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Arterial pressure: agreement between a brachial cuff-based device and radial tonometry

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Objectives: Aortic (central) blood pressure (BP) differs from brachial BP and may be a superior predictor of cardiovascular events. However, its measurement is currently restricted to research settings, owing to a moderate level of operator dependency. We tested a new noninvasive device in a large UK cohort. The device estimates central BP using measurements obtained with an upper arm cuff inflated to suprasystolic pressure. We compared these estimates with those obtained using radial tonometry as well as with invasively acquired measurements of aortic BP in a limited number of individuals.

Methods: Consecutive cuff-based and tonometry-based estimates of the pressure waveform and the central BP were obtained from 1107 individuals (70 ± 6 years). Short-term and long-term reproducibility studies were performed on 28 individuals. Simultaneous cuff-based and invasively measured pressure traces were acquired and compared in an additional six individuals (65 ± 20 years).

Results: Central systolic BP, as estimated by the cuff-based device, was found to be highly reproducible (coefficient of variation 4 and 8% for short and long-term reproducibility, respectively) and was comparable to that estimated by tonometry (average difference 3 ± 6 mmHg, intraclass correlation coefficient = 0.91). The cuff-based pressure waveforms were similar to those acquired invasively (cross-correlation coefficient 0.93), and the difference in the estimated central systolic BP was −5 ± 8 mmHg ($P = 0.2$).

Conclusion: Cuff-based devices show promise to simplify the measurement of central BP, whilst maintaining a similar fidelity to tonometry. This could lead to improved adoption of estimates of central BP in clinical practice.

Keywords: brachial cuff, central blood pressure, invasive, noninvasive, tonometry

Abbreviations: AMMI, American Association for the Advancement of Medical Instrumentation; bDBP, brachial diastolic pressure; bSBP, brachial systolic pressure; BP, Blood pressure; bSBP, brachial systolic BP; CHD, coronary heart disease; CVD, cardiovascular disease; cDBP, central DBP; cSBP, central systolic BP; DBP, brachial DBP; HR, heart rate; ICC, intraclass correlation coefficient; MAP, mean arterial pressure; PP, pulse pressure; SABRE, Southall And Brent REvisited

INTRODUCTION

Hypertension is a major determinant of cardiovascular disease (CVD) [1], and measurement of blood pressure (BP) using a brachial cuff is one of the most widely performed clinical investigations. Systolic and diastolic BP are determined by the shape of the BP waveform, which is itself influenced by the interaction between left ventricular ejection and the biomechanical properties of the arterial system. Pulse pressure increases as it travels from the aorta to peripheral locations such as the brachial artery [2], and the difference between aortic and brachial systolic BP (bSBP) can be substantial [3]. In adults, peripheral systolic BP exceeds aortic pressure by approximately 10 mmHg; however, this difference can be much greater especially in younger individuals and with increased heart rate. Differences between central (aortic) and brachial BP could be clinically important, as central BP is more closely correlated with target organ damage in hypertension [4]; is differentially influenced by antihypertensive therapy compared with brachial BP [5]; and may be a superior predictor of cardiovascular events than brachial BP [6]. These three factors emphasize the potential importance of routine measurement of central BP in research and clinical settings.

Radial artery applanation tonometry is an established methodology for noninvasive measurement of central BP and has been widely used for research. It involves the use of a generalized transfer function to derive a central BP waveform from the measured tonometry signal [7,8]. However, the technique requires both a moderate level of operator skill and also requires calibration by conventional sphygmomanometry. Furthermore, the mode of calibration has been reported to influence the results considerably [9]. A second option is a new, automatic, noninvasive, cuff-based

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BP measurement device that estimates central systolic BP (cSBP) from suprasystolic waveforms [10] as part of a routine brachial BP measurement.

In this study, we compared noninvasive estimates of central BP calculated by the cuff-based device and by applanation tonometry in a multiethnic cohort of older individuals with varying levels of cardiovascular risk. In addition, we compared the cuff-based measurements against invasive measurements of central aortic BP in a small sample of patients with established disease.

MATERIALS AND METHODS

Participating patients

Noninvasive measurements were performed on 1107 participants aged 70 ± 6 years recruited from the Southall And Brent REvisited (SABRE) study. SABRE is a large population-based tri-ethnic longitudinal study consisting of white Europeans, first-generation migrant South Asians and African-Caribbean people living in the UK. Participants were originally recruited from primary care without exclusions in 1988–1991 [11], and data for the current study were collected as part of the 20-year follow-up that was conducted between June 2008 and March 2011. Approval was obtained from the local research ethics committee, and all participants gave written informed consent. The study adheres to the principles of the Declaration of Helsinki.

Preliminary clinical assessment

All participants fasted overnight and refrained from taking any medication on the morning of their visit to the clinic. A questionnaire was completed, which detailed health behaviours, medical history and medication. Height, weight and waist circumference were measured, as previously described [11]. Coronary heart disease (CHD) was defined as a coronary event or revascularization identified by medical record review, and adjudicated by an independent committee. Fasting blood plasma and serum samples were taken for biochemical analysis and those without known diabetes also had an oral glucose tolerance test (OGTT) performed. Diabetes was defined according to the 1999 WHO guidelines [12], and hypertension was defined as physician-diagnosed hypertension or participant-reported hypertension accompanied by receipt of BP-lowering medication.

Noninvasive estimates of central blood pressure

Participants rested in a sitting position in a quiet, dark, temperature-controlled room for at least 10 min prior to measurements. We performed two noninvasive measurements of pressure (in the left brachial and radial arteries). For these, we used a cuff-based device (Pulsecor R6.5; Auckland, New Zealand) and a tonometry-based device (SphygmoCor; AtCor, Sydney, Australia).

A variety of different cuff sizes were available to use with the cuff-based device. Arm circumference was measured prior to choosing which cuff to use according to the British Society of Hypertension guidelines. The cuff-based device was calibrated by recording BP in the brachial artery using oscillometry employing a British Society of Hypertension validated algorithm [13]; details about the device and algorithms have been published [10]. The cuff was then deflated for 3–5 s, and reinflated to nearly 30 mmHg above the recorded brachial systolic pressure (i.e. suprasystolic pressure), to occlude the brachial artery. The resulting wideband suprasystolic cuff pressure signals were recorded for 10 s (approximately two respiratory cycles) before cuff deflation. The device calculated central BP measurements from the ensemble-averaged suprasystolic brachial cuff waveforms calibrated to brachial BP as described previously [10,14].

SphygmoCor measurements were acquired immediately after taking the Pulsecor measurements, according to the manufacturer's instructions. First, calibration was performed using the measurements of BP acquired by the cuff device. Two different calibration schemes were used: bSBP and brachial diastolic BP (bDBP); and calibration using brachial mean arterial pressure (MAP) and bDBP, where $\text{MAP} = \text{bDBP} + (0.4 * \text{pulse pressure})$, as described by Bos *et al.* [15]. The SphygmoCor device is a hand-held tonometer with a strain gauge pressure sensor; it was used to applanate the left radial artery and record pressure waveforms over at least six cardiac cycles. Central BP was calculated using the manufacturer's software, which employs a generalized transfer function.

Repeatability and reproducibility of cuff-based estimates of central blood pressure

Short-term repeatability data for the cuff-based device was collected on 28 volunteers average age 53 ± 20 years (20 men) by recording two measurements 5–10 min apart on the same day. Long-term reproducibility was performed on a different set of 28 individuals, average age 71 ± 5 years (23 men): measurements were repeated on two occasions that were separated by an interval of approximately 1 month.

Comparison with invasive central blood presure measurements

In the invasive study, six patients (four men, aged 65 ± 20 years) undergoing diagnostic catheterization procedures in the Cardiac Catheterization Unit, Hammersmith Hospital, London, UK, participated. The protocol was approved by the local research ethics committee, met with the requirements of the Research Governance Framework and all participating patients gave informed consent.

Invasive and noninvasive central BP was measured simultaneously over a period of seven to 10 cardiac cycles. Noninvasive estimates of central BP were derived using the Pulsecor device, as described previously. Invasive ascending aortic pressure measurements were recorded using a high-fidelity pressure wire (Combowire XT Guidewire; Volcano Europe BVBA, Brussels, Belgium), which was calibrated prior to each measurement. The raw data were passed from the transducer into a Wavemap console in which the analogue signal was converted into a digital signal by a 12-bit analogue-to-digital converter. Aortic pressure signals were processed off-line using custom-written software in Matlab (The MathWorks Inc., Natick, Massachusetts, USA), and seven to 10 cycles were analysed. The beats in the invasively measured pressure

corresponding to the beats used to calculate the cuff-based pressure were identified and ensemble averaged off-line. The form factor for both waveforms was calculated for each patient as form factor = (MAP – bDBP)/pulse pressure [16].

Statistical analysis

Statistical analyses were performed using Stata 12.0 (StataCorp, College Station, Texas, USA). All numerical measurements are reported as mean ± SD. The data were examined for skewness and were log-transformed if necessary: the repeatability and reproducibility of data from the brachial cuff-based device, comparison of cuff-based and tonometry-based central BP estimates, and comparison of cuff-based estimate vs. invasive pressures were each performed using Bland–Altman analysis [17]. Repeatability and reproducibility were also assessed using the within-individual coefficient of variation. Comparisons of cSBP measured by the two devices were also assessed using intraclass correlation coefficients (ICCs). Comparisons of cSBP estimated by the two noninvasive devices in subgroups stratified by age, ethnicity, diabetes, hypertension, CHD and type of antihypertensive medication (in those with known hypertension) were made using Student's *t*-test or analysis of variance (ANOVA) as appropriate. Agreement between the waveforms of the ensemble averages of the invasively measured pressures and cuff-based measurements was determined by the cross-correlation coefficient calculated over the cardiac cycle for each patient. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Cuff-based device repeatability and long-term reproducibility

The difference between the two estimates of the cSBP taken 5–10 min apart was 1 ± 4 mmHg and that of the cDBP was 0 ± 4 mmHg (Fig. 1a, b). The intraobserver coefficient of variability was 4% for bSBP and 5% for bDBP, 4% for cSBP and 5% for cDBP.

The average difference between the two estimates taken 1 month apart was 0 ± 11 mmHg for cSBP and 2 ± 11 mmHg for cDBP (Fig. 1c, d). The coefficient of variability was 7% for bSBP and 8% for bDBP and 8% for cSBP and 13% for cDBP.

Comparison of cuff-based and tonometry-based central blood pressure estimates

The characteristics of the 1107 participants in the noninvasive study are presented in Table 1. Average resting brachial BP was 142/84 mmHg and 67% of participants were taking antihypertensive therapy. Comparison of the cSBP estimated using the tonometer (calibrated with the bSBP and bDBP) and the cuff-based device revealed that the cSBP was 3 ± 6 mmHg higher when measured using the cuff-based device (Table 2, Fig. 2a). This value is within the American Association for the Advancement of Medical

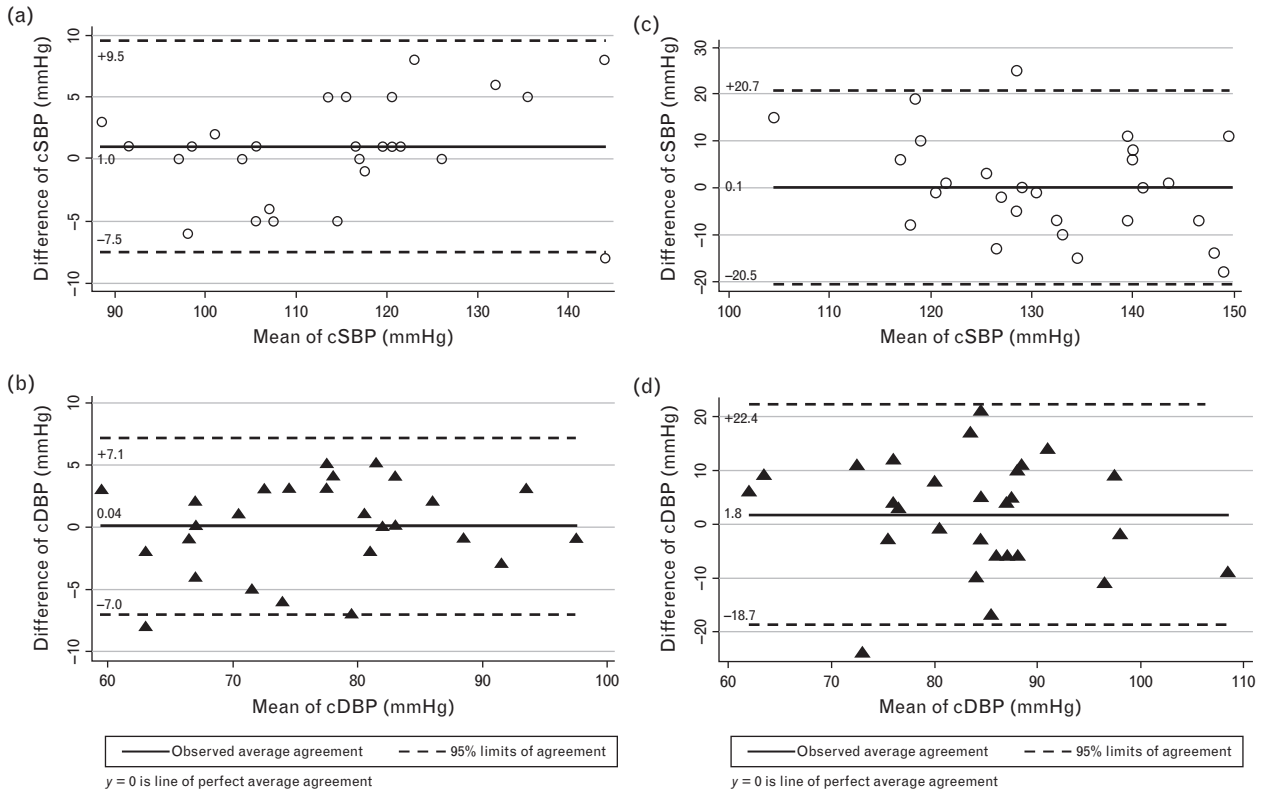

FIGURE 1 Comparison of the repeatability and reproducibility of central systolic (cSBP) and diastolic (cDBP) pressure obtained using the cuff-based device. (a) repeatability of cSBP; (b) repeatability of cDBP; (c) reproducibility of cSBP; (d) reproducibility of cDBP.

TABLE 1. Characteristic of participants in noninvasive study ($n = 1107$)

Variable	Value
Men, *n* (%)	840 (76)
Age (years)	70 ± 6
Ethnicity (European/South Asian/ African Caribbean), *n* (%)	520 (47)/396 (36)/191 (17)
Height (cm)	168 ± 9
Weight (kg)	77.2 ± 14.1
BMI (kg/m^2)	27.4 ± 4.5
Waist (cm)	98.4 ± 11.7
Brachial systolic BP (mmHg)	142 ± 16
Brachial diastolic BP (mmHg)	84 ± 10
Heart rate (beats/min)	68 ± 2
Antihypertensive treatment, *n* (%)	739 (67)
CHD, *n* (%)	271 (25)
Diabetes, *n* (%)	342 (31)

Data are mean ± SD or *n* (%). CHD, diagnosed coronary heart disease.

Instrumentation (AAMI) standards (mean <5 mmHg, or SD <8 mmHg). The cDBP did not differ between the two noninvasive devices (Table 2, Fig. 2b). When the tonometer was calibrated using the MAP and bDBP, the cuff-based estimates of cSBP were 5 ± 8 mmHg lower than tonometry estimates (Table 2, Fig. 3).

Stratified comparison of cuff-based and tonometry-based central blood pressure estimates

A more detailed assessment of the comparability of the estimates of the cSBP obtained using the two noninvasive devices was achieved by stratifying the patients according to their sex, age more than 69 years, ethnicity, BMI, hypertension status, diabetes status, presence of diagnosed CHD and class of antihypertensive medication. Table 3 shows that all comparisons still fell within the AAMI standards. The differences between the two devices were not significantly different when stratified by age, sex, ethnicity, obesity, hypertension and CHD (Table 3). However, there was a larger difference in the estimates of the cSBP produced by the cuff-based device and tonometry in participants with diabetes ($P = 0.002$) and a progressively larger difference in overweight and obese individuals ($P = 0.003$). Differences between cuff-based device and tonometry in people with diabetes were similar when they were stratified into normal overweight or obese categories (data not shown), suggesting that the influence of diabetes was not attributable to more obese participants in the group with diabetes.

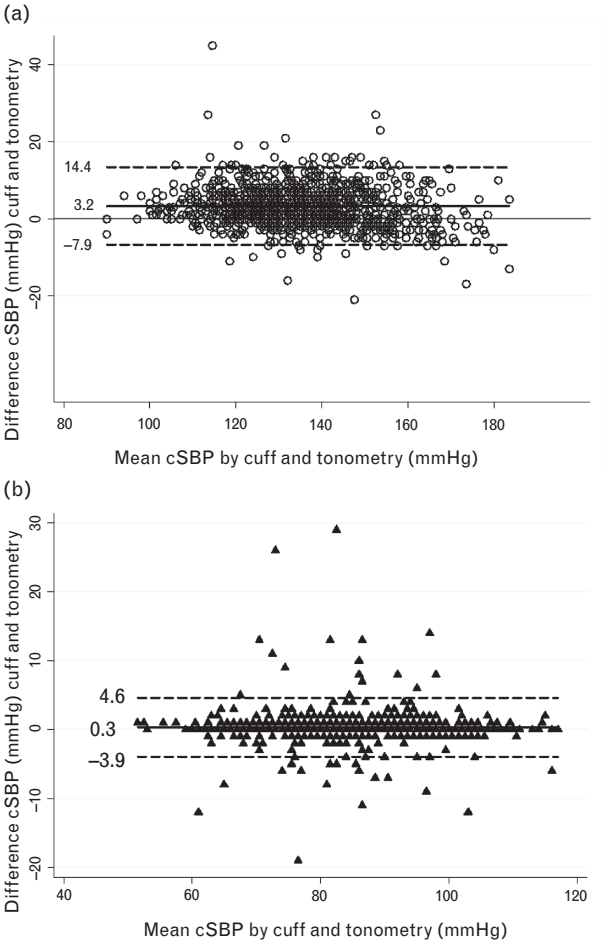

FIGURE 2 Comparison of central systolic pressure (cSBP) obtained using the cuff-based device and tonometry calibrated using brachial systolic and diastolic pressure.

Comparison of noninvasive cuff-based and invasive pressure waveforms

The average resting brachial BP for the invasive study participants ($n = 6$, 67% men) was 126/82 mmHg. Figure 4a shows the ensemble average of the invasively measured pressure and noninvasive pressure waveforms for one of the participants. In all patients, the cSBP tended to be higher, whereas the cDBP was significantly lower in invasive than in noninvasive measurements. Figure 4b shows

TABLE 2. Comparison of noninvasive central blood pressure measurements ($n = 1107$)

	Cuff-tonometry (calibration using bSBP and bDBP)				Cuff-tonometry (calibration using MAP and bDBP)			
Variable	Mean ± SD	Mean$_{diff}$ ± SD$_{diff}$	Limits of agreement	ICC	Mean ± SD	Mean$_{diff}$ ± SD$_{diff}$	Limits of agreement	ICC
MAP (mmHg)	104 ± 11	1 ± 4	−7, 8	0.94	107 ± 11	−2 ± 3	−7, 3	0.95
cDBP (mmHg)	85 ± 10	0 ± 2	−4, 5	0.98	85 ± 10	0 ± 2	−3, 4	0.99
cSBP (mmHg)	132 ± 16	3 ± 6	−8, 14	0.91	141 ± 17	−5 ± 8	−20, 10	0.85
Central PP (mmHg)	48 ± 13	2 ± 5	−8, 11	0.88	56 ± 16	−5 ± 9	−22, 11	0.77

All data are presented as mean ± SD, mean difference ± SD of difference (Mean$_{diff}$ ± SD$_{diff}$) and limits of agreement and intraclass correlation coefficients (ICC). cDBP, central diastolic pressure; cSBP, central systolic pressure; MAP, mean arterial pressure; PP, pulse pressure.

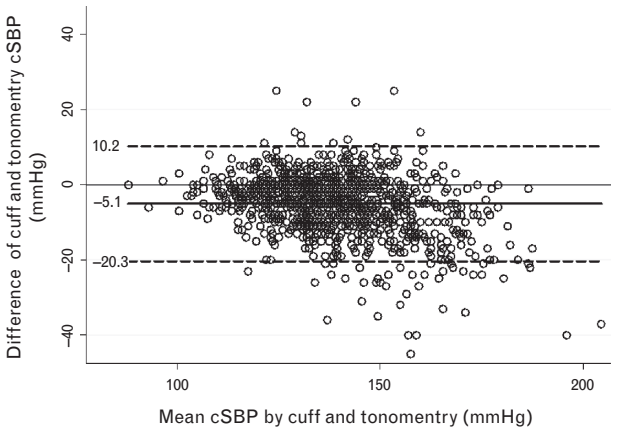

FIGURE 3 Comparison of central systolic pressure (cSBP) obtained using the cuff-based device and tonometry calibrated using brachial mean and diastolic pressure.

the normalized pressure waveforms obtained from the same patient. In this case, the noninvasively acquired cuff-based pressure waveforms correlated closely with the normalized invasively acquired waveform with a cross-correlation coefficient of 0.93.

The average difference between the invasively and noninvasively estimated cSBP was -5 ± 8 mmHg ($P = 0.2$; Table 4), while that for cDBP was 8 ± 3 mmHg ($P < 0.001$). The mean aortic pressure difference over the cardiac cycle between the noninvasive and invasively measured data was $-\pm 3$ mmHg ($P = 0.6$). The average cross-correlation coefficient between noninvasive and invasive waveforms was 0.97 ± 0.02. The form factor was lower for the noninvasively measured data (0.39 ± 0.01) than for invasively measured data (0.47 ± 0.05).

DISCUSSION

Measurement of central BP appears to offer advantages over brachial BP for risk stratification [4,6] and assessment of therapeutic efficacy [5]. If it is to be widely adopted in the clinic, devices that estimate central BP should be easy to operate, reproducible and accurate. Analysis of a large data set from a multiethnic population-based study provided evidence that the new cuff-based technique was easy to use, reproducible and gave similar results to applanation tonometry. In a small study, the noninvasive cuff-based device also gave acceptably accurate estimates of central pressure waveforms compared with invasive aortic measurements.

Tonometry is regarded as the 'gold standard' method for noninvasive measurement of central BP [4,18–20]. However, it has been well documented that, when calibrated with brachial systolic and diastolic pressures, tonometry underestimates invasively measured cSBP by nearly 4–13 mmHg [21–23]. Recalibration of the data using MAP and bDBP has been reported to reduce these differences [15]. With respect to our noninvasive study, the agreement between the cSBP estimated by the two devices was acceptable when using either bSBP/bDBP or MAP/bDBP [15] to calibrate the tonometry device. These results are in agreement with those of Climie *et al.* [14] who found a mean difference ± standard deviation in cSBP of 1 ± 2 mmHg comparing Pulsecor and Sphygmocor devices in a small

TABLE 3. Comparison of central systolic blood pressure (cSBP) measured by cuff or tonometry, stratified by sex, ethnicity, age and presence of cardiovascular disease

Stratifying factor	Difference in cSBP (Cuff-tonometry), mmHg	Limits of agreement (mmHg)	*P*
Male	3 ± 6	(−8, 15)	0.1
Female	3 ± 5	(−8, 13)	
European	3 ± 6	(−9, 16)	0.8
South Asian	3 ± 5	(−7, 13)	
African Caribbean	3 ± 5	(−7, 13)	
Age			
≤69 years	3 ± 6	(−9, 15)	0.6
>69 years	3 ± 5	(−7, 14)	
No diabetes	3 ± 6	(−8, 14)	0.002
Diabetes	4 ± 5	(−5, 13)	
No Hypertension	3 ± 5	(−7, 13)	0.3
Hypertension	3 ± 6	(−9, 15)	
No CHD	3 ± 6	(−8, 15)	0.1
CHD	4 ± 5	(−6, 14)	
Normal weight	3 ± 5	(−8, 13)	0.003
Overweight	3 ± 6	(−9, 15)	
Obese	4 ± 5	(−6, 15)	
Antihypertensive medication			
No beta blocker	3 ± 6	(−9, 16)	0.5
Beta blocker	3 ± 5	(−7, 13)	
No CCB	3 ± 7	(−10, 16)	0.5
CCB	4 ± 5	(−7, 14)	
No ARB/ACEI	3 ± 5	(−7, 13)	0.1
ARB/ACEI	4 ± 7	(−9, 17)	

Data are mean differences ± SD of difference and (limits of agreement) for cuff cSBP- tonometry cSBP (calibrated using brachial systolic and diastolic pressure). Comparisons of stratified groups were made using a Student's *t*-test or analysis of variance (ANOVA). A *P* value of <0.05 was considered statistically significant. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CHD, coronary heart disease.

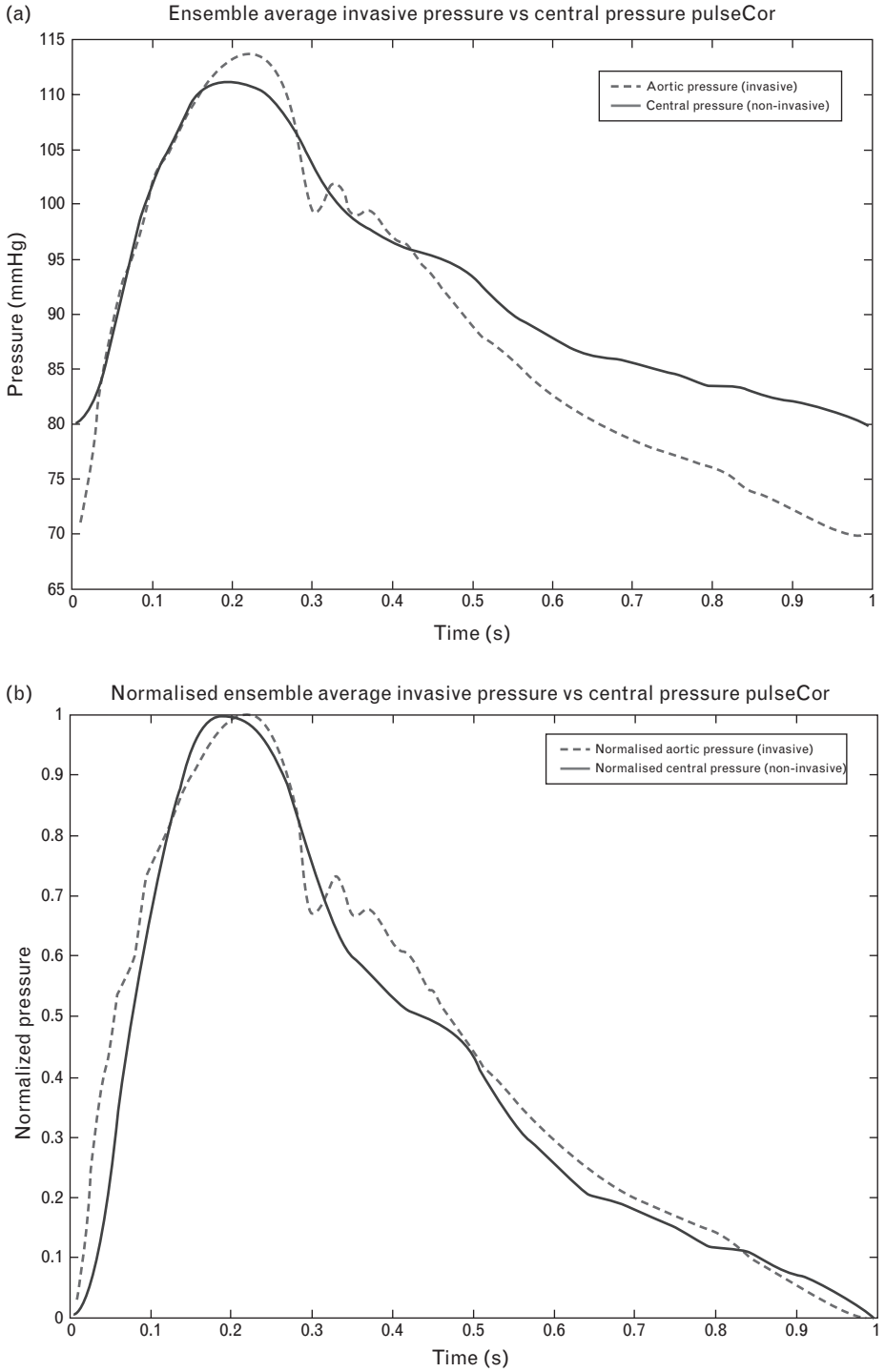

FIGURE 4 Ensemble average invasive pressure vs. cuff-based device derived central pressure. (a) Invasive aortic (red) and noninvasive (blue) central pressure waveforms acquired in the same patient. (b) Normalized pressure waveforms acquired from the same patient.

TABLE 4. Comparison of cuff-based estimates of central blood pressure and invasively acquired aortic measurements ($n = 6$)

	Noninvasive	Invasive	Difference (noninvasive – invasive)	*P*
cSBP (mmHg)	121 ± 16	126 ± 23	−5 ± 8	0.2
cDBP (mmHg)	83 ± 12	75 ± 10	8 ± 3	<0.001
MAP (mmHg)	98 ± 13	99 ± 16	−1 ± 3	0.6

All data are presented as mean ± SD or mean difference ± SD of the difference. cDBP, central diastolic pressure; cSBP, central systolic pressure; MAP, mean arterial pressure.

sample of younger individuals. The results of our present study stress the importance of correctly calibrating the tonometry device [24], although they do not resolve the question of which calibration method is superior.

Several noninvasive devices have been designed to estimate cSBP. Such systems include a modified tonometer sensor embedded into a wrist strap (BPro), brachial oscillometric devices that incorporate the transfer function method (Mobil-O-Graph, SphygmoCor XCEL, WatchBP Office, Vicorder, CardioMon) and those that adopt an occlusive cuff 'stop-flow' approach similar to that adopted by the Pulsecor (Arteriograph). All these systems have been tested and show potential. Brachial cuff-based approaches do not require separate calibration and circumvent problems related to brachial-radial amplification. Moreover, learning to operate the device requires little additional training beyond the training in the measurement of BP. However, these devices cannot overcome the inherent inaccuracy of cuff-based techniques [25,26].

This study expands on previous work by comparing noninvasively obtained pressure waveforms with aortic pressure waveforms measured invasively with high-fidelity catheters. Noninvasive estimates of cSBP were nearly 5 mmHg lower than measured aortic SBP, whereas estimated central DBP was 8 mmHg higher than aortic DBP. These findings are consistent with previous studies showing average differences of 8–18 mmHg comparing noninvasive and invasive DBP [25,26]. Form factors were higher for invasively measured data, although in both cases, the values were within the range (0.35–0.53) reported by Chemla *et al.* [27] for central BP. Both the systolic upstroke and the diastolic decay of the invasively and noninvasively acquired pressure waveforms showed excellent agreement, but agreement of the waveforms around the dicrotic notch was less good. This may be a consequence of damping of the signal due to the properties of arm tissue and cuff and/or effects due to ensemble averaging cardiac cycles with inherently variable ejection periods. Despite this limitation, the fidelity of the central pressure waveforms was acceptable.

There are several strengths to this study: it used a large population-based cohort, which included men and women of varying ethnicities, age and cardiovascular health. The agreement between the two devices remained high when stratified by age, sex, ethnicity, obesity, hypertension, diagnosed CHD and antihypertensive medication class. The largest interdevice differences were observed in participants with diabetes; however, these differences were small and still fell within the AAMI standards. A possible explanation for the increased difference in people with diabetes is that the generalized transfer function used by the tonometer to derive central BP may be less accurate in diabetes due to increased arterial stiffness/calcification. Concerns regarding inaccuracies in the transfer function for deriving central BP in patients with diabetes mellitus have been raised previously [28].

A possible limitation to the noninvasive study was that the devices were not used in a randomized order. The cuff-based device was always used first to allow calibration to be performed. However, the cuff-acquired brachial BP measurement was used to calibrate the tonometer and patients were well rested before any measurements were taken. A further limitation is the age of our cohort. We only compared the devices in older individuals; consequently, our findings may not necessarily apply to a younger population. The main limitations for the invasive study were the small number of participants and the lack of simultaneous tonometry data.

In conclusion, cSBP obtained from noninvasive cuff-based measurements of brachial pressure showed acceptable agreement with estimates based on radial tonometry. A cuff-based device requires minimal additional training and may facilitate measurement of central pressure in trials, observational studies and the clinic.

Central BP may be a superior predictor of cardiovascular events and is differentially influenced by antihypertensive therapy. We show that a brachial cuff-based device provides reliable and accurate estimates of central BP. This approach could facilitate adoption of measurement of central BP in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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Reviewers' Summary Evaluations

Reviewer 1

In a large and heterogeneous cohort of subjects with different levels of cardiovascular risk, the authors compared two noninvasive methods for measuring central BP (a cuff-based device and applanation tonometry). The cuff-based method was found to be easy to use, as well as reproducible and accurate in most patients.

As strengths of this study count the population included and the rigorous methods used; the results are interesting and for sure a good base for future studies.

Weaknesses: the data could not be extended for subjects younger than the population included (70 ± 6 years). The inter-device difference in diabetic patients needs further investigations.

Reviewer 2

The authors have conducted an elegant study in a broad population of 1107 individuals, on noninvasive central blood pressure using a technique easier to apply in clinical practice, and less dependence on the ability of the researcher or clinician that will measure blood pressure, so it is of interest for application in clinical practice.

Among the weaknesses of this study should be noted that it was conducted in an aging population, so the results cannot be extrapolated to younger population. Moreover, the invasive study was conducted in a very small number of subjects.