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ORIGINAL ARTICLE

A new oscillometric method for pulse wave analysis: comparison with a common tonometric method

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In the European Society of Cardiology–European Society of Hypertension guidelines of the year 2007, the consequences of arterial stiffness and wave reflection on cardiovascular mortality have a major role. But the investigators claimed the poor availability of devices/methods providing easy and widely suitable measuring of arterial wall stiffness or their surrogates like augmentation index (AIx) or aortic systolic blood pressure (aSBP). The aim of this study was the validation of a novel method determining AIx and aSBP based on an oscillometric method using a common cuff (ARCSolver) against a validated tonometric system (SphygmoCor). aSBP and AIx measured with the SphygmoCor and ARCSolver method were compared for 302 subjects. The mean age was 56 years with an s.d. of 20 years. At least two iterations were performed in each session. This resulted in 749 measurements. For aSBP the mean difference was −0.1 mm Hg with an s.d. of 3.1 mm Hg. The mean difference for AIx was 1.2% with an s.d. of 7.9%. There was no significant difference in reproducibility of AIx for both methods. The variation estimate of inter- and intraobserver measurements was 6.3% for ARCSolver and 7.5% for SphygmoCor. The ARCSolver method is a novel method determining AIx and aSBP based on an oscillometric system with a cuff. The results agree with common accepted tonometric measurements. Its application is easy and for widespread use.

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Introduction

The medical research regarding hypertension has fairly changed during the last two decades. Around the year 1990, the diastolic blood pressure was the most important value to look at,[1] approximately 10 years later the focus was on the systolic blood pressure. Today, we know that both systolic and diastolic blood pressures are prognostically important.[2] But other vascular parameters seem to be of importance for evaluating the hypertensive patient with respect to his prognosis and potentially therapeutical options. With the beginning of the new millennium the topic of arterial stiffness of major vessels related to hypertension slowly arose in clinical practise. This issue was together with its indicators for the first time mentioned in the ESH–ESC (European Society of Hypertension–European Society of Cardiology) guidelines for hypertension treatment in the year 2003.[3] As parameters to measure arterial stiffness primary the methods of pulse wave analysis and pulse wave velocity have been suggested. The pulse wave analysis evaluates shape and amplitude of the aortic pulse wave. The resulting parameters of relevance are the aortic systolic blood pressure (aSBP) and the so-called augmentation index (AIx).

Owing to the differences in impedances between central and peripheral vessels and the moderate presence of wave reflection for healthy people, the systolic blood pressure at the aortic root is significantly lower than in the upper arm in such subjects. Diastolic and mean blood pressures do not differ significantly.[4] Different diameters and elasticities are responsible for the occurrence of these different wave impedances and the resulting differences in blood pressure. As a result of aging

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and pathological changes (for example, arteriosclerosis or subclinical organ damage) stiffening of vessels and therefore an increase of aSBP as well as an increased peripheral arterial resistance may occur. As a consequence of these changes, increased and premature pressure reflections emerge, which superimpose the generic pulse wave ejected by the heart earlier and more intensely. Their accumulation leads to an elevation of the aSBP and is called augmentation. The percent ratio of augmentation to the aortic pulse pressure is called AIx. The superposition may cause a pathological increase of the aSBP and subsequently an increase of the cardiovascular risk.[5,6] It has been shown that both elevated aSBP and AIx are independent predictors of mortality in patients with end-stage renal disease[7,8] and coronary heart disease.[5,9,10] Furthermore, it is reported that the AIx correlates with the left ventricular mass in normotensive men as well as in hypertensive ones.[11] Moreover, the increase in cardiovascular risk can be estimated better from central than from brachial blood pressure measurements.[7,12,13]

In the update of the ESH–ESC guidelines for hypertension treatment in the year 2007,[14] the consequences of arterial stiffness on cardiovascular mortality have a major role. These guidelines additionally claim to provide widely suitable measuring devices for the measurement of arterial wall stiffness and its influence on aortic blood pressure. The increase of the aSBP is *ad hoc* not noticeable in the A. brachialis and therefore *per se* not to be measured by common oscillometric methods. Therefore, the aim of this study was the validation of a novel method determining AIx and aSBP based on an oscillometric method using a common cuff (ARCSolver, Austrian Institute of Technology, Vienna, Austria) against a validated tonometric system (SphygmoCor, AtCor Medical Pty Ltd, West Ryde, Australia)).

Materials and methods

Study population
The examinations have been carried out in two hospitals, at the Institution of Hypertoniker, Vienna, Austria and at the cardiology department in the University teaching hospital of Wels-Grieskirchen, Wels, Austria. The measurements were authorized by the local ethics commissions. Exclusion criteria were atrial fibrillation or unstable clinical presentation. Overall 302 patients and healthy volunteers have been included.

Method of investigation
To get a robust estimation of the performance of the system, the measurements were performed within the clinical routine by several examiners. Beside that the international recommendations for the measurement of arterial stiffness were respected.[15] The measurements took place at convenient room temperature and under avoidance of external influences.

The systolic and diastolic blood pressure values used for the ARCSolver method were also entered to the SphygmoCor system to calibrate the radial pressure curve. The consecutive recording of the pulse waves was carried out in random order on the left arm. Usually, at least two iterations were performed in each session. This resulted in 749 measurements.

SphygmoCor
Using the SphygmoCor device, the peripheral pulse wave is measured at A. radialis by applanation tonometry and recorded on a personal computer. The quality of the recording can be appreciated using the provided operator index. Thereafter, the pulse wave has to be calibrated by externally determined blood pressure values. The personal computer-software of ShpygmoCor calculates the aortic pulse wave using a transfer function. This transformation provides the first parameter under investigation, the aSBP and the aortic pulse pressure. Now a characteristic point of the pressure curve, the inflection point, is identified within the time domain, indicating the arrival of the reflected wave in the ascending aorta. The blood pressure at this point of time is called 'inflection pressure'. The difference between aSBP and inflection pressure is called 'augmentation pressure (AP)'. The AIx is then calculated by $AP/aPP \times 100$ for positive values as illustrated in Figure 1b.

ARCSolver
The ARCSolver method aims to be a novel method for the determination of the aSBP and AIx based on oscillometric blood pressure measurement with a common cuff. The method[16] has been developed by the Austrian Institute of Technology, Vienna, Austria. The method uses the pulse waves assessed at A. brachialis. The recordings are carried out at diastolic pressure level for approximately 10 s using a conventional blood pressure cuff for adults available in two sizes (24–34 and 32–42 cm) and a high fidelity pressure sensor (MPX5050, Freescale Inc., Tempe, AZ, USA). The sensor is connected to a 12 bit A/D converter by means of an active analogue band bass filter ($0 < > 25$ Hz). After digitalization, the signal processing is performed using a three level algorithm. In a first step, the single pressure waves are verified for their plausibility by testing the position of minima and the corresponding wavelengths. During the second stage, all single pressure waves are compared with each other to recognize artifacts. Thereafter, an aortic pulse wave is generated by the means of a generalized transfer function. The idea behind a transfer function is

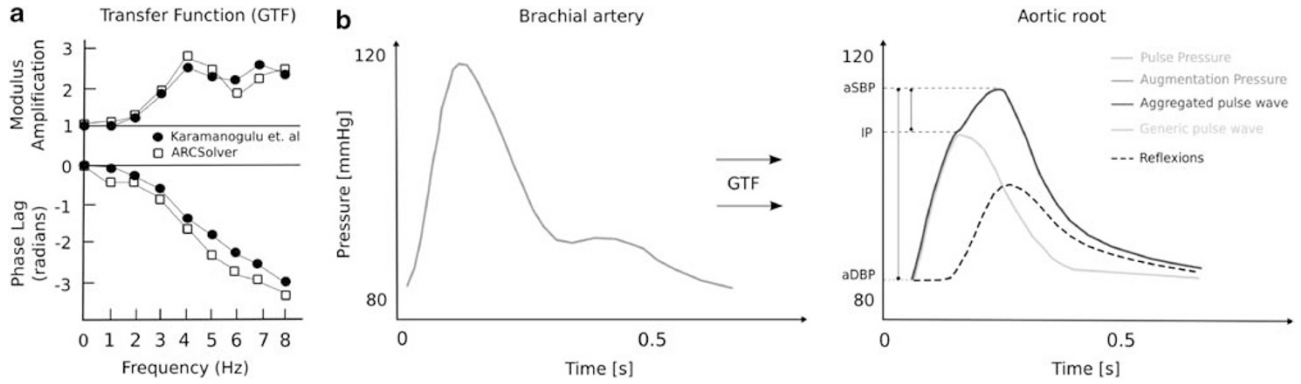

Figure 1 (**a**) Characteristic modulus amplifications and phase shifts of pressure wave harmonics between aortic root and brachial artery used for the ARCSolver—generalized transfer function and data published by Karamanoglu *et al*.[17] (**b**) Principles to derive aSBP and AIx from the brachial waveform.

the modification of a certain frequency range within the acquired pulse signal to get the aortic pressure wave. Modulus and phase characteristics of the ARCSolver transfer function are illustrated in Figure 1a. Compared with data published by Karamanoglu *et al*.[17] similar parameters have been obtained.[18] The first positive zero crossing of the fourth-order time derivative of the generated aortic pulse wave represents the desired inflection point.[19] Finally, the coherence of the measured parameters is verified. Therefore, the inflection point of each single pulse wave is compared with the mean inflection point. The determination of aSBP and AIx is carried out in the same way as in SphygmoCor (see Figure 1b).

Statistics

Basically, all measurements are stated by mean and s.d. Furthermore, they are analysed using the methods presented by Bland–Altman.[20] Those are mainly helpful to represent the data graphically and to analyse the reproducibility of measurements according to the different methods and the resulting corrections for the s.d. To examine the accordance of the measurements with regard to age groups a *t*-test at 95% significance level is applied. For the analysis the statistical software of Matlab 7.5 (The Mathworks Inc., Natick, MA, USA) is used.

Results

Clinical parameters of the cohort

Overall 302 subjects were measured, 129 women and 173 men. The mean age was 56 years with an s.d. of approximately 20 years. The lower age limit was 16 years, the upper one was 92 years. Medical treatment was not withheld for the measurements. The mean blood pressure was systolic 129 mm Hg with an s.d. of 18 mm Hg and diastolic 77 mm Hg with an s.d. of 11 mm Hg. For detailed base line characteristics we kindly refer to Table 1.

Table 1 Baseline characteristics

Men/Women	173/129
Hypertension	192
Diabetes	44
Smoker	52
Previous myocardial infarction or stroke	21
CAD	45
LVH	57
Mitral regurgitation or CHF	14
Carotis plaque	45
Renal disease	26
Age (years)	56 (20)
Height (cm)	171.1 (9.5)
Weight (kg)	79 (16.9)
Mean SBP (mm Hg)	129 (18)
Mean DBP (mm Hg)	77 (11)
Heart rate (1 min^{-1})	69.5 (11.2)
SBP 0–99 (mm Hg)	12
SBP 100–129 (mm Hg)	159
SBP 130–159 (mm Hg)	114
SBP 160–179 (mm Hg)	17

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.
Values are numbers or mean (s.d.).

Comparison of reproducibility of measurements

Beside the biological variability of a human being, the reproducibility depends on two technical factors. On the one hand the variation of the measurement method and on the other the effect of the investigator. Several investigations can be found regarding this topic for SphygmoCor in literature. Wilkinson *et al*.[21] report an intra-investigator variability of 5.3% and Siebenhofer *et al*.[22] an inter-operator variability of 6.4%. Savage *et al*.[23] state up to 9% inter-operator variability. The denoted ranges of values could be reproduced in our study. There was no significant difference for reproducibility of AIx for both methods. The variation estimate of inter- and intraobserver measurements was 6.3% for ARCSolver and 7.5% for SphygmoCor.

Comparison of aSBP

Brachial systolic blood pressure was measured at least two times per subject leading to 749 data sets. The systolic and diastolic blood pressure values retrieved were used to calibrate the peripheral pulse waves for both methods. After transforming the brachial into aortic pressures, the mean difference between the two methods was −0.1 mm Hg with an s.d. of 3.1 mm Hg.

Thereby 93% of the differences were ⩽5 mm Hg, 99% ⩽10 mm Hg and 100% ⩽15 mm Hg. In total, 7 of 302 subjects had more than one reading beyond 5 mm Hg difference. Only three of them had all their comparisons over 5 mm Hg. A Bland–Altman plot in Figure 2 shows a very satisfying spreading of residues.

Comparison of AIx and AP

AIx/AP was measured at least two times per patient, averaged and then compared. The mean difference for AIx was 1.2% (7.9 s.d.) and 0.4 mm Hg (4.1 s.d.) for AP. Subsequently, 85% of the AP comparisons were ⩽5 mm Hg, 98.5% ⩽10 mm Hg and 100% ⩽15 mm Hg. In total, 23 of 302 subjects had more than one reading beyond 5 mm Hg difference whereby 12 of them had all their comparisons over 5 mm Hg. Figure 3 illustrates the uniform distri-

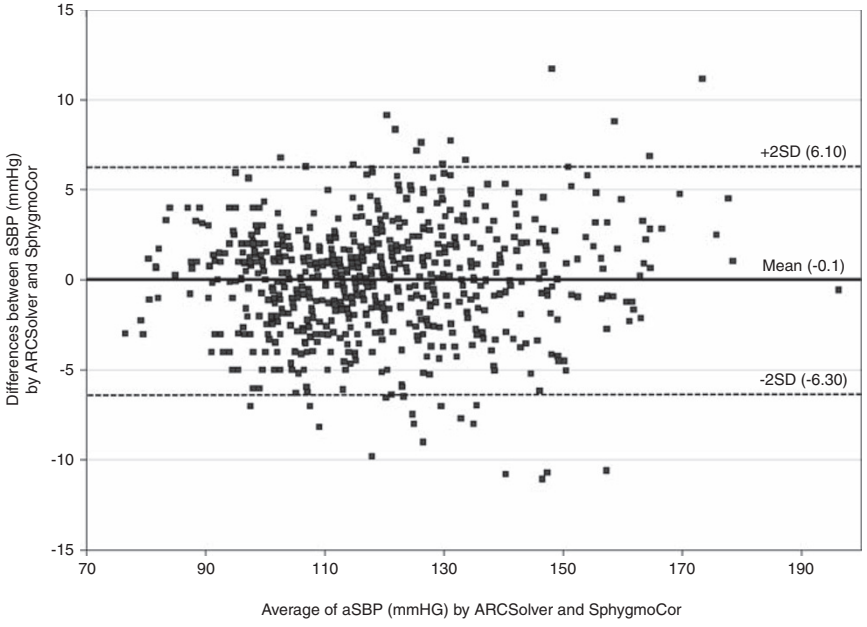

Figure 2 Bland–Altman analysis of aSBP ARCSolver vs SphygmoCor.

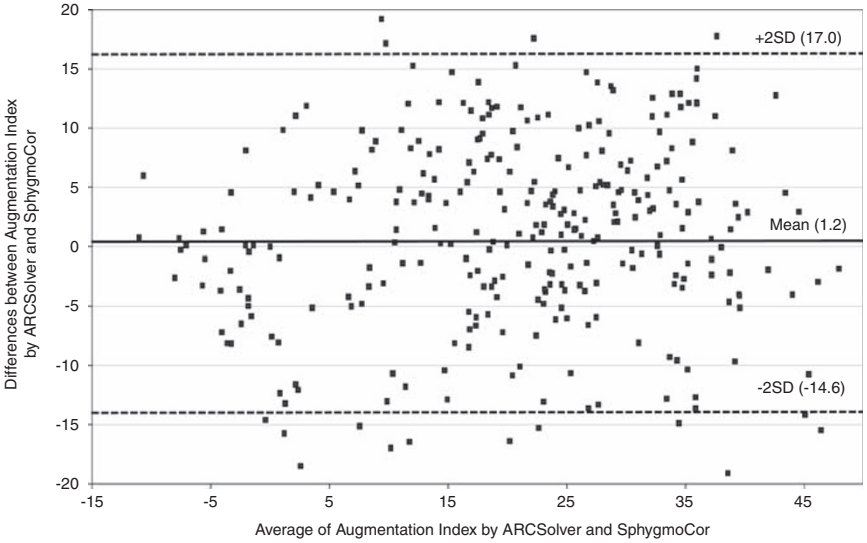

Figure 3 Bland–Altman analysis of Alx ARCSolver vs SphygmoCor.

Table 2 Comparison of AIx mean values and differences by age groups

Age group	*Mean values AIx*	*Mean differences AIx*	P-*values*
16–24	−0.50	−5.13	0.0001
25–39	8.13	2.8	0.0603
40–49	20.30	−0.03	0.2388
50–59	23.36	0.41	0.1586
60–69	25.84	0.58	0.5316
70–79	27.34	−0.17	0.2302
80+	31.41	1.71	0.1665

Abbreviation: AIx, augmentation index.

bution of the residuals. This suggests an independency of measurement differences to the measurement values, which is essential for an objective measuring procedure.

Comparison of AIx regarding age groups
The AIx is reported to correlate strongly with age. Owing to this reason, we divided our sample into age groups and compared their AIx mean values. The analysis has been carried out using a *t*-test. The null hypothesis was that the means of AIx for each age group do not differ for both methods. The desired significance level was 95%. Therefore, the null hypothesis for a group has to be rejected if $P<0.05$. In our cohort, there was no significant mean difference for any group but one as illustrated in Table 2.

Discussion

The aim of this comparison was the analysis for clinical suitability of the ARCSolver algorithms compared with SphygmoCor, which served as a reference device because of its wide distribution and acceptance. The parameters under investigation were the aSBP and the AIx. Both are surrogates for increased cardiovascular risk caused by increased and premature arterial wave reflections.

The trials showed satisfactory accordance of the two methods. Thus, the ARCSolver algorithms are suitable for the use in oscillometric cardiovascular measuring devices. This is emphasized by the fact that the measurements were taken by a representative sample of healthy volunteers and patients during clinical routine.

Bland–Altman analysis
aSBP mean difference and s.d. are far below the thresholds of ± 5 (8 s.d.) mm Hg for mean difference and s.d. recommended by the Association for the Advancement of Medical Instrumentation.[24] For Association for the Advancement of Medical Instrumentation and both the British Hypertension Society[25] as well as the ESH[26] recommendations the aSBP results meet the highest levels of accuracy with respect to the various defined accumulative error bandwidths and measurement procedures (if applicable). Furthermore, the Bland–Altman analysis in Figure 2 shows an exemplary spreading of residues and therefore no dependences on mean and difference.

The reasons for this good accordance may be based on the fact that for the transformation to determine the aortic blood pressure, the lower frequency bands of the pulse wave are dominant. This frequency bands are very robust and stable during measurement.[27] The mentioned dominance may also blur the effects of high-frequency impedance changes between brachial and radial artery and its influence on central pressure. In spite of the promising results, we suggest additional invasive trials to reinforce the actual findings.

The results of the analysis of the AIx comparison show sufficient accuracy. The variation values determined in our studies are in the same range as those published for SphygmoCor. The ARCSolver is based on an user-independent recording method. Considering this, the measured values of the mean difference and the s.d. show consistency. In general, the determination of the AIx is discussed controversial in the scientific community up to now[28] and the exact SphygmoCor method has not been disclosed and invasively validated yet[29] and therefore comparisons are limited. The agreement for AIx/AP show reasonable good results with regard to the recommendations of Association for the Advancement of Medical Instrumentation, British Hypertension Society and ESH. S.d. of differences is slightly higher compared with aSBP and may be further analysed by invasive trials.

Comparison of age groups
The comparison of age groups gives good results. In none of the existing age groups but one the mean values of SphygmoCor and ARCSolver differ significantly. For the age group below 25, we observed a moderate over estimation of AIx for negative values by ARCSolver. This effect seems to result from a different AIx calculation method used by SphygmoCor for negative values but may be of minor clinical relevance.

In summary, the results of this study indicate that the measurements for AIx and aSBP agree for the suggested methods. The shown equivalence between both measuring devices recommends the use of ARCSolver algorithms in oscillometric methods. Actually, there are two upcoming commercial devices using the method (CardioMon by Medifina, Vienna, Austria and Mobil-O-Graph NG—ABPM by IEM, Stolberg, Germany). In addition, further invasive comparisons should be performed to prove the actual evidence. The principal easiness of clinical appliance provided by oscillometric methods offer the opportunity for wide spread use. This may ultimately lead to an improvement in common efforts to prevent cardiovascular disease.

What is known about the topic

- In the ESC-ESH guidelines of the year 2007, the consequences of arterial stiffness and wave reflection on cardiovascular mortality play a major role.
- But the investigators claim the poor availability of devices/methods providing easy and widely suitable measuring of arterial wall stiffness or their surrogates like augmentation index (AIx) or aortic systolic blood pressure (aSBP).

What this study adds

- A novel method determining AIx and aSBP based on an oscillometric method with a cuff is introduced and evaluated.
- The clinical application of the method is easy and suitable for widespread use.
- The obtained results agree with common accepted tonometric measurements.

Conflict of interest

SW and CCM are inventors of a patent, which is partly used in ARCSolver. The remaining authors declare no conflict of interest.

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