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ORIGINAL ARTICLE

Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method

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Abstract Pulse transit time (PTT) and pulse wave velocity (PWV), respectively, were shown to have a correlation with systolic blood pressure (SBP) and have been reported to be suitable for indirect BP measurements. The aim of this study was to create a function between SBP and PWV, and to test its reliability for the determination of absolute SBP using a non-linear algorithm and a one-point calibration. 63 volunteers performed exercise to induce rises in BP. Arterial PTT was measured between the R-spike of the ECG and the plethysmographic curve of finger pulse-oximetry. The reference BP was measured using a cuff-based sphygmomanometric aneroid device. Data from 13 of the 63 volunteers served for the detection of the PWV–BP relationship. The created non-linear function was used to calculate BP values after individual correction for the BP offset in a group of 50 volunteers. Individual correlation coefficients for SBP measured by PTT (SBP_{PTT}) and by cuff (SBP_{CUFF}) varied between $r = 0.69$ and $r = 0.99$. Taking all data together, we found $r = 0.83$ (276 measurements in 50 volunteers). In the Bland–Altman plot, the limits of agreement were $mean_{SBP_{PTT},SBP_{CUFF}} \pm 19.8$ mmHg. In conclusion, comparing SBP values using the PTT-based method and those measured by cuff resulted in a significant correlation. However, the Bland–Altman plot shows relevant differences between both methods, which are partly due to greater variability of the SBP_{PTT} measurement during intensified exercise. Results suggest that PTT can be used for measuring absolute SBP when performing an individual correction for the offset of the BP–PWV relation.

Keywords Blood pressure · Pulse transit time · Exercise

Introduction

Non-invasive measurement of blood pressure (BP) using cuff-based methods provides adequate data for many applications in medicine. However, cuff-based methods have some disadvantages, which limit their use in certain clinical situations. First, a continuous measurement of blood pressure is not possible, since a pause of at least 1–2 min between two BP measurements is necessary to avoid errors in the measurement (Campbell et al. 1990). Therefore, short-term changes in BP cannot be detected. Furthermore, the inflation of the cuff may disturb the patient and the consequences of these disturbances are alterations of the BP. Both problems are, for example, important when investigating BP fluctuations during sleep. The blow up of the cuff leads to an arousal going along with an increase in the systemic blood pressure (personal observation). Thus, in this case, blood pressure measurement may result in false-positive values. An alternative approach for a continuous, non-invasive and indirect measurement of BP is based on changes in pulse wave velocity (PWV). PWV is the speed of a pressure pulse propagating along the arterial wall and can easily be

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calculated from pulse transit time (PTT). PTT is the time between two pulse waves propagating on the same cardiac cycle from two separate arterial sites. PTT has been shown to be quasi-linear to low BP values, but increase exponentially at higher pressures (Pruett et al. 1988; Callaghan et al. 1984).

The velocity of a longitudinal pressure wave is related to the elasticity of the arterial vessel and to the vessel dimension by the equation of Moens and Korteweg (Callaghan et al. 1984; Wippermann et al. 1995). PWV depends both on the arterial pressure and the intrinsic elastic properties of the arterial wall. In practice, it is difficult to estimate how well PWV reflects BP and in how far severe age-dependent or disease-related changes (e.g., atherosclerosis) influence the arterial wall stiffness. In fact, investigations in a larger number of subjects showed that age, BP, gender, and cardiovascular risk factors significantly influence PWV (Yamashina et al. 2003; Mitchell et al. 2004; Schiffrin 2004; Foo and Lim 2006). These results suggest that PWV can only be used for measurement of relative BP changes as it has been shown by a number of studies in human beings and animals (Ochiai et al. 1999; Barschdorff and Erig 1998). However, determination of the individual the PWV–BP relation and calibration of the system would allow the measurement of the absolute BP using the indirect method using PTT. This procedure is time consuming and not feasible in most of the situations. Therefore, we developed a one-point calibration of the PWV–BP relation, which needs only one measurement of BP using a cuff-based reference method.

The aim of the present study was (1) to develop a PWV–BP function on the basis of the physiological properties of arterial walls and (2) to test if a one-point calibration of the PWV–BP relation offers an adequate measure of the absolute SBP.

Methods and materials

Subjects

We included a total of 63 subjects (see Tables 1, 2). All subjects underwent a physical examination on a bicycle ergometer with the aim the induce blood pressure increases.

Group 1 consisted of 13 persons (6 females, 7 males) who served for the determination of the PWV–BP function. To test for the applicability of this function for measurement of absolute SBP a second group of 50 volunteers (21 females, 29 males, group 2) was investigated. The main exclusion criterion for all subjects was cardiovascular diseases, which were potent to influence the ECG or

Table 1 Gender, height, and correlation coefficients of volunteers (group 1)

Subj.	Sex	Height (cm)	CC	#
1	m	173	0.988	5
2	m	171	0.995	3
3	f	165	0.946	5
4	f	168	0.878	4
5	f	163	0.940	4
6	m	180	0.942	6
7	f	172	0.853	4
8	f	176	0.892	5
9	m	184	0.782	6
10	f	170	0.747	4
11	m	192	0.973	3
12	m	188	0.941	6
13	m	171	0.999	3

Subj. subject, *CC* correlation coefficient, # number of data pairs

Table 2 Gender, height, and correlation coefficients of volunteers (group 2)

Subj.	Sex	Height (cm)	CC	#	Subj.	Sex	Height (cm)	CC	#
1	m	191	0.875	6	26	m	181	0.739	6
2	m	180	0.931	6	27	m	165	0.985	4
3	m	187	0.852	6	28	f	161	0.699	6
4	m	177	0.781	6	29	f	163	0.724	6
5	f	161	0.987	6	30	f	162	0.956	6
6	f	169	0.977	6	31	f	165	0.975	5
7	m	185	0.986	3	32	m	186	0.951	5
8	m	173	0.968	5	33	m	172	0.986	6
9	f	163	0.855	5	34	m	193	0.888	5
10	m	183	0.958	6	35	m	160	0.905	5
11	m	183	0.999	6	36	m	183	0.915	5
12	f	163	0.978	4	37	f	160	0.995	6
13	f	171	0.994	5	38	f	164	0.962	6
14	m	197	0.998	5	39	f	171	0.854	5
15	f	167	0.992	5	40	f	178	0.991	5
16	f	176	0.99	5	41	f	168	0.908	6
17	f	165	0.969	6	42	m	177	0.952	3
18	m	182	0.952	6	43	f	177	0.928	6
19	m	189	0.925	6	44	f	178	0.807	4
20	m	183	0.94	6	45	m	180	0.92	4
21	m	173	0.972	6	46	m	185	0.885	6
22	m	187	0.999	3	47	m	169	0.998	4
23	m	182	0.975	6	48	m	174	0.925	6
24	f	168	0.976	6	49	f	157	0.92	5
25	m	168	0.986	6	50	m	187	0.985	6

Subj subject, *CC* correlation coefficient, # number of data pairs

plethysmography signal and thereby impeding an accurate detection of the PTT.

All subjects gave their written informed consent to participate in the study. The local ethical commission approved of the study (EA1/127/06).

Equipment

Exercise was performed on a bicycle ergometer EGT 1000 (ELMED, Zimmer Elektromedizin GmbH in Neu-Ulm, Germany). The electrocardiogram (ECG) and the finger plethysmography curve were recorded with the SOMNOscreen^{TM} polysomnography device (SOMNOmedics GmbH, Randersacker, Germany). The determination of PTT and calculation of PWV and BP was performed with the DOMINO-Software (DOMINO 2.2.0 supplied with the SOMNOscreen^{TM}). To obtain the ECG, a modified lead after Nehb was applied. Two bipolar electrodes were fixed: parasternal 2. ICR, right, and 5. ICR, left. Another electrode was affixed to the lower arm and served for the electrical ground. The plethysmography signal was obtained using a probe for finger plethysmography/pO_2 (SOMNOmedics GmbH, Randersacker, Germany). The cuff of the sphygmomanometric devise was placed at the contra lateral upper arm.

Measurement procedure

Exercise protocols

Group 1 The maximum load and size of the incremental increase of exercise in this group depended on the physical abilities of the subjects and their anthropometric data. Increment was either 25 or 50 W. We obtained 3–6 data pairs per subject (Table 1).

Group 2 The subjects underwent a standardized incremental load on a bicycle ergometer. The increment was 0.5 W/kg BM. Five load steps were performed up to 2.5 W/kg BM.

Calibration procedure

Groups 1 and 2 Before starting exercise on the bicycle ergometer, volunteers relaxed in a sitting position. Then the SOMNOscreen^{TM} was started. BP was measured by a calibrated sphygmomanometric aneroid device. A single sphygmomanometric measurement (cuff) was performed to obtain BP_{cal}. The point in time was indicated by pressing the marker button of the SOMNOscreen^{TM}. This procedure allowed a correct time alignment of BP measured by cuff (BP_{cal}) and BP measured using the PTT ($BP_{PTT,cal}$). The difference between $BP_{PTT,cal}$ and BP_{cal} at this distinct time point was used for the one-point calibration of the PWV–BP function.

Data collection BP was measured by cuff (BP_{cuff}) at the end of each level of exercise (steady-state conditions). Cycling was stopped for 1 min during the measurement to reduce disturbances due to the movements. The measurement time was marked in the SOMNOscreen^{TM}. BP calculated from PTT (BP_{PTT}) was obtained continuously for each heart cycle after calibration in the software. BP values were averaged using a 5-value moving window to reduce the influence of artifacts (e.g., changes caused by breathing). Corresponding values of BP_{PTT} and BP_{cuff} were used for the statistical comparison of methods.

Determination of PTT

PTT is defined as the time delay between the R-wave of the ECG and the arrival of the pulse wave in the periphery (finger). The R-wave was detected from a chest lead of the ECG (Nehb) using amplitude and slope criteria. The arrival of the pulse wave was defined by the peak value of the differentiated signal, which corresponds to the steepest part of the ascent of the plethysmography signal (Fig. 1).

The PWV was calculated using the following formula (Davies and Struthers 2003):

$$\text{PWV (cm/ms)} = \frac{\text{BDC} \times \text{height (cm)}}{\text{PTT (ms)}}$$

with BDC = body correlation factor, and height = body length. BDC is 0.5 for adults when taken the finger for detection of the peripheral pulse wave as used in the

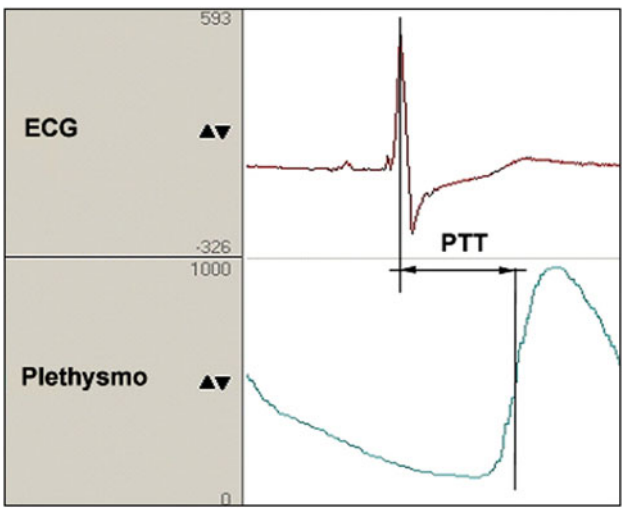

Fig. 1 Original traces of the electrocardiogram (ECG, *upper trace*) and peripheral pulse wave (Plethysmo) showing the detection of R-wave and pulse wave arrival and the calculation of the pulse transition time (*PTT*)

present study. This parameter is based on several studies showing a highly significant correlation between arm span and body height and small absolute differences between both measures (Versluis et al. 1999; Nygaard 2008). The BDC corresponds to the distance from sternal notch to the tip of the middle finger.

Statistics

The relation between BP_{cuff} and BP_{PTT} was examined using linear regression analysis. Correlation coefficients for BP_{cuff} versus BP_{PTT} were calculated for individuals as well as for the whole group. The latter was corrected for multiple measurements according to the formula by Bland and Altman (1995). The bias was estimated according the procedure suggested by Hopkins (2004). The table of variance was calculated using "R: A Language and Environment for Statistical Computing", package "hh", (R Development Core Team 2010). In addition, a Bland–Altman plot was done. In the Bland–Altman plot, the mean value calculated from corresponding BP values obtained from both methods is plotted against the corresponding difference of the mean BP minus the BP_{PTT}. The agreement limits were defined by mean ± 1.96 of the standard deviation (SD) of the differences. The plot helps to assess the disagreement between the two methods of BP measurement (Bland and Altman 1986).

Model for the PWV–BP relation

An empiric mathematical function was created to fit the data of PWV and SBP obtained from 13 subjects of group 1. The function consists of three terms: (1) an exponential term, (2) a second non-linear term, and (3) a correction constant, which is the difference of the BP_{PTTcal} and the BP_{cal} measured by the reference cuff method. This correction corresponds to a one-point calibration and shifts the curve to the reference BP. The following function was obtained:

$$BP_{PTT} = P1 \times PWV \times e^{(P3 \times PWV)} + P2 \times PWV^{P4} - (BP_{PTT,cal} - BP_{cal})$$

with the parameters $P1 = 700$, $P2 = 766{,}000$, $P2 = -1$, and $P4 = 9$, $BP_{PTT,cal}$ as the calculated BP (from PTT) corresponding to the BP measured by the reference method, and BP_{cal} as the BP measured at a distinct time at the beginning of the experiment using the reference method (cuff). The parameters $P1$–$P4$ were estimated by least square fitting of the function to the data of 13 subjects (see "Subjects"). The non-linear regression coefficient was $r^2 = 0.626$. Figure 2 depicts the individual graphs of the two components of the function, of the resulting function, the original data, and the effect of the one-point calibration. The algorithm used is matter of a patent (11/364 174 US 2006/0217616 A1, 7374542).

Results

PWV–BP relation

Applying the algorithm for the calculation of the SBP (including the one-point-calibration) to data of the first group resulted in a significant correlation between BP_{PTT} and BP_{cuff}. Individual correlation coefficients ($n = 13$) varied between $r = 0.75$ and $r = 0.99$ (see Table 1). The correlation coefficient for all data of the 13 volunteers was $r = 0.89$ after correction for repeated measurements ($p < 0.05$, $n = 58$, Fig. 2).

Application of the PWV–BP function

The created function was used to calculate BP values after individual correction for the offset in SBP in a group of 50 volunteers. In this group, load was increased in 5 steps resulting, theoretically, in 300 measurements. However, the number was reduced due to muscle exhaustion or reaching stop criteria ($n = 25$). Further eight measurements were lacking because of technical disturbances in the ECG and/or finger plethysmography. At the end, 267 data pairs were analyzed. Figure 3 shows the plot of BP_{cuff} and BP_{PTT} and the regression for this group. The individual ($n = 50$) correlation coefficients of BP_{cuff} versus BP_{PTT} varied between $r = 0.69$ and $r = 0.99$ (see Table 2). The correlation coefficient for data of all 50 volunteers and measurements was $r = 0.83$ after correction for repeated measurements ($n = 267$, $p < 0.05$).

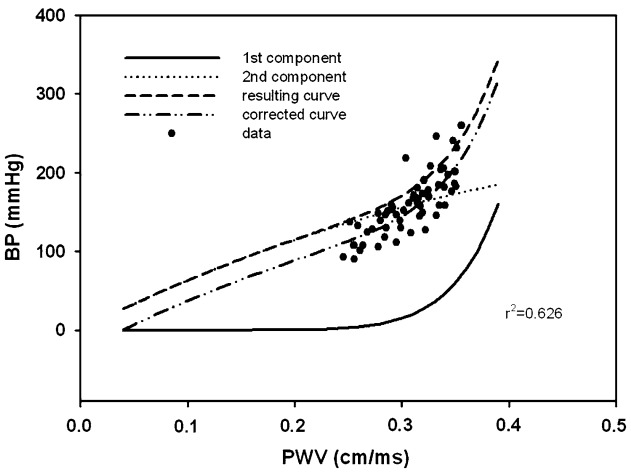

Fig. 2 Graphical demonstration of the two components of the empiric PWV–BP function (1st and 2nd component) and the resulting function without correction (*dashed line*), and with correction (*dashed + dotted line*) using one-point calibration (for details see "Methods" section). *Filled dots* represent the measured data (from group 1)

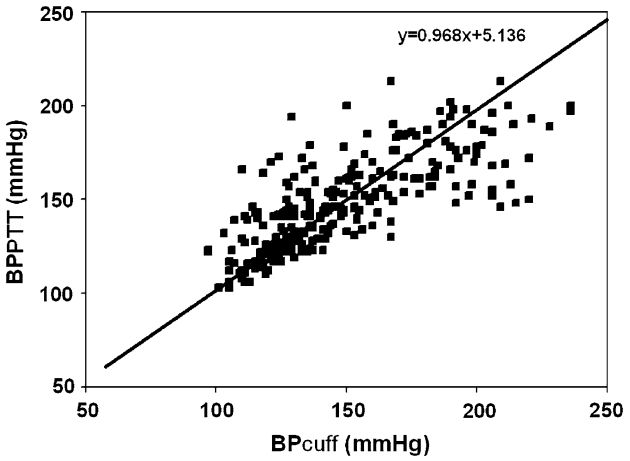

Fig. 3 Plot of systolic blood pressure measured by cuff (BP_{cuff}) versus systolic blood pressure calculated from the pulse transit time (BP_{PTT}) of group 2. The *straight line* represents linear regression (see inserted formula)

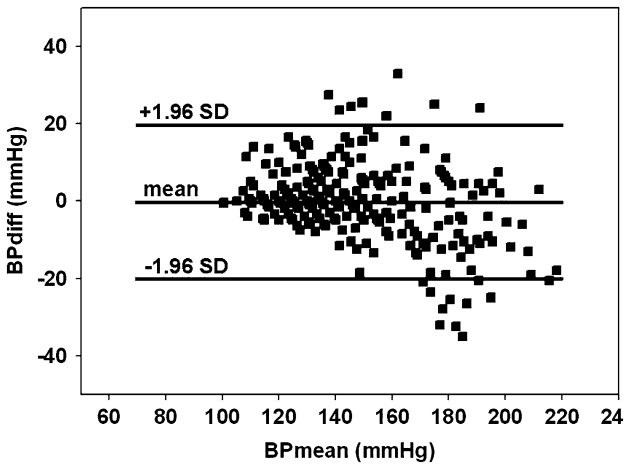

Fig. 4 Bland–Altman plot of the systolic blood pressure (BP) data of 50 volunteers (group 2) obtained during cycling with increasing load (for details see "Methods" section). 18 of 276 pairs are located beyond the agreement limits (mean ± 1.96 SD). Mean represents the average of all differences calculated from $(BP_{cuff} + BP_{PTT})/2 - BP_{PTT}$. The plot gives an idea about the disagreement between the two measures

Figure 4 shows the Bland–Altman plot of the data. The analysis reveals agreement limits of $mean_{SBP_{PTT},SBP_{CUFF}} \pm 19.8$ mmHg. Higher BP values were associated with a greater scatter of the data.

Discussion

The present study shows that the SBP calculated from the pulse transit time using a one-point calibration correlates significantly with the SBP measured by the cuff method. The Bland–Altman plot of the data shows differences of about 20 mmHg between both methods.

In the present paper, the relation between PWV and measured SBP followed a non-linear function. Similar non-linear relations between BP and brachial–ankle PWV were described by Yamashina et al. 2003 in human beings. Other authors obtained a non-linear relationship between PVW and BP, which was inverted to that of the above cited studies (Chen et al. 2009; Zheng and Murray 2009). Linear as well as non-linear PTT-BP functions have been described in isolated canine common carotid arteries (Callaghan et al. 1984), while a number of authors reported linear relations (Geddes et al. 1981; Payne et al. 2006).

The innovation of the presented method is the non-linear algorithm and the one-point calibration. Latter reduces the influence of the structural properties of arteries by shifting the PWV–BP relationship along the *y*-axis. Normally, individual age and/or disease-dependent differences in the arterial stiffness do not allow calculating absolute BP values. This difficulty can only be avoided by creating individual calibration points. Indeed, high correlation between BP derived from the PTT and SBP as well as errors smaller than 10% were observed using an intermitted calibration of the SBP (Chen et al. 2000). However, this procedure seems not to be practicable under clinical conditions. The one-point calibration requires only one BP measurement using a reference method (cuff) in the beginning of the patient's investigation. It has to be considered that patients may differ more or less in regard to the steepness of their PWV–BP relation. Therefore, the one-point calibration represents a compromise between clinical practicability and the need for a complete calibration curve. Nevertheless, the application of the PWV–BP function to the data of the first group serving for the creation of the PWV–BP relation resulted in highly significant individual correlation coefficients.

To test if the method presented here leads to clinically useful determinations of the absolute SBP, a group of 50 volunteers were investigated. Their individual correlation coefficients were significantly high and the values were similar to those that of the first group. While differences between BP_{PTT} and mean BP did not exceed 20 mmHg in the lower pressure range (up to 160 mmHg), the scatter increased in the upper BP range. Individual differences in the PTT–BP relation can be responsible for this effect. Another reason may be the higher frequency of disturbances of the ECG lead and the plethysmography signal during increased load and motor activity on the bicycle ergometer. Such effects have bigger impacts on the PWV calculation when the PTT is short as during high load and high SBP periods. To prevent a significant influence of, e.g., breathing disturbances, the calculated PTTs were averaged for five cycles in the present study.

The calculation of PTT from the ECG (R-spike) and the peripheral plethysmographic signal has the advantage of good availability of both signals under several clinical situations when the ECG and the oxygen saturation are monitored, for example, during sleep. The ECG signal was used as the proximal timing point because it is easy to detect and shows lesser artifacts compared to the phonocardiogram. On the other hand, PTT calculated from the ECG includes the pre-ejection period (PEP), which is the time between the onset of electrical cardiac activity and the start of mechanical ventricular ejection. It has recently been shown that PEP contributes significantly to the PTT. This was shown in studies where BP was varied over a wide range using several pharmacological agents and in short-term physical stress tests, respectively (Payne et al. 2006; Muehlsteff et al. 2006). The data also show that PEP accounts for a variable proportion of PTT suggesting that the PTT estimated from ECG does not only reflect arterial stiffness (Payne et al. 2006).

One limitation of the present study is the use of the cuff method for the reference BP which cannot be considered as the "Gold standard". This is mentionable, since sphygmomanometric measurements have inaccuracies compared with arterial BP measurements (Brown et al. 1994; Turjanmaa 1989; Rebenson-Piano et al. 1987; Van Bergen et al. 1954). Possibly, such inaccuracies contribute to the scatter of the plots in the present study. Remarkably, a recent clinical study, comparing the BP measured by PTT with that of an invasive measurement of the arterial blood pressure, demonstrated similar results in comparison with the present study (Bartsch et al. 2010). The differences shown in the Bland–Altman plot extended to about 15 mmHg in patient without cardiac arrhythmias and hypotension, while the 1.96 SD was clearly greater (>25 mmHg) in a group including patients with arrhythmias and hypotension. This, on the other hand, suggests that the cuff methods used in the present study does not offer serious disadvantages versus intra-arterial measurements in this context.

The 1.96 SD of about 20 mmHg in the present study is debatable in sense of the usability of the PTT method. Whether such a variability of differences is clinically acceptable depends on the application of these methods. Interestingly, mean values of BP calculated from PTT and of BP measured intra-arterially did not differ in a group of 40 volunteers (19,200 data points) (Bartsch et al. 2010). Thus, long-term measurement and calculation of mean BP via PTT gives reliable values. For short-term investigations, as performed in the present study, and for evaluation of transient events, the advantages of the continuous, non-invasive, and non-expensive method via PTT has to be weighted with the disadvantage of higher variability of calculated values.

The present study suggests the usefulness of BP measurement by using the PTT for continuous recording of the SBP. Further studies have to be performed to check if this method is suitable for the measurement of SBP in patients under clinical conditions.

Portapres®, Finapres® and similar method/equipments based on Penaz's principle can also be used for non-invasive measurement of the systemic blood pressure. Their advantage is the continuous registration of blood pressure. These methods have been largely applied in scientific and clinical investigations. Several studies showed that these systems also have disadvantages. The absolute blood pressure measured using this technique can differ compared to intra-arterial and cuff-based methods due to many reasons (Eckert and Horstkotte 2002; Molhoek et al. 1984; Kugler et al. 1997; Kermode et al. 1989). Physical and physiological factors influence the measurement (Imholz et al. 1998). Further, the equipment is cost intensive, which limits the widespread use in the clinic. The current system for calculation of the SBP does not require additional hardware, for example, in most of the diagnostic or therapeutic measurements in the sleep laboratory. ECG and finger plethysmography are routine methods (monitoring). The presented algorithm allows calculating exclusively the SBP in the present study. This is a limitation, since diastolic and mean BP values are also of clinical interest.

In conclusion, the results show that the created PWV–BP function, including a one-point calibration, produces significant correlation between BP derived from the PWV and the SBP measured by sphygmomanometry. Although differences in SBP between both methods reached values up to 20 mmHg, we think that the results form a base for further studies with the aim to evaluate the applicability under clinical conditions.

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Conflict of interest There are no conflicts of interest for the authors Heiko Gesche, Detlef Grosskurth, and Andreas Patzak. Gert Küchler holds the patent cited in the manuscript and is owner of the Somnomedics GmbH. There was no financial support from any company.

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