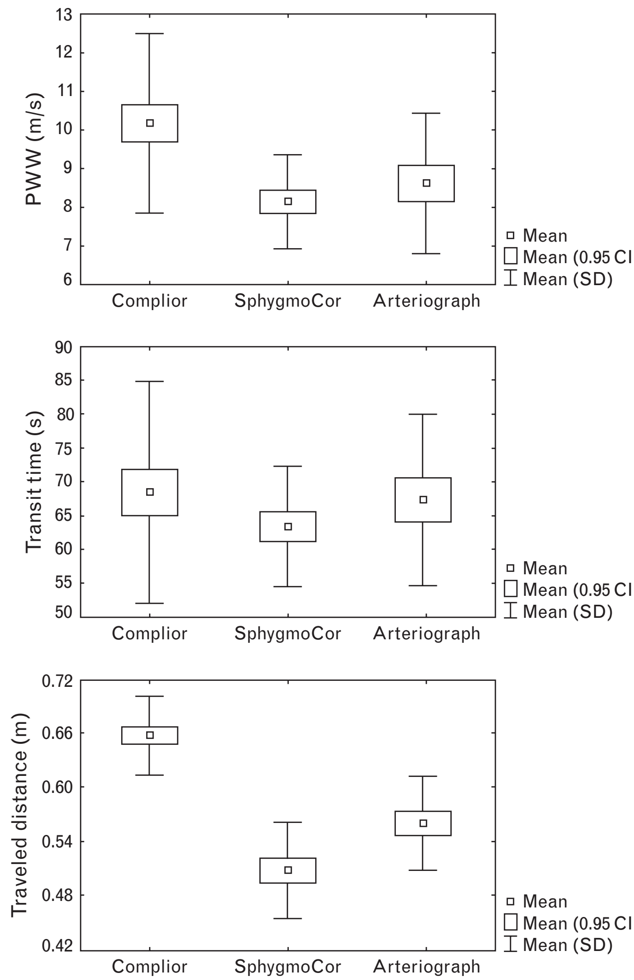
Results

Table 1 summarizes the clinical characteristics of the study group. Aortic PWV measured using Complior was significantly higher than that obtained using SphygmoCor or Arteriograph. PWV measured using SphygmoCor and Arteriograph did not differ (Fig. 1 and Table 2). According to the basic formula, PWV depends on wave transit time (TT) and traveled distance (D), that is, PWV = D/TT. Between-method comparison of these two variables – the main determinants of PWV – in ANOVA revealed that differences in traveled distance, but not in transit time, were statistically significant (Fig. 1).

The highest Δ mean for wave traveled distance was observed when comparing Complior and SphygmoCor (0.15 m). However, in post-hoc testing, all differences in traveled distance were significant (Table 2). Strong positive correlations were observed for PWV values measured using each pair of devices (Fig. 2).

Bland–Altman analysis performed in the same manner confirmed the acceptable accuracy (differences below double standard deviation) of PWV measurements for all devices, under the assumption that mean difference in

Fig. 1



Comparison of pulse wave velocity, transit time and traveled distance obtained using three devices: Complior, SphygmoCor and Arteriograph by analysis of variance. ANOVA: $P < 0.001$ for PWV; $P = 0.72$ for transit time; $P < 0.001$ for traveled distance. CI, confidence interval.

Table 1 Clinical characteristics of the study group ($n = 64$)

Variable	Mean or number of patients	SD or %
Age (years)	54.6	13.6
Weight (kg)	81.4	16.5
Height (cm)	169.8	10.4
BMI (kg/m^2)	28.3	4.7
Duration of hypertension (years)	12.5	7.8
Smoking (patients)	15	23.0
Heart rate (bpm)	64.0	9.7
SBP (mm Hg)	148.5	23.7
DBP (mmHg)	89.6	12.9
Biochemical data		
Na (mmol/l)	140.1	3.1
K (mmol/l)	4.32	0.4
Creatinine (mmol/l)	69.6	15.08
Total cholesterol (mmol/l)	5.3	0.81
Triglycerides (mmol/l)	1.16	0.62
HDL (mmol/l)	1.35	0.4
LDL (mmol/l)	2.77	0.77

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2 Post-hoc analyses for pulse wave velocity and traveled distance differences

	Δ mean	CI	P (Tukey test)
PWV (m/s)			
Complior–Arteriograph	1.55	0.80–2.29	<0.05
Complior–SphygmoCor	2.01	1.27–2.76	<0.05
Arteriograph–SphygmoCor	0.46	−0.34–1.27	NS
Distance (m)			
Complior–Arteriograph	0.09	0.08–0.12	<0.05
Complior–SphygmoCor	0.15	0.13–0.16	<0.05
Arteriograph–SphygmoCor	0.05	0.03–0.07	<0.05

CI, confidence interval; PWV, pulse wave velocity.

PWV between Complior and SphygmoCor method is 1.4 m/s, as well as between Complior and Arteriograph is 1.1 m/s (Fig. 2).

Discussion

Comparison of two methods to measure the traveled distance by the pulse wave

The main finding of our study is the significant difference in aortic pulse wave velocity measured by three commercially available devices. Two of them (Complior and SphygmoCor) are well known and widely used in clinical practice, applying registration of carotid and femoral pulse waves for calculating transit time. Complior records both waves simultaneously, whereas SphygmoCor records consecutively using ECG-gating. Variation in transit time obtained using the SphygmoCor may be determined by changes in heart rate between the two recordings. Moreover, transit time acquisition in the SphygmoCor device based on the foot-to-foot method may cause the difference with the Complior implementing correlation method [11].

Millasseau *et al.* [16], when comparing carotid–femoral PWV and transit time obtained using Complior and SphygmoCor devices, found that SphygmoCor and Complior devices do significantly differ with respect to transit time, in which shorter times were obtained using SphygmoCor compared with Complior. The difference in transit time with the Complior and transit time with the SphygmoCor detected by Millasseau *et al.* was 5.9 ms, SD = 5.5 ms with the absolute value of transit time approximating 65 ms (the last values are similar to our study). Because in above mentioned study authors used the same traveled distance for both SphygmoCor and Complior devices in carotid–femoral PWV calculation (total distance between the carotid and femoral sites of pulse registration) PWV measured by SphygmoCor was higher than measured by Complior. Our results did not reveal a significant difference in transit time between the Sphygmocor and Complior methods in contrast with a significant difference in traveled distance and subsequently in carotid–femoral PWV. In our study, we measured traveled distance precisely according to the manufacturer recommendations: total distance between the carotid and femoral sites of measurement for Complior and total distance between carotid and femoral pulse recording sites minus the distance from the carotid location to the sternal notch for SphygmoCor. As a consequence, distance in the SphygmoCor technique was shorter than in the Complior method and pulse wave velocity obtained by Complior was higher than those calculated by SphygmoCor.

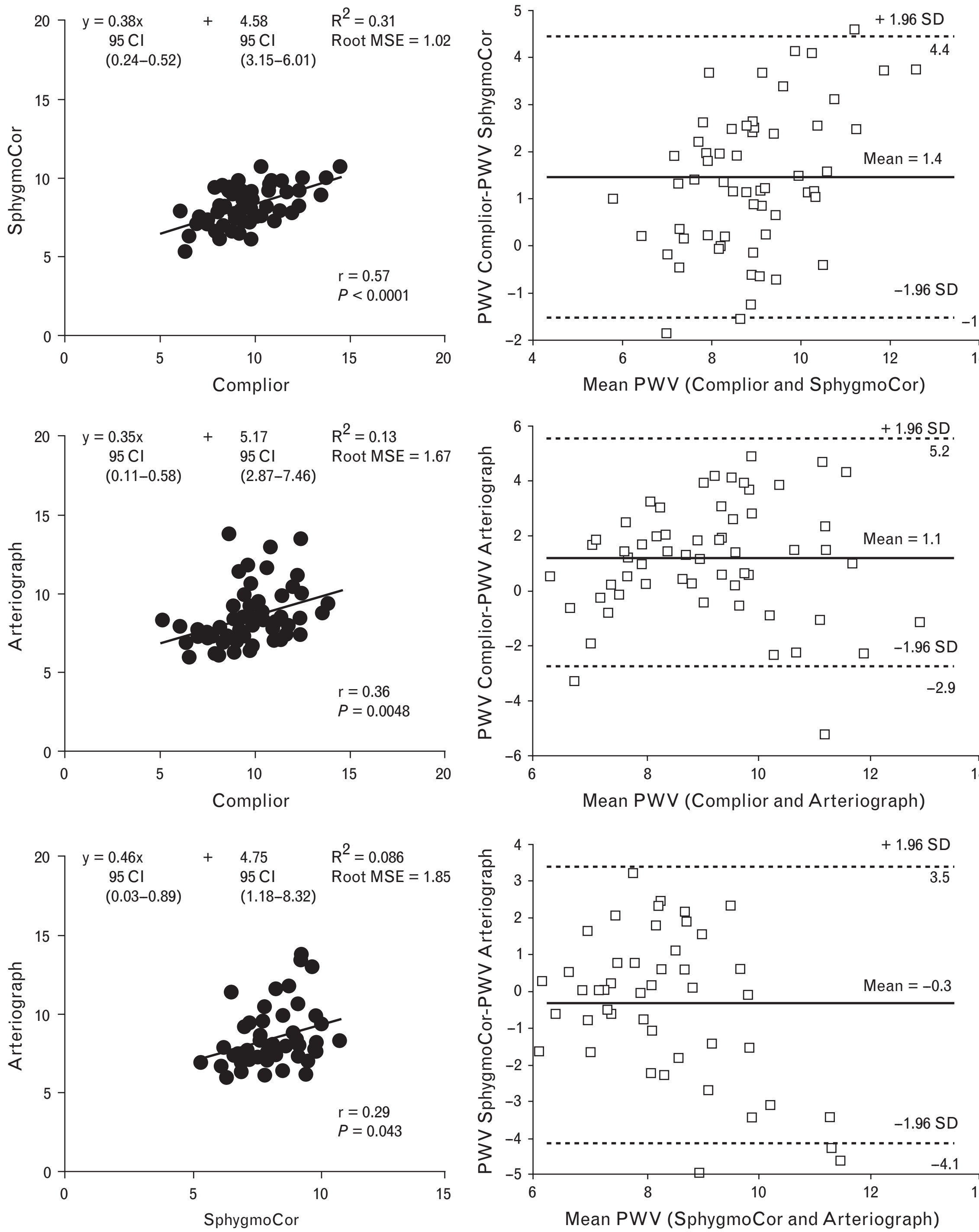
The ‘Expert consensus document on arterial stiffness’ [1] describes three methods for measuring traveled distance: using the total distance between the carotid and femoral sites of measurement, subtracting the distance from the carotid location to the sternal notch from the total distance, or subtracting the distance from the carotid location to the sternal notch from the distance between the sternal notch and the femoral site of measurement. This document identified many problems regarding traveled distance measurement on body surface, such as abdominal obesity, large bust in women, peripheral artery disease. Very important in the context of between-method comparison is the sentence: ‘The shorter the distance between two recording sites, the greater the absolute error in determining transit time’. In our study we overcome this problem by using the same recording sites for Complior and SphygmoCor methods.

Two other methodological aspects of traveled distance measurement should be underlined. First, for subtracting the distance from the carotid location to the sternal notch from the total distance, one should measure two distances, which doubles the chance of observer error. Second, even if transit times for Complior and SphygmoCor are not different, as in our study, the shorter traveled distance for SphygmoCor may increase absolute error in calculated PWV.

In the literature including the information about aortic PWV measurement, other methods of traveled distance calculation are used: based on measurements from the sternal notch to the femoral site [17], from the sternal notch to the aortic bifurcation, localized by Doppler probes on the body surface [18]. Besides using manufacturers recommendations with accuracy in measurement of distance in Complior and SphygmoCor technique, one should remember that implemented distances are only approximations of the real distance traveled by the pulse wave in the aorta.

References quoted in the 2007 ESH/ESC guidelines, regarding carotid–femoral PWV greater than 12 m/s as the threshold for subclinical organ damage, were studies which assessed the total distance between carotid and femoral measurement sites, irrespective of the technique for pulse wave recording (Doppler probe, mechanotransducers) [3–5,19]. Carotid–femoral PWV greater than 12 m/s as a prognostic factor was first referred to by Blacher *et al.* [20] in patients with renal failure. The

Fig. 2



Relationships of aortic pulse wave velocities obtained using three devices: Complior, SphygmoCor and Arteriograph. Analyses of regression, correlations and Bland–Altman plots for comparison pairs. MSE, mean standard error; PWV, pulse wave velocity.

investigators measured the total distance between the carotid and femoral sites on body surface. Doppler probes were used for recording of the carotid and femoral pulse waveforms. In another study from the same institution – using the Complior device – the PWV exceeded 12 m/s in patients with diabetes mellitus or renal failure as compared with healthy controls in whom the mean carotid–femoral PWV was below 12 m/s [21].

Again, using the Complior to measure carotid–femoral PWV and calculate traveled distance between carotid and femoral sites directly on body surface, a relationship was found between PWV greater than 13 m/s and reduced survival in patients with arterial hypertension [22].

Most prognosis/survival studies apply direct, point-to-point measurement of the total distance between carotid and femoral sites to calculate carotid–femoral (aortic) PWV. It is also the only method used to measure traveled distance using the Complior device [3–5,11,22].

There are several ways of calculating traveled distance, when using the SphygmoCor device, namely as the total distance between the carotid and femoral sites of pulse wave recording [8]. Most frequently, this includes subtracting the carotid location-sternal notch distance from the sternal notch-femoral site distance [7,12,13] or sometimes the distance from the sternal notch-femoral site of pulse measurement [17]. Some investigators using SphygmoCor do not provide any information on the technique used for measuring distance traveled, as if it yielded an insignificant impact on PWV values obtained using this device [23].

Comparison between three methods to measure pulse wave velocity

Arteriograph, newly developed device for measuring aortic pulse wave velocity, calculates transit time based on brachial pulse oscillations, without pulse wave registration on the carotid and femoral artery. In fact, the half of return time S35 is an equivalent of the pulse wave transit time when calculated by Complior and SphygmoCor method [15].

Our results confirm that the half of return time S35 and transit time measured by Complior as well as transit time measured by SphygmoCor are not significantly different. Tensiomed Company recommends – for Arteriograph in PWV calculation – measurement of the distance between sternal notch (*jugulum*) and pubic symphysis. This distance once again is only the approximation of the real distance traveled by the pulse wave in aorta. The Arteriograph technique, like Complior and SphygmoCor devices, is based on the same simple equation for calculation of PWV as a ratio of traveled distance and transit time. The similarity of approaches implemented in these devices permits the between-method comparisons.

In our study, distances measured in the three compared methods were significantly different: the longest was the distance used by Complior method, the shortest used by SphygmoCor. The biggest was the difference between the distances measured from Complior and SphygmoCor (Δmean = 0.15 m), but significant differences were observed between distances measured from Complior and Arteriograph (Δmean = 0.09 m), as well as from SphygmoCor and Arteriograph (Δmean = 0.05 m) devices. Probably due to this slight difference (Δmean = 0.05 m) in traveled distance and lack of difference in transit times obtained by SphygmoCor and Arteriograph, the last pair of devices did not differ in estimated aortic PWV, in our study as well as in the study by Magometschnigg [9].

In the present study, PWV values obtained with the Complior device were significantly higher as compared with those obtained with SphygmoCor and Arteriograph. This PWV differences could be attributed to differences in arbitrarily selected traveled distance and not transit time.

Our study does not indicate which of the three methods for measuring PWV is more correct. A comparison with a definitive method would be ideal, but there is no consensus as to what constitutes the definitive method. In our opinion, if aortic PWV is expected to be a reliable tool for determining arterial stiffness it is necessary to establish uniform principles of calculating traveled distance. Because a large number of prognosis/survival studies use direct distance between carotid and femoral sites of pulse wave recording for PWV calculation, this distance should be mostly recommended. Until there is no equivocal recommendation, three different cutoff points for determining arterial stiffness, as a subclinical organ damage, should be considered. According to our results in the Bland–Altman analysis, taking into account assumption that cutoff point for Complior is 12.0 m/s, the cutoff points for SphygmoCor and Arteriograph should be 12–1.4 = 10.6 m/s and 12–1.1 = 10.9 m/s, respectively.

Conclusion

(1) Values of aortic PWV obtained using Complior are significantly higher than those obtained using the other two devices.
(2) Complior, SphygmoCor and Arteriograph do not differ significantly in calculating transit time.
(3) Differences in pulse wave velocity obtained using the three devices are attributable to differences in calculating traveled distance.
(4) It appears reasonable to establish uniform principles for measuring traveled distance in further recommendations.

References

1 Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, *et al.* Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J* 2006; **27**:2588–2605.
2 2007 Guidelines for the Management of Arterial Hypertension. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC). *J Hypertens* 2007; **25**:1105–1187.
3 Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, *et al.* Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; **37**:1236–1241.
4 Laurent S, Katsahian S, Fassot C, Tropeano AI, Laloux B, Boutouyrie P. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. *Stroke* 2003; **34**:1203–1206.

5 Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, Laurent S. Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients; a longitudinal study. *Hypertension* 2002; **39**:10–15.

6 Baulmann J, Homsi R, Uen S, Düsing R, Fimmers R, Vetter H, Mengden T. Pulse wave velocity is increased in patients with transient myocardial ischemia. *J Hypertens* 2006; **24**:2085–2090.

7 Shiburi CP, Staessen JA, Maseko M, Wojciechowska W, Thijs L, Van Bortel LM, *et al.* Reference values for SphygmoCor measurements in South Africans of African ancestry. *Am J Hypertens* 2006; **19**:40–46.

8 Schillaci G, Mannarino MR, Pucci G, Pirro M, Helou J, Savarese G, *et al.* Age-specific relationship of aortic pulse wave velocity with left ventricular geometry and function in hypertension. *Hypertension* 2007; **49**:317–321.

9 Magometschnigg D. Blood pressure and arterial stiffness. A comparison of two devices for measuring augmentation index and pulse wave velocity. *Wien Med Wochensch* 2005; **155**:404–410.

10 El Assad M, Topouchian J, Asmar R. Evaluation of two devices for self-measurement of blood pressure according to the international protocol: the Omron M5-I and the Omron 705IT. *Blood Press Monit* 2003; **8**:127–133.

11 Asmar R, Benetos A, Topouchian J, Laurent P, Pannier B, Brisac AM, *et al.* Assessment of arterial distensibility by automatic pulse wave velocity measurement. Validation and clinical application studies. *Hypertension* 1995; **26**:485–490.

12 Kucerova J, Filipovsky J, Staessen JA, Cwynar M, Wojciechowska W, Stolarz K, *et al.* Arterial characteristics in normotensive offspring of parents with or without a history of hypertension. *Am J Hypertens* 2006; **19**:264–269.

13 Raggi P, Bellasi A, Ferramosca E, Block GA, Muntner P. Pulse wave velocity is inversely related to vertebral bone density in hemodialysis Patients. *Hypertension* 2007; **49**:1278–1284.

14 Borresen ML, Wang D, Strangaard S. Pulse wave reflection is amplified in normotensive patients with autosomal- dominant polycystic kidney disease and normal renal function. *Am J Nephrol* 2007; **27**:240–246.

15 Brinton TJ, Kailasam MT, Wu RA, Cervenka JH, Chio SS, Parmer RJ, *et al.* Arterial compliance by cuff sphygmomanometer application to hypertension and early changes in subjects at genetic risk. *Hypertension* 1996; **28**:599–603.

16 Millasseau SC, Stewart AD, Patel SJ, Redwood SR, Chowieñczyk PJ. Evaluation of carotid-femoral pulse wave velocity: influence of timing algorithm and heart rate. *Hypertension* 2005; **45**:222–226.

17 Stewart AD, Jiang B, Millasseau SC, Ritter JM, Chowienczyk PJ. Acute reduction of blood pressure by nitroglycerin does not normalize large artery stiffness in essential hypertension. *Hypertension* 2006; **48**:404–410.

18 Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, Gosling RG. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? *Circulation* 2002; **106**:2085–2090.

19 Willum-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, Ibsen H, Jeppesen J. Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. *Circulation* 2006; **113**:664–670.

20 Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM. Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; **99**:2434–2439.

21 Aoun S, Blacher J, Safar ME, Mourad JJ. Diabetes mellitus and renal failure: effects on large artery stiffness. *J Hum Hypertens* 2001; **15**:693–700.

22 Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 1999; **33**:1111–1117.

23 Stewart AD, Millasseau SC, Kearney MT, Ritter JM, Chowienczyk PJ. Effects of inhibition of basal nitric oxide synthesis on carotid-femoral pulse wave velocity and augmentation index in humans. *Hypertension* 2003; **42**:915–918.