

Comparison of central SBP in children estimated from a brachial cuff alone, brachial cuff-calibrated applanation radial tonometry and brachial cuff-calibrated carotid wall-tracking

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Objectives: We compared the agreement between different techniques to estimate central SBP (cSBP) in children and the relative impact of different methods of measuring peripheral blood pressure (BP).

Methods: A total of 135 children, aged 12.9 ± 3.0 years including 67 boys, 85 with chronic kidney disease were studied. We measured cSBP using radiofrequency ultrasound carotid wall-tracking (Esaote ART.LAB system, a previously validated reference method), transformation of the radial artery pressure waveform obtained by tonometry (SphygmoCor) and a cuff-based system (cBP301; Centron Diagnostics) during a single visit. Carotid and radial tonometric-derived values were calibrated from mean and diastolic values of brachial BP obtained by aneroid sphygmomanometer. Brachial cuff only values were calibrated from the same aneroid sphygmomanometer values and from oscillometric values obtained from the brachial cuff.

Results: cSBP values estimated from radial tonometry were closely correlated with those obtained from the carotid ($r = 0.959$, mean difference -0.61 ± 3.5 mmHg). cSBP values estimated by the brachial cuff only method agreed reasonably well with those obtained from the carotid ($r = 0.847$, mean difference 5 ± 7.4 mmHg) when calibrated by the same method but when calibrated by oscillometric values from the brachial cuff, agreement was less good ($r = 0.659$, mean difference 8.7 ± 11.4 mmHg).

Conclusion: Radial tonometry with a radial-to-central transfer function can be used to estimate cSBP in children with acceptable accuracy when compared with the invasively validated carotid reference method. All methods are subject to errors introduced by calibration from peripheral BP.

Keywords: central blood pressure, cuff-based oscillometry, radial tonometry, radiofrequency ultrasound carotid wall-tracking

Abbreviations: BP, blood pressure; CKD, chronic kidney disease; cSBP, central SBP; MAP, mean arterial pressure; pSBP, peripheral SBP

INTRODUCTION

SBP is amplified along conduit arteries such that peripheral SBP (pSBP) exceeds central SBP (cSBP) measured at the aortic root as a result of the phenomenon of peripheral pressure wave reflection [1–4]. By contrast, mean arterial pressure (MAP) and DBP remain nearly identical throughout the arterial tree [1]. Amplification is greater in children than in adults and, may be more closely related to target organ damage than peripheral blood pressure (BP) as has been shown to be the case in adults [4,5].

We have previously verified that central aortic SBP can be derived from wall-tracking of the carotid artery using the ART.LAB system (Esaote, Maastricht, The Netherlands) in children [6]. There are currently several devices available that use different technologies to determine central aortic pressure using noninvasive techniques. Elmenhorst *et al.* [7] published percentiles for cSBP in children and adolescents, specific for sex and age or height using an oscillometric technique. However, there are currently no data in children comparing agreement between different techniques to estimate cSBP and the relative impact of different methods of measuring peripheral BP (pBP) on estimated cSBP levels using different technologies.

In this study, at the time of a single visit, we compared estimates of cSBP obtained by applanation tonometry with the SphygmoCor device (AtCor Medical, West Ryde, New South Wales, Australia) and from a brachial cuff-based device (Centron cBP301 device; Centron Diagnostics Ltd, London, UK) with wall tracking of the carotid artery (as the reference method). All methods were calibrated from the

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same peripheral measurements of BP and, in addition, we compared the influence of using oscillometric and aneroid-derived values of peripheral BP for calibration of the cuff-derived cSBP values.

METHODS

Study population

One hundred and thirty-five children were recruited from the nephrology and hypertension outpatient clinics at the Evelina London Children's Hospital, United Kingdom, including healthy children as controls ($n=37$) who were recruited from the local community. The study was approved by the Local Research Ethics Committee and written informed consent and/or assent as appropriate was obtained from parents and children for participation in the study.

Inclusion and exclusion criteria

Any child more than 2 and less than 18 years attending the renal and hypertension clinics at the study centre was eligible if they could understand the proposed investigations and tolerate the cSBP measurements using different instruments. We excluded children with arrhythmias or clinical evidence of heart failure. In those with chronic kidney disease (CKD), in accordance with published definitions, renal function was categorized by stages of CKD [8]. Renal function was estimated using the modified Schwartz formula published previously [9].

Peripheral blood pressure

Peripheral SBP and DBP were measured in participants seated for 5 min in a quiet environment. Trained observers measured peripheral BP at the brachial artery thrice by auscultation using a calibrated aneroid sphygmomanometer and appropriate size arm cuff in accordance with the British Hypertension Society recommendations. The mean of three measurements was used for further analyses. The brachial BP measurements were performed initially followed by measurements of central BP using different instruments. Hypertension was defined as one or both SBP and DBP above the 95th percentile for age and height or if the patient was on antihypertensive medication(s) [10].

Central blood pressure

- (1) *Carotid wall tracking by ultrasound*: Determination of local pressure from noninvasive carotid pressure waveform was initially shown by Van Bortel *et al.* [12]. Carotid distension waveforms were acquired by radiofrequency ultrasound wall tracking of the right common carotid artery, using the ART.LAB system (Esaote) [11–13]. Each carotid waveform recording was obtained over ~10 s. Carotid distension waveforms were ensemble averaged to estimate cSBP ($cSBP_{CWT}$) using custom in-house software developed in MATLAB (MathWorks, Cambridge, UK). Waveforms were calibrated from values of MAP and DBP derived as for method (2) below.
- (2) *Applanation tonometry*: Radial artery applanation tonometry was performed on the right wrist of each subject by lightly applying a high-fidelity

micromanometer (SPC-301; Millar Instruments, Houston, Texas, USA) to the radial artery. All readings were processed by the SphygmoCor device (AtCor Medical). Radial waveforms meeting the inbuilt quality control criteria of the SphygmoCor device were ensemble-averaged and converted to a corresponding aortic waveform using the inbuilt SphygmoCor generalized radial-aortic transfer function (derived in adults) from which central BPs ($cSBP_{RT}$) were calculated. Peripheral measures of brachial SBP and DBP obtained by aneroid sphygmomanometry were used for SphygmoCor radial pulse wave calibration, from which MAP was calculated by integrating the radial waveforms. The subsequent MAP and DBP were used to calibrate the estimated aortic waveforms transferred from radial waveforms to give $cSBP_{RT}$.

- (3) *Cuff-based oscillometry*: We estimated central BP using the Centron cBP301; Centron Diagnostics Ltd, a device that incorporates the measurement of cuff pressure and applies a validated oscillometric algorithm derived in adults to determine the SBP, DBP and mean brachial BP [14]. The cuff was then reinflated to a pressure between the MAP and SBP, and oscillations in the cuff pressure recorded over 15 s. Measurements were performed on the right arm of the child in the supine position.

Brachial cuff only values were calibrated from the same MAP and DBP values used in method (2) ($cSBP_{CUFF}$) and from oscillometric values obtained from the brachial cuff at the same time as the measurement of the cuff waveform ($cSBP_{CUFF/OSC}$). Thus, for all three methods ($cSBP_{CWT}$, $cSBP_{RT}$ and $cSBP_{CUFF}$), the same values of peripheral MAP and DBP obtained from peripheral measures of SBP and DBP by aneroid sphygmomanometry, and integration of SphygmoCor-derived radial pressure waveforms (to obtain MAP), were used for calibration. In addition, cuff-based values were calibrated from oscillometric estimates of MAP and DBP to give $cSBP_{CUFF/OSC}$ (Fig. 1). In all children, three sequential estimates of cSBP were attempted using all three instruments and the average of three measurements calculated.

Statistics

Results are expressed as mean \pm SD. The correlation between methods was assessed using Pearson's correlation analysis. Bland–Altman plots were used to evaluate the agreement between methods; mean difference to reflect systematic bias and the SD of the differences to indicate the level of agreement. Differences between cSBP estimates of the three instruments were assessed using paired Student's *t* tests. All statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, Illinois, USA). *P* values less than 0.05 were considered statistically significant.

RESULTS

One hundred and thirty-five children including 67 boys, aged 12.9 ± 3.0 years successfully underwent planned cSBP assessments. Eighty-five children had CKD with stages 1, 2, 3, 4 and 5 of CKD in 22, 26, 27, 7 and 3, respectively; of

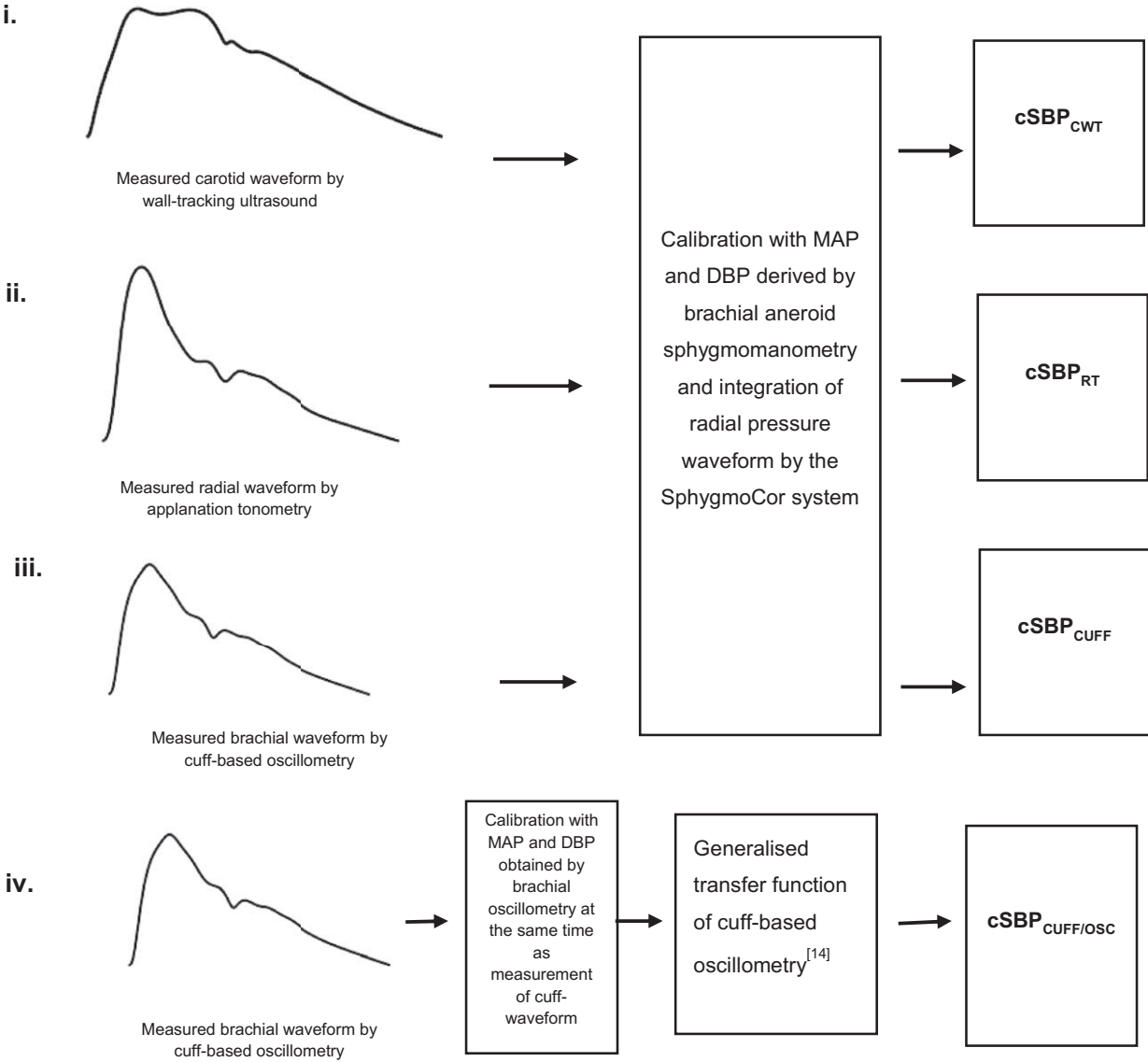


FIGURE 1 Illustration of the methodology of the calibration of the noninvasive estimations of central SBP. (i–iii) Estimation of central SBP with calibration of waveforms by mean arterial pressure and DBP derived using an aneroid sphygmomanometer to measure peripheral SBP and DBP and integration of the radial pressure waveform by the SphygmoCor system to obtain mean arterial pressure [6]. (iv) Estimation of central SBP with calibration of waveforms by mean arterial pressure and DBP derived using brachial oscillometry [14].

whom 23 children with CKD were on antihypertensive medication. Thirteen children had hypertension with normal renal function, of whom four were on antihypertensive medications. Thirty-seven children including 14 boys were healthy controls from the local population. The population characteristics of the subgroups are shown in Table 1.

Overall, 87% of the study cohort had two or more sequential estimates of cSBP using carotid wall-tracking, 86% using radial tonometry and 94% using the brachial cuff-based device. Those aged over 10 years, had more sequential estimates performed with the cuff device than with the other methods, but this was not statistically significant. There was no significant difference in success of cSBP measurement using any instrument between boys and girls ($P=0.21$).

There were no significant differences for cSBP_{RT} and cSBP_{CWT} between sexes and those at least 10 years; but cSBP estimated using radial tonometry is underestimated in

TABLE 1. Demographic characteristics of 135 children included in the study

Variable	
Number of children	135
Age (year)	12.9 ± 3.0
Male, n (%)	67 (50)
Ethnicity	
White, n (%)	112 (83)
Black, n (%)	9 (7)
Asian, n (%)	7 (5)
Other, n (%)	7 (5)
Height (cm)	154.4 ± 18.0
Weight (kg)	50.8 ± 18.4
BMI (kg/m ²)	20.7 ± 4.9
Controls, n (%)	37 (27)
CKD patients, n (%)	85 (63)
Hypertensive patients, n (%)	13 (10)
Antihypertensive drugs, n (%)	27 (20)
pSBP (mmHg)	107.4 ± 13.9
pDBP (mmHg)	60.6 ± 11.8

All values are mean ± SD unless stated otherwise. CKD, chronic kidney disease; pDBP, peripheral DBP; pSBP, peripheral SBP.

TABLE 2. Age and sex differences in central SBP by radial tonometry (cSBP_{RT}) and by carotid wall tracking (cSBP_{CWT}) values

	N	cSBP _{RT}	cSBP _{CWT}	Mean difference	P values
Age (years)					
<10	24	84.5	87.1	-2.6	<0.001
≥10	111	91.1	91.2	-0.1	0.676
Sex					
Male	67	90.8	91.5	-0.7	0.154
Female	68	89.1	89.5	-0.4	0.202

TABLE 3. Age and sex differences in central SBP by cuff-based oscillometry calibrated with auscultatory-derived peripheral blood pressure (cSBP_{CUFF}) and by carotid wall tracking (cSBP_{CWT}) values

	N	cSBP _{CUFF}	cSBP _{CWT}	Mean difference	P values
Age (years)					
<10	24	76.4	87.1	-10.7	<0.001
≥10	111	87.5	91.2	-3.7	<0.001
Sex					
Male	67	86.0	91.5	-5.5	<0.001
Female	68	85.1	89.5	-4.4	<0.001

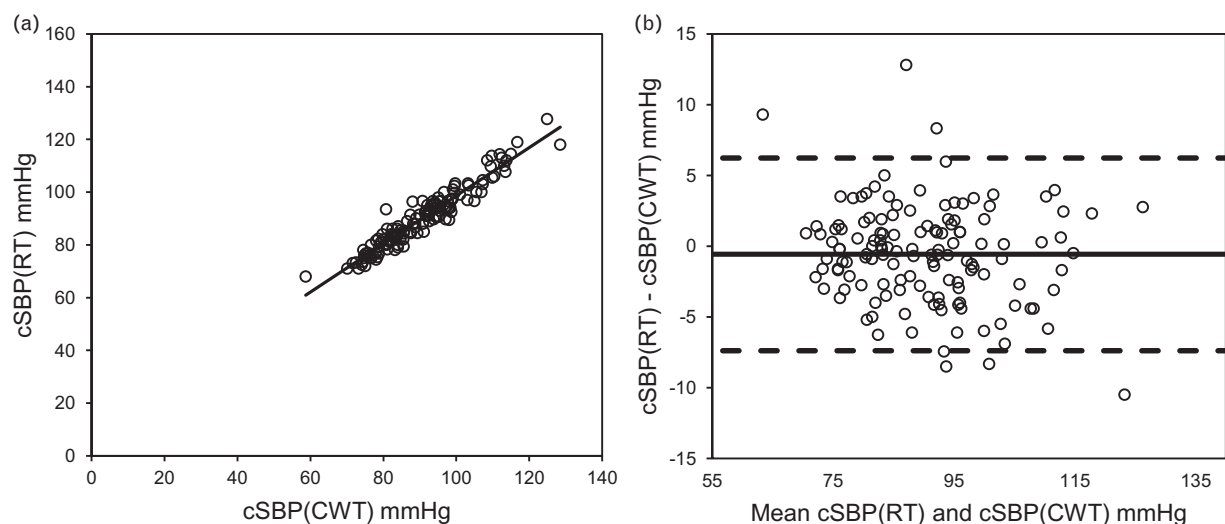
younger children (Table 2). There were significant differences in cSBP_{CUFF} and cSBP_{CWT} and in cSBP_{CUFF/OSC} and cSBP_{CWT} between sexes and age groups (Tables 3 and 4); except in those less than 10 years for cSBP_{CUFF/OSC} and cSBP_{CWT} in whom cSBP levels were similar. The mean difference between cSBP_{CUFF} and cSBP_{CWT} is slightly greater in males than in females (Table 2) in comparison with the mean difference between cSBP_{CUFF/OSC} and cSBP_{CWT} which is greater in females than in males (Table 3).

Comparison of radial tonometry with carotid wall-tracking

Values of cSBP obtained by radial tonometry were highly correlated with estimates obtained by carotid wall-tracking cSBP_{RT} vs. cSBP_{CWT} ($r=0.959$, $P<0.001$; Fig. 2a). Bland–Altman analysis revealed a small but significant difference in the estimation of cSBP by the two methods (Fig. 2b) when considering the whole study population. The mean cSBP_{RT} was 89.9 ± 11.6 mmHg and mean cSBP_{CWT} was

TABLE 4. Age and sex differences in central SBP estimated by cuff-based oscillometry (cSBP_{CUFF/OSC}) and by carotid wall tracking (cSBP_{CWT}) values

	N	cSBP _{CUFF/OSC}	cSBP _{CWT}	Mean difference	P values
Age (years)					
<10	24	89.6	87.1	2.5	0.263
≥10	111	101.3	91.2	10.1	<0.001
Sex					
Male	67	98.1	91.5	6.6	<0.001
Female	68	100.4	89.5	10.9	<0.001

**FIGURE 2** Comparison of central SBP measured by radial tonometry (cSBP_{RT}) and by carotid wall tracking (cSBP_{CWT}) when both devices are calibrated from the same peripheral blood pressure measures (brachial aneroid sphygmomanometry). (a) The correlation between cSBP_{RT} and cSBP_{CWT}. (b) The mean difference between cSBP_{RT} and cSBP_{CWT}.

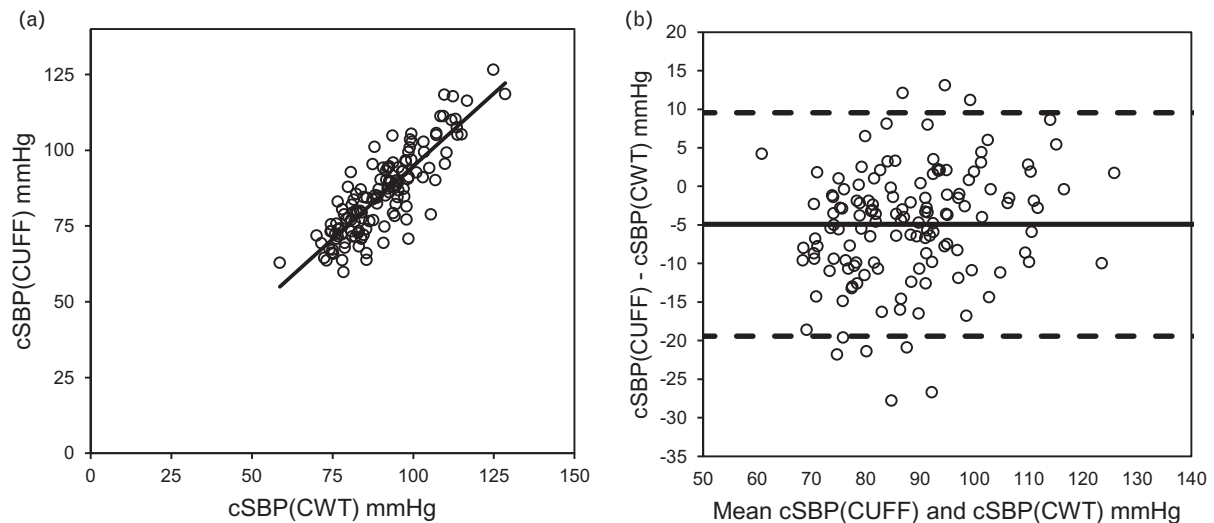


FIGURE 3 Comparison of central SBP estimated by cuff-based oscillometry calibrated with auscultatory-derived peripheral blood pressure ($cSBP_{CUFF}$) and by carotid wall tracking ($cSBP_{CWT}$). (a) The correlation between $cSBP_{CUFF}$ and $cSBP_{CWT}$. (b) The difference between $cSBP_{CUFF}$ and $cSBP_{CWT}$.

90.5 ± 12.2 mmHg. The difference in absolute values between the $cSBP_{RT}$ and $cSBP_{CWT}$ was -0.61 ± 3.5 mmHg [95% confidence interval (CI), -1.20 to -0.22 , $P = 0.042$]. However, in children less than 10 years, radial tonometry produced values that were significantly less than those obtained by carotid wall-tracking (mean difference -2.6 mmHg, $P < 0.001$, Table 2). The coefficient of variation for $cSBP_{RT}$ was less than 1.5% suggesting excellent repeatability of measurements.

Comparison of brachial cuff with carotid wall-tracking (with same peripheral blood pressure calibration)

Estimates of $cSBP_{CUFF}$ obtained off-line by inputting the same auscultatory-derived MAP and DBP measures used to calibrate the other methods, and $cSBP_{CWT}$ were also closely correlated ($r = 0.847$; $P < 0.001$; Fig. 3a). However, Bland–Altman analysis demonstrated a significant systematic difference in the estimation of cSBP by the two methods (Fig. 3b) with mean $cSBP_{CUFF}$ 85.5 ± 13.9 mmHg and mean $cSBP_{CWT}$ 90.5 ± 12.2 mmHg. The mean difference between $cSBP_{CUFF}$ and $cSBP_{CWT}$ was -5.0 ± 7.4 mmHg (95% CI, -6.23 to -3.72 , $P < 0.001$). The underestimation of cSBP by cuff compared with carotid wall-tracking was most marked in children less than 10 years in whom the mean difference between the two methods was -10.7 mmHg (Table 3). $cSBP_{CUFF}$ values also correlated well with those estimated by radial tonometry ($r = 0.924$, but with a mean difference: -4.36 ± 5.4 mmHg, $P < 0.001$).

Comparison of brachial cuff (with oscillometric peripheral blood pressure calibration) with carotid wall-tracking (with aneroid peripheral blood pressure calibration)

Estimates of cSBP obtained by cuff-based oscillometry using the Centron device calibrated by oscillometric values of peripheral BP ($cSBP_{CUFF/OSC}$) and $cSBP_{CWT}$ (calibrated from aneroid-derived peripheral BP) were moderately

correlated ($r = 0.659$; $P < 0.001$; Fig. 4a). Bland–Altman analysis demonstrated a significant difference in the estimation of cSBP by the two methods (Fig. 4b). The mean $cSBP_{CUFF/OSC}$ was 99.2 ± 14.8 mmHg and mean $cSBP_{CWT}$ was 90.5 ± 12.2 mmHg. The overestimation of cSBP by the cuff using oscillometric peripheral BP calibration relative to $cSBP_{CWT}$ was less marked in children less than 10 years (Table 4). The mean difference was 8.7 ± 11.4 mmHg (95% CI, 6.77 – 10.65 , $P < 0.001$). cSBP values obtained by the cuff device correlated well with those obtained by radial tonometry but with a systematic error ($r = 0.742$, mean difference: 9.32 ± 10.0 mmHg, $P < 0.001$).

Peripheral to central amplification

The mean systolic amplification (peripheral–central SBP) was 16.8 ± 1.8 , 17.4 ± 2.3 and 21.8 ± 0.1 mmHg for carotid wall tracking, radial tonometry and cuff-based oscillometry calibrated with aneroid sphygmomanometer values (Fig. 5). The mean systolic amplification for cuff-based oscillometry calibrated with oscillometric peripheral values was 8.1 ± 0.9 mmHg (Fig. 5).

DISCUSSION

Our study is the first to investigate the agreement between the SphygmoCor radial tonometry and a cuff-based device for estimating cSBP and to compare these methods with a validated method for measuring central systolic pressure using carotid-wall tracking ultrasound in children [6].

The technique of applanation tonometry using the SphygmoCor, has been used extensively in adults and recently in studies in children by us and others [6,11,12,14,15]. In the current study, values of cSBP obtained by radial tonometry and carotid-wall tracking were highly correlated similar to our previous report [6]. The mean difference was low at -0.61 mmHg with a low SD reflecting good agreement between these methods. Hence, regardless of the SphygmoCor's radial-to-aortic transfer function being derived in adults, these results suggest that

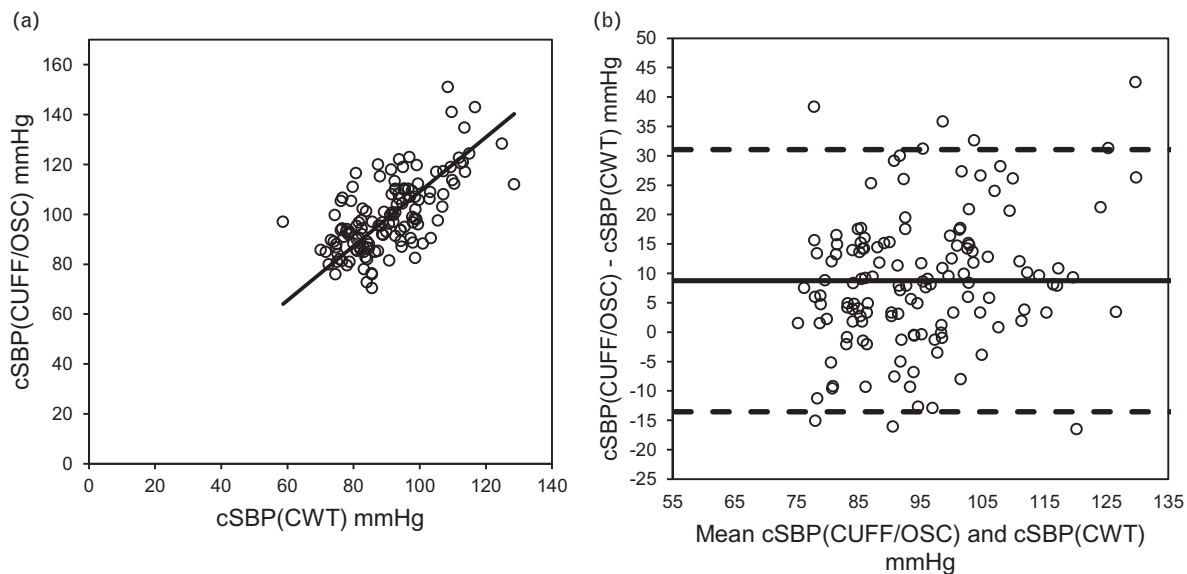


FIGURE 4 Comparison of central SBP estimated by cuff-based oscillometry ($cSBP_{CUFF/OSC}$) and by carotid wall tracking ($cSBP_{CWT}$). (a) The correlation between $cSBP_{CUFF/OSC}$ and $cSBP_{CWT}$. (b) The difference between $cSBP_{CUFF/OSC}$ and $cSBP_{CWT}$.

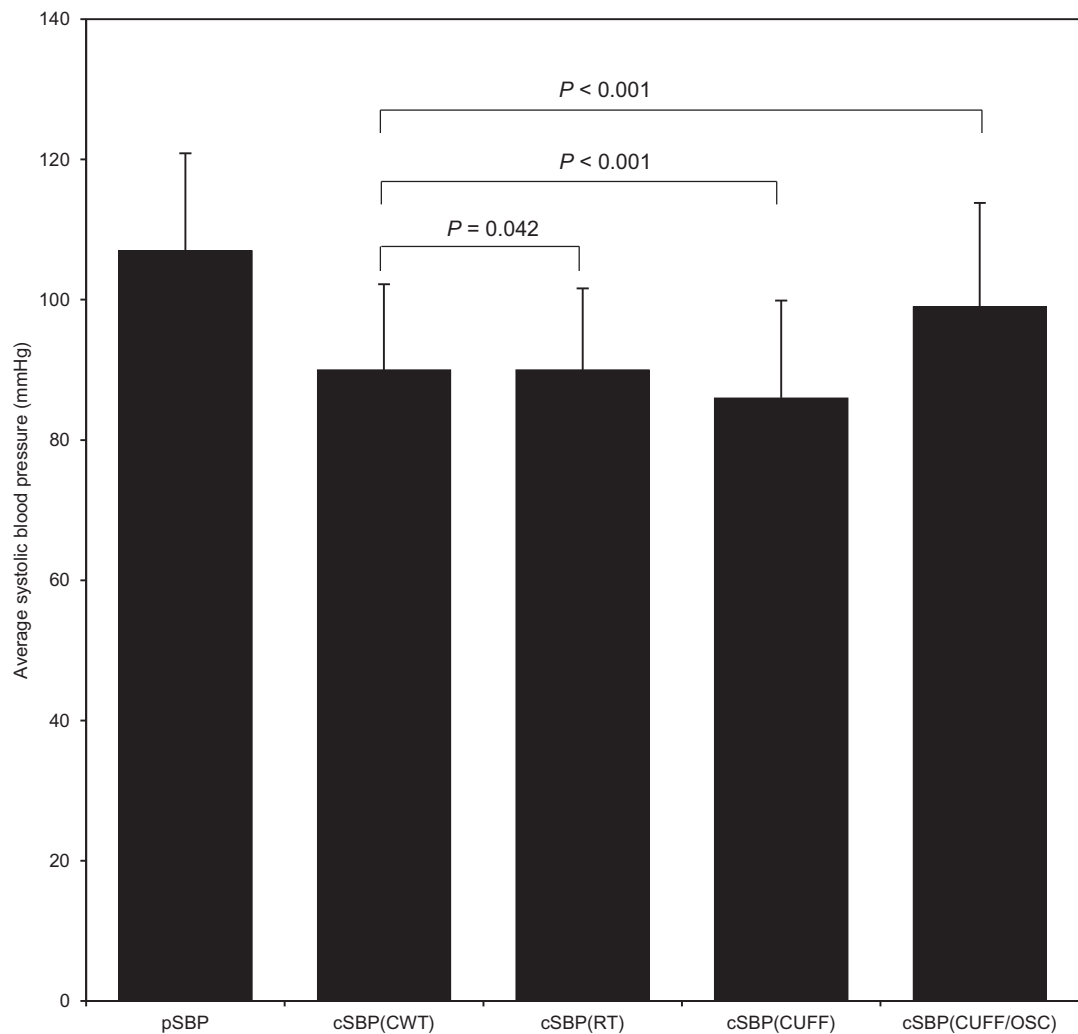


FIGURE 5 Mean peripheral SBP and central SBP measured by carotid ultrasound ($cSBP_{CWT}$), radial tonometry ($cSBP_{RT}$) and by cuff oscillometry calibrated with auscultatory-derived peripheral SBP ($cSBP_{CUFF}$) and cuff oscillometry calibrated with oscillometry-derived peripheral SBP ($cSBP_{CUFF/OSC}$).

it holds to a close estimation in children. However, in children less than 10 years there was a slightly greater difference between values obtained by these two methods.

The Centron cuff-based device, is an alternative technology that uses processing of cuff-derived waveform to estimate central systolic pressure. Our results demonstrate reasonable correlation between cuff-derived cSBP and the carotid reference method when both were calibrated from the same peripheral BP. However, the agreement was less good than that between radial tonometry-derived values and the reference carotid wall tracking-derived values.

It is important to note that the accuracy of any method for estimating cSBP that is based on waveform processing (i.e. all three of methods used here) is dependent on the peripheral BP used from calibration. The good agreement between the radial tonometry and carotid wall tracking-derived values probably arose in large part because of the use of the same method of peripheral BP calibration. It does not mean that absolute values of cSBP derived by these methods are accurate (although we have previously shown that to be the case for the carotid wall tracking method). The importance of calibration from peripheral BP is illustrated by the difference between cSBP values derived from the cuff method when these were calibrated by the aneroid and oscillometric values.

Cuff-based oscillometry with oscillometric calibration (which is how a device would be used in practice) systematically overestimates the cSBP when compared with the validated carotid wall-tracking method. The Centron device uses an algorithm that has been previously been developed and validated against invasive measurements obtained in adult participants and has been shown to provide reasonable measurements of cSBP in adults [14,16]. The inaccuracy of this cuff-based oscillometric technique in children may be a result of the algorithm being developed in adults. The resulting overestimation of the cSBP, could be corrected by subtracting 5.0 mmHg from cSBP estimated by cuff-based oscillometry. Naturally, this requires further prospective validation to confirm that this is a plausible and true means of adjustment for the systematic error.

In adults, the amplification of SBP from the aorta to the upper limb is usually in the order of 10 mmHg with reports of a significant inverse relationship between the degree of the amplification and age [17]. In children, there is typically a greater amplification in SBP of ~20 mmHg from the central to peripheral arteries [6,18]. Significantly, the current study demonstrated that cuff-based oscillometry shows a smaller amplification as a result of overestimation of the cSBP ~8 mmHg and this is in line with the findings of Elmenhorst *et al.* [7] who reported lower amplification in children using a different oscillometric device.

It is important to note that despite calibration with the same auscultatory-derived peripheral BP, the differences in estimation of cSBP between the three methods remained and are likely due to differences in the transfer functions between different instruments. Therefore, values of cSBP estimated by different techniques are not interchangeable and this may have significant implications when employed for clinical purposes.

We observe differences between techniques by age (but not by sex). In those aged less than 10 years, cSBP estimated

using radial tonometry is underestimated compared with the validated method (cSBP_{CWT}); cSBP using brachial cuff was overestimated when pBP was directly measured (cSBP_{CUFF/OSC}) but cSBP was underestimated when brachial cuff was calibrated with auscultatory-derived peripheral DBP and MAP (cSBP_{CUFF}). In those more than 10 years, there were no significant difference in cSBP level when measured using radial tonometry and wall tracking; whilst the direction of difference from cSBP_{CWT} remained similar for cSBP_{CUFF/OSC} and cSBP_{CUFF} the magnitude of the difference was smaller. There was no difference between the sexes in estimation of cSBP using radial tonometry and wall tracking; while the magnitude of difference in cSBP levels in boys and girls were different when using cuff-based techniques.

Although the methods have proven to be reliable, clinical utilization presents its own challenges. Essentially, a device routinely used clinically to determine central pressure should be easy to operate with minimal training and well tolerated by children, whilst maintaining accuracy. Unlike radial tonometry and carotid-wall tracking, cuff-based oscillometry is quick to perform and the device used is portable and does not require a trained operator. Nevertheless, all three methods appeared to have been equally well tolerated by subjects as assessed by the higher percentage of children in whom two or more readings of satisfactory quality could be acquired. However, as shown here in our study, cuff-based oscillometry is inferior in its accuracy in estimating cSBP when compared with radial tonometry and wall tracking.

In conclusion, close agreement between available techniques suggest that, relative to pSBP, they provide a reasonable estimate of cSBP although estimates by different techniques are not interchangeable. The clinical significance of these findings need further evaluation.

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Conflicts of interest

P.C. and King's College London have an interest in Centron Diagnostics, a company that produces instruments for the measurement of blood pressure.

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