ORIGINAL ARTICLE

Central blood pressure estimation by using N-point moving average method in the brachial pulse wave

Rie Sugawara, Shigeo Horinaka, Hiroshi Yagi, Kimihiko Ishimura and Takeharu Honda

Recently, a method of estimating the central systolic blood pressure (C-SBP) using an N-point moving average method in the radial or brachial artery waveform has been reported. Then, we investigated the relationship between the C-SBP estimated from the brachial artery pressure waveform using the N-point moving average method and the C-SBP measured invasively using a catheter. C-SBP using a N/6 moving average method from the scaled right brachial artery pressure waveforms using VaSera VS-1500 was calculated. This estimated C-SBP was compared with the invasively measured C-SBP within a few minutes. In 41 patients who underwent cardiac catheterization (mean age: 65 years), invasively measured C-SBP was significantly lower than right cuff-based brachial BP (138.2 ± 26.3 vs 141.0 ± 24.9 mm Hg, difference -2.78 ± 1.36 mm Hg, $P = 0.048$). The cuff-based SBP was significantly higher than invasive measured C-SBP in subjects with younger than 60 years old. However, the estimated C-SBP using a N/6 moving average method from the scaled right brachial artery pressure waveforms and the invasively measured C-SBP did not significantly differ (137.8 ± 24.2 vs 138.2 ± 26.3 mm Hg, difference -0.49 ± 1.39 , $P = 0.73$). N/6-point moving average method using the non-invasively acquired brachial artery waveform calibrated by the cuff-based brachial SBP was an accurate, convenient and useful method for estimating C-SBP. Thus, C-SBP can be estimated simply by applying a regular arm cuff, which is greatly feasible in the practical medicine.

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INTRODUCTION

Heart and major arteries supplying blood to the brain are exposed to central aortic pressure rather than brachial arterial pressure. Particularly in heart, central aortic pressure directly reflects cardiac afterload in systole and controls coronary circulation in diastole. As a consequence, central aortic pressure may be a more powerful predictor of the cardiovascular events than brachial arterial pressure.^{1–3} The Conduit Artery Function Evaluation study, a sub-study of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), suggested that the two different blood pressure lowering regimens could have expected the different effects on central blood pressures despite similar brachial blood pressures, and concluded that the difference in central blood pressure may explain the different clinical outcomes.⁴

Central blood pressure is regulated by cardiac output, peripheral resistance, stiffness of aorta and the timing and magnitude of pressure wave reflection. Although diastolic arterial pressure is comparatively constant, systolic pressure is up to 40 mm Hg higher in the brachial artery than in the central aorta.^{5–7} As the pressure wave travels from the elastic central conduit artery to the stiffer muscular brachial artery, the systolic pressure increases in the brachial artery as compared with the proximal ascending aorta especially in young subjects.^{5,6}

The gold standard measurement of central blood pressure is the direct recording of the blood pressure in the proximal ascending aorta by using a pressure-sensing catheter. However, this is unsuitable for routine clinical practice and the numbers of non-invasive methods have been developed. The corresponding central blood pressure derived from peripheral arteries (brachial or radial) by using a generalized transfer function^{7,8} or identification of the late systolic shoulder, so called SBP2,^{9,10} Very recently, Shih *et al.*¹¹ demonstrated that the N-point moving average method using a mathematical low-pass filter with a common dominator of the N/6 (where N is acquisition sampling frequency) eliminated peaked systolic augmentation of the brachial pressure waveform by the reflection wave of the peripheral arteries, and that could estimate central systolic pressure accurately. Cuff-based device (Vasera VS-1500, Fukuda Denshi, Tokyo, Japan) is able to obtain brachial waveform from pulse volume plethysmography and blood pressure measured by brachial cuff. Therefore, we examined whether the non-invasively determined central aortic pressure that is obtained by N/6-point moving average method of the scaled brachial waveform in Vasera VS-1500 can estimate the direct recording central aortic pressure in the proximal ascending aorta in the cardiac catheterization.

METHODS

Study population and data collection

We recruited patients who had chest pain, suspicious of ischemic heart disease and underwent first coronary angiography for diagnosis or exclusion of coronary artery disease at Dokkyo Medical University Hospital. Patients who had acute myocardial infarction, congenital heart diseases, valvular heart diseases, aortic aneurysm and atrial fibrillation were excluded.

The patients were instructed to assume a supine position for 10 min before measurements in the catheter laboratory. This room was semi-clean and temperatures were 26°C and 24°C in summer and winter, respectively, and humidity was 50%. Patients were fasting state and were prohibited caffeine intake and smoking since 24 h before measurements. The pre-treatments such as anti-hypertensive agents were continued until 4 h before measurements.

We divided two study groups.

Comparison group study. First, in the comparison group ($n=31$), the cuff-based left brachial systolic and diastolic blood pressures (SBP and DBP) and invasive proximal ascending aortic systolic (i-CSBP) and diastolic blood pressures (i-CDBP) (measured using fluid-filled manometer system with the breath lightly hold that was confirmed stable in the blood pressure waves by the pressure recording monitor; AXIOM Sensis XP, Siemens AG, Muenchen, Germany) were simultaneously measured, and these blood pressures were compared. Because using the right arm for catheterization in many cases, we could not be attached simultaneously to the cuff on the right arm. The present specification of the VS-1500 is able to measure the brachial pulse waveform only when the cuffs were attached on both arms.

Validation group study. Second, in the validation group ($n=41$), the non-invasively calculated C-SBP (N/6-moving average systolic blood pressure (MASBP)) that was obtained by N/6-point moving average method from the scaled right brachial pulse pressure waveform and the cuff-measured brachial SBP after resting for 10 min before cardiac catheterization in the supine position in the catheter laboratory. Then within the 10 min, i-CSBP was measured, and the values were compared with N/6-MASBP.

Cardiac catheterization

All patients underwent diagnostic cardiac catheterization with a right transradial or transbrachial approach, which unable the measurement of right brachial blood pressure and the recording of right pulse pressure waveform simultaneously. First, the pigtail catheter (5-French size, tube outer/inner diameter = 1.70/1.20 mm, Fukuda Denshi) or Judkins catheter (5-French size, tube outer/inner diameter = 1.67/1.15 mm, Gadeliusmedical K.K., Tokyo, Japan) was inserted to the proximal aorta, which was just above to the aortic valve and directly measured i-CSBP and i-CDBP by fluid-filled manometer system. The transducer (TruWave disposable pressure transducer, Edwards Lifescience, Irvine, CA, USA, Infus Medical, Tambon, Thailand) was kept at the level of mid-axillary line during the examination and zero calibrated to atmosphere before catheterization. Then, the patients were underwent coronary angiography and the coronary heart disease was defined when the major coronary artery exhibited at least 75% organic stenosis after intracoronary injection of a nitrate drug.

Principles and methods of measuring cuff-based brachial blood pressure and brachial pulse waveform measurements

The VaSera VS-1500N (Fukuda Denshi) was utilized. The measurements were executed using plethysmography cuffs placed on the left or right upper arm with installation of the semiconductor pressure sensors. The brachial pulse waveforms were obtained by the volume plethysmographic method at the cuff pressure of 50 mm Hg by the sample frequency of 1 KHz. Consecutively, cuff-based SBP and DBP were obtained by the oscillometric method. Two blood pressure measurements were performed; the first measurement was used when the difference of these was less than 10 mm Hg. If it more than 10 mm Hg, then lower value was used.

Non-invasively calculated C-SBP by using N/6-MABP of the brachial pulse waveform

The non-invasive brachial pulse waveform data were transferred to the personal computer with the data management software VSS-10 (Fukuda Denshi). These data were calibrated to the cuff-based brachial SBP. The N-point moving average method with dominator of N/6 ($1000/6=167$), which was suitable for analyzing brachial cuff-based waveform, was used to estimate the C-SBP as previously described by Shih *et al.*¹¹

Furthermore, we calculate the standard deviation (s.d.) of consecutive five beats in the N/6-MASBP. Average s.d. was 0.621 ($n=40$). Thus, the reproducibility of the non-invasive method itself might be good.

Central systolic pressure was determined to the maximum value of the moving average array curve as shown in Figure 1.

The Institutional Review Board of Dokkyo Medical University approved the study protocol. The written informed consent was obtained from all patients.

Statistical analysis

All calculated data are expressed as mean $\pm$ standard deviation. Paired samples *t* test and the Bland-Altman analysis were performed to determine the agreement between measurements. Comparisons between the two groups were done by chi-square test. The correlation coefficient was calculated for paired data with or without adjustment of age. Multiple stepwise regression analysis was performed when there were many variables. A 2-tailed $P<0.05$ was considered significant. Statistical analysis was performed using JMP 10.0 software (SAS Institute, Carry, NC, USA).

RESULTS

Comparison group: Comparison between cuff-based brachial SBP and i-CSBP, cuff-based brachial DBP and i-CDBP

Baseline subject characteristics are shown in Table 1. Mean age was 66.7 years old and 58.1% of subjects were male. Almost two-third of the patients received antihypertensive drugs and half of patients received statins, and 29% of patients received anti-diabetic hypoglycemic medication. Eighteen subjects (58.1%) had coronary artery disease. As a whole, blood pressure was high normal.

Figure 1 Central systolic blood pressure (C-SBP) was calculated by using a N/6 moving average method from the scaled right brachial artery pressure waveforms. The N/6 ($1000/6=167$ points) moving averages were plotted to a brachial artery pressure waveform acquired using plethysmography with a sampling frequency of 1000 Hz. Cuff-based SBP and N/6 moving average SBP (estimated central systolic blood pressure) were 123 and 121.5 mm Hg, respectively. BP, blood pressure.

The cuff-based left brachial SBP was correlated with i-CSBP ($R=0.860$, $P<0.0001$) as shown in Figure 2a, the cuff-based SBP however, was significantly higher than i-CSBP (difference = 4.0 ± 12.0 mm Hg, $P=0.0053$, Table 2 and Figure 3). Although the age was not significant covariates in the multiple stepwise regression analysis ($P=0.128$), the correlation coefficient between the cuff-based brachial SBP and i-CSBP slightly improved with adjustment of age as shown in Figure 2b ($R=0.871$, $P<0.0001$). Interestingly, the cuff-based brachial SBP – i-CSBP difference between the age group of younger than (9.6 ± 8.6 mm Hg) and that of older than 60 years old (2.0 ± 12.5 mm Hg) was significant ($F=6.32$, $P=0.014$) as shown in Figure 4.

Table 1 Characteristics of the study subjects

	Comparison group (n = 31)	Validation group (n = 41)
Age (years)	66.7 $\pm$ 12.2	64.8 $\pm$ 9.8
Male, n (%)	18 (58.1)	31 (75.6)
Body height (cm)	158.6 $\pm$ 10.3	160.3 $\pm$ 8.5
Body weight (kg)	58.5 $\pm$ 12.7	62.8 $\pm$ 12.9*
Body mass index (kg m ⁻²)	23.1 $\pm$ 3.2	24.3 $\pm$ 3.8
Systolic blood pressure (mm Hg)	140.2 $\pm$ 18.3	143.3 $\pm$ 21.9
Diastolic blood pressure (mm Hg)	79.8 $\pm$ 12.7	87.0 $\pm$ 11.3*
Pulse rate (bpm)	72.2 $\pm$ 12.7	67.3 $\pm$ 13.3*
Current smoking, n (%)	3 (9.7)	2 (0.5)
Hypertension, n (%)	23 (74.2)	32 (78.1)
Diabetes mellitus, n (%)	9 (29.0)	15 (36.6)
Dyslipidemia, n (%)	15 (48.4)	16 (36.0)
Coronary artery disease, n (%)	18 (58.1)	31 (75.6)
Chronic kidney disease	5 (16.1)	8 (19.5)
<i>Use of medications, n (%)</i>		
Angiotensin-converting enzyme inhibitors	1 (3.2)	4 (9.8)
Angiotensin receptor blockers	13 (48.4)	22 (53.7)
β -Blockers	4 (12.9)	13 (31.7)
Calcium channel blockers	14 (45.2)	23 (56.1)
Diuretics	0 (0)	2 (4.9)
Statins	18 (58.1)	12 (29.3)

Values are mean $\pm$ s.d. or number of subjects (%).

* $P<0.05$.

This indicates the subjects who are younger than 60 years old have higher in the cuff-based brachial SBP than in the i-CSBP.

The cuff-based left brachial DBP was also correlated with i-CDBP ($R=0.685$, $P<0.0001$); the cuff-based DBP, however, was significantly higher than i-CDBP (difference = 12.3 ± 8.1 mm Hg, $P<0.0001$) as shown in Table 2.

Validation group: non-invasively calculated C-SBP (N/6-MASBP) and i-CSBP

Patient's characteristics and physiological data were also shown in Table 1. Age, cuff-based left brachial SBP, other patient characteristics and use of medications were comparable between the comparison and validation groups (Table 2). The slopes of the correlation line in the left brachial SBP between the comparison and validation groups were almost equivalent (the validation group: $y=1.050x-15.196$, $R=0.908$, $P<0.0001$ as compared with the comparison group as shown in Figure 2a). Moreover, cuff-based right and left brachial SBPs also did not differ significantly ($P=0.062$). i-CSBP was closer to cuff-based right brachial SBP than left brachial SBP but there was still statistically significant difference ($P=0.048$). On the other hand, i-CSBP and N/6-MASBP were quite similar and did not significantly differ (difference = -0.5 ± 8.9 mm Hg, $P=0.728$ Figure 5). Moreover, the good correlation between N/6-MASBP and i-CSBP was observed ($R=0.941$, $P<0.0001$) as shown in Figure 6a. The correlation coefficient between N/6-MASBP and i-CSBP did not improve with adjustment of age as shown in Figure 6b ($R=0.938$). The N/6-MASBP – i-CSBP difference between the age group of younger than (3.4 ± 2.0 mm Hg) and that of older than 60 years old (3.2 ± 1.5 mm Hg) was not significant ($F=0.25$, $P=0.619$). This indicates that N/6-MASBP – i-CSBP difference is independent of age.

DISCUSSION

The present study confirmed a close correlation between N/6-MASBP and i-CSBP. Although the cuff-based brachial SBP was significantly different from i-CSBP, the values of N/6-MASBP and i-CSBP did not differ significantly. The cuff-based SBP but not N/6-MASBP was significantly higher than i-CSBP in subjects with younger than 60 years old, which was coincident with the previous reports.^{5,6} This finding may implicate important suggestion that SBP measured by brachial cuff is likely to overestimate compared with central blood pressure especially in subjects with younger than 60 years old.

Very recently, Shih *et al.*¹¹ reported that mean difference between non-invasively estimated central aortic systolic pressure by the N-point moving average with a dominator of N/6 and invasively measured

Figure 2 (a) Relationship between i-CSBP and cuff-based left brachial SBP in the comparison group. SBP, systolic blood pressure. (b) Relationship between i-CSBP and cuff-based left brachial SBP after adjustment of age in the comparison group. n, number of simultaneous measurements.

Table 2 The cuff-based brachial blood pressure and invasive central blood pressure

	Cuff-based brachial BP	Invasive central BP	Difference
<i>Comparison group</i>			
<i>Left brachial</i>			
Systolic (mm Hg)	140.2 ± 18.3	136.2 ± 23.4*	-4.0 ± 12.0*
Diastolic (mm Hg)	79.8 ± 12.7	67.5 ± 11.6*	-12.3 ± 8.1*
Pulse rate (bpm)	72.2 ± 12.7		
<i>Validation group</i>			
<i>Left brachial</i>			
Systolic (mm Hg)	143.3 ± 21.9	138.2 ± 26.3*	-7.9 ± 12.0*
Diastolic (mm Hg)	87.0 ± 11.3	63.4 ± 11.9*	-17.0 ± 8.8*
<i>Right brachial</i>			
Systolic (mm Hg)	141.0 ± 24.9	138.2 ± 26.3 ⁺	-2.8 ± 8.7 ⁺
Diastolic (mm Hg)	81.0 ± 10.9	68.4 ± 11.9*	-12.6 ± 10.7*
Pulse rate (bpm)	67.3 ± 13.3	70.7 ± 12.9	3.4 ± 7.9*
	<i>N/6-MASBP</i>	<i>Invasive central BP</i>	<i>Difference</i>
Systolic (mm Hg)	137.8 ± 24.2	138.2 ± 26.3	-0.5 ± 8.9

Abbreviations: BP, blood pressure; N/6-MASBP, N-point moving average with a dominator of N/6 of the scaled right brachial pulse pressure waveform by the cuff-measured right brachial systolic blood pressure; * $P < 0.01$, ⁺ $P < 0.05$.

Figure 3 Bland-Altman comparison of the cuff-based left brachial SBP and i-CSBP in the comparison group. CI, confidential interval.

central aortic systolic pressure using a pressure-sensing catheter was -0.6 ± 7.6 mmHg, which was almost identical to the our data by using water-filled system (-0.5 ± 8.9 mmHg). The theoretical aspect of the N-point moving average method is noteworthy. The N/6-point moving average removes all pulse wave components above 4 Hz that is typically dominated by the wave reflection in the brachial artery waveform, and also heart rate alteration modifies more than this frequency band.¹²

Currently, the most popular method for estimating the central blood pressure is to convert to the aortic pressure waveform from radial artery waveform using the generalized transfer function.^{4,7,8,10} However, the radial and central aortic pressure waveforms were much different when the mean pressure was lower that was lower vascular compliance as well as the slower timing and lesser magnitude of reflected waves.¹³ These factors vary with age and vascular disease^{14–16} and might affect the population-based generalized transfer function. The transfer functions are different in each subject especially in a diseased patient.^{17,18} Furthermore, Verbeke *et al.*¹⁹ suggested that the calibration of radial arterial pressure waveform on brachial arterial pressure should be avoided since the amplification from the brachial to radial pulse pressure was average 12%.

Figure 4 Relationship between the cuff-based left brachial SBP - i-CSBP difference and age in the comparison group.

Figure 5 Bland-Altman comparison of the i-CSBP and estimated C-SBP by using N/6 moving average to scaled brachial artery pressure waveform in the validation group.

In this study, invasive central blood pressure measurements were underwent using a fluid-filled monometer system. This system is known to have a chance to occurrence of damping and attenuation of pressure waves due to microbubbles, coagulation and leakage, which

Figure 6 (a) Relationship between i-CSBP and estimated C-SBP by using N/6 moving average to scaled brachial artery pressure waveform in the validation group. MASBP, moving average systolic blood pressure. (b) Relationship between i-CSBP and estimated C-SBP by using N/6 moving average to scaled brachial artery pressure waveform in the validation group after adjustment of age. n, number of simultaneous measurements.

becomes a problem.^{20,21} However, it has the advantage that an external zero is kept constant, which offsets the catheter-mounted sensor records irrespective of the vertical position of the sensor in the body. Although a catheter-tip pressure transducer has no chance of occurrence of damping and attenuation, it possibly exhibit DC electrical drift.^{22,23}

We found that i-CSBP more closely correlated with N/6-MASBP in the right brachium than that of the left. Theoretically, the just position above the aortic valve that is nearest from the heart is ideal for the location of central blood pressure measurement, since the pulse waveform is gradually amplified by the reflection wave with the away from the heart. The possible location of the blood pressure measurement using a cuff is the right upper arm, which is nearest to the heart. Actually, several previous studies have used carotid tonometry to non-invasively estimate central aortic pressure waveform alterations with aging and to assess aortic impedance^{24–26} and a surrogate for central aortic waveform analysis.²⁷ Because carotid artery is directly separated from ascending aorta and nearest to the heart.

Anatomically, the reflection wave, the water column pressure correction, was more prominent in the wrist than in brachium.^{28,29} Moreover, Williams *et al.*³⁰ demonstrated that N-point moving average method using a common dominator of the N/4 but not N/6 to a non-invasively acquired radial artery waveform with the applanation tonometry, calibrated to cuff-based brachial blood pressure, defined C-SBP most accurately. Thus, the most sophisticated common dominator might be different in the radial (N/4) artery and the brachial artery (N/6).

Notably, the most important factor inducing error in the estimation of central blood pressure was the inaccuracy of cuff-based brachial blood pressures. Currently, all central blood pressure measuring device was corrected by the brachial cuff pressure, which was measured by oscillometric method. The algorithms and experimentally obtained coefficients were used to adjust the oscillometric results to give readings that match the auscultatory results as well as possible. Since many oscillometric devices have not been validated, the commercially available oscillometric devices might have different algorithms.

The 1993 modified British Hypertension Society protocol,³¹ the 2002 International Protocol and the 2002/2003 Association for the Advancement of Medical Instrumentation³² standards required measurement error of 5 ± 8 mm Hg to peripheral automatic blood pressure monitors as compared with auscultatory results but not direct measurement result by the catheter-tip or fluid-filled catheter. The oscillometric devices ordinarily underestimate brachial SBP and

overestimate brachial DBP.³³ In our study, cuff-based brachial DBP was significantly higher than the i-CDBP. This discrepancy may be explained by the reasons of above mentioned and these have also suggested by Williams *et al.*³⁰ Therefore, the oscillometric device should be accurately integrated when they are used to estimate central BP especially in DBP.

In conclusion, N-point moving average method using a common dominator N/6 to a non-invasively acquired brachial artery waveform obtained by the volume plethysmography and calibrated to cuff-based brachial SBP was an ideal, convenient and useful method for estimating C-SBP. Furthermore, C-SBP can be estimated by simply applying regular cuffs. There is a large merit in the usage of this method in the practical medicine. Central blood pressure may be a better predictor of future cardiovascular events than peripheral blood pressure. However, the most required data will clarify whether the lowering N/6 MASBP by antihypertensive drugs is actually associated with the improvement of hypertension-induced target organ damage and clinical outcome.

Limitations

Various limitations apply to the present study. First, the direct central blood pressure was not measured by using a pressure-sensing catheter. This may lead to underestimation of the C-SBP. Second, although the left brachial SBPs were comparable in the comparison and validation groups, the direct central systolic pressure and right cuff-based brachial SBP were not simultaneously measured. Currently, the study is ongoing to measure simultaneously the right invasive and left non-invasive brachial blood pressures and compare the central blood pressure. Third, pharmacological treatment may influence the N/6-MASBP and the influence should be investigated. However, the antihypertensive agents have been reported to have no effects on the result of N-point moving average method.¹¹ Forth, N/6-MASBP requires the calibration of cuff-based brachial blood pressure, which greatly depends on the accuracy of the brachial artery blood pressure measurement. Fifth, further study needs to demonstrate the reproducibility of N/6-MASBP at the several different time points. Finally, although the sample size was relatively small, Bland-Altman analysis revealed the agreement between N/6-MASBP and i-CSBP.

CONFLICT OF INTEREST

N/6 point moving average program was gift from Fukuda Denshi, Tokyo, Japan. The authors declare no other conflict of interest.

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