

Central Aortic Blood Pressure From Ultrasound Wall-Tracking of the Carotid Artery in Children Comparison With Invasive Measurements and Radial Tonometry

Laura Milne, Louise Keehn, Antoine Guilcher, John F. Reidy, Narayan Karunanithy, Eric Rosenthal, Shakeel Qureshi, Phil J. Chowienzyk, Manish D. Sinha

Abstract—Differences between central aortic root (c) and peripheral (p) systolic blood pressure (SBP) may be particularly marked in children, but noninvasive methods for assessing cSBP in children have not been validated. We compared estimates of cSBP obtained from radiofrequency ultrasound wall tracking of the carotid artery (ART.LAB system) with that measured directly by a catheter in the aortic root at the time of arterial cannulation. Carotid waveforms were calibrated from invasive measurements of mean and diastolic pressures. In 9 children aged 10.5 ± 5.0 years (mean \pm SD), cSBP obtained from carotid wall tracking was highly correlated with invasive measures of cSBP ($r=0.99$) with mean (\pm SD) difference 3.9 ± 2.5 mmHg. Second, we compared values of cSBP obtained from the carotid with those obtained using noninvasive applanation tonometry at the radial artery and a radial-to-aortic transfer function (SphygmoCor). Both carotid and radial tonometric measurements were calibrated from the same peripheral mean and diastolic measurements of blood pressure obtained by sphygmomanometry. In 84 children aged 13.2 ± 3.2 years, there was excellent agreement between the 2 methods ($r=0.95$; $P<0.001$) with mean difference 0.71 ± 3.7 mmHg (95% confidence interval = -1.53 to 1.01). This invasive validation study confirms that cSBP as estimated by carotid wall tracking provides an acceptable measurement of true cSBP when calibration is from true mean and diastolic pressures. Close agreement of cSBP obtained by carotid wall tracking and radial tonometry suggests that these provide similar results when calibrated from the same peripheral blood pressure measurements. (*Hypertension*. 2015;65:1141-1146. DOI: 10.1161/HYPERTENSIONAHA.115.05196.)

Key Words: applanation tonometry ■ central blood pressure ■ hypertension ■ pediatrics ■ renal disease

Systolic blood pressure (SBP) is amplified along conduit arteries such that peripheral SBP (pSBP) measured at the brachial or radial artery usually exceeds central aortic systolic pressure (cSBP) at the aortic root.¹ By contrast, mean arterial pressure (MAP) and diastolic blood pressure (DBP) are almost identical at central and peripheral sites.² In adults, cSBP is thought to relate more closely to target organ damage than pSBP.^{3,4} Differences between cSBP and pSBP are more marked in younger compared with older adults⁵ and may be particularly important in children.⁶ However, noninvasive estimates of cSBP have not been validated in children, and there is limited information on the magnitude of SBP amplification in children.^{7,8}

The aim of the study was to (i) compare estimates of central aortic systolic pressure obtained from radiofrequency ultrasound wall tracking of the carotid artery^{9,10} with that measured directly using a pressure-tipped catheter placed in the aortic root at the time of arterial cannulation; (ii) to compare the values of cSBP obtained from noninvasive radiofrequency ultrasound wall tracking of the carotid artery with those obtained

using applanation tonometry at the radial artery and a radial-to-aortic transfer function¹; (iii) to determine typical SBP amplification in children with and without chronic kidney disease (CKD) and hypertension.

Methods

The study was performed at Evelina London Children's Hospital, UK, with the approval of the local Research Ethics Committee. Written informed consent was obtained from parents and assent from children as appropriate for participation in the study.

Study 1: Invasive Validation of Carotid Wall Tracking-Derived Compared With Measured Aortic cSBP

Children aged 2 to 18 years ($n=9$) attending for diagnostic or interventional arteriography for the investigation/treatment of suspected renovascular disease or congenital heart disease were recruited from the Paediatric Nephrology and Cardiology departments at Evelina London Children's Hospital. Children with arrhythmias or clinical evidence of heart failure were excluded from the study. After standard preparations for arteriography, vascular access to the femoral artery was established with a homeostatic sheath. A 4-FR

Received January 26, 2015; first decision February 5, 2015; revision accepted February 25, 2015.

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Hypertension is available at <http://hyper.ahajournals.org>

DOI: 10.1161/HYPERTENSIONAHA.115.05196

pig-tail catheter was passed through the femoral arterial sheath over a guidewire and a high fidelity pressure-tipped Volcano wire (diameter 0.014", ComboWire®, Volcano Corporation, CA) placed at the proximal aortic root under radiographic guidance. Aortic pressure waveforms were digitally recorded at 1 kHz, over a 5 to 10 second period during simultaneous measurement of carotid distension waveforms. Carotid distension waveforms were obtained by radio-frequency ultrasound wall tracking of the carotid artery, using the ART.LAB system (Esaote, Maastricht, Netherlands).^{9–11} Up to 5 repeat recordings of 5 to 10 second periods of simultaneous carotid and aortic waveform recordings were obtained. Carotid distension and aortic waveforms were postprocessed using custom in-house software developed in MATLAB (MathWorks, Cambridge, UK). Waveforms from each 5 to 10 second period of recording were ensemble averaged. Invasive values of cSBP, MAP, and DBP ($cSBP_{inv}$, MAP_{inv} , and DBP_{inv}) were obtained from the ensemble-averaged aortic waveforms. Ensemble-averaged carotid waveforms were calibrated from MAP_{inv} and DBP_{inv} and used to obtain an estimate of cSBP ($cSBP_{carotid}$). Processing was performed automatically, but an experienced observer first inspected all waveforms to exclude artifacts.

Study 2: Noninvasive Comparison of Radial Tonometry-Derived Versus Carotid Wall Tracking-Derived Estimates of cSBP

Children aged 2 to 18 years ($n=84$) were recruited from the hypertension and nephrology outpatient clinics of the Evelina London Children's Hospital, and healthy control children were recruited from the local population. Hypertension was defined as systolic, diastolic, or both systolic and diastolic BP above the 95th percentile for age and height or if the patient was on antihypertensive therapy, using the Fourth Report Criteria (National High Blood Pressure Education Program Working Group). Renal function was determined by estimated glomerular filtration rate using the Schwartz formula,^{12,13} and CKD stage was defined according to published definitions.¹⁴ Children with arrhythmias or clinical evidence of heart failure were excluded from the study. Measurements were made with children seated in a quiet environment. Peripheral systolic and diastolic BP were measured in triplicate by a trained observer by auscultation using a calibrated aneroid sphygmomanometer and appropriate-size arm cuff according to British Hypertension Society guidelines.

Radial pressure waveforms were obtained from the right wrist over a 10 second period by applanation tonometry using a high-fidelity micromanometer (SPC-301; Millar Instruments, Houston, TX) and processed by the SphygmoCor device (Atcor medical, Australia). 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-to-aortic transfer function (derived in adults) from which central blood pressures were calculated. Radial waveforms were calibrated from peripheral brachial measures of SBP and DBP, from which MAP was calculated by integrating the radial waveform. Transformed radial waveforms (ie, estimated aortic waveforms) were calibrated from these values of MAP and DBP to give a radial tonometric estimate of cSBP ($cSBP_{RT}$) calibrated from noninvasive peripheral measures of SBP and DBP.

Radiofrequency ultrasound wall tracking of the carotid artery was performed as in the invasive validation study. Carotid distension waveforms were calibrated using the same values of MAP and DBP used to calibrate transformed radial waveforms to estimate cSBP ($cSBP_{carotid}$). Thus, errors in the noninvasive peripheral measures of SBP and DBP contributed equally to both radial tonometry and carotid wall tracking-derived estimates of cSBP. In all children, 3 sequential estimates of cSBP were attempted using radial tonometry and carotid wall tracking.

Statistics

Results are expressed as means \pm SD. Agreement between methods was assessed by measuring the Pearson correlation coefficient,

mean difference, and SD of difference. Bland–Altman plots were used to examine systematic bias and random error. In the case of the comparison of carotid wall tracking–derived cSBP with invasive measurements, a modified Bland–Altman plot was used whereby the reference invasive measurement was substituted for the mean of the 2 methods on the abscissa of the Bland–Altman plot. All analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, Illinois, USA). P values <0.05 were considered statistically significant.

Results

Invasive Validation of Carotid Wall Tracking–Derived Compared With Measured Aortic cSBP

Of the 9 children studied, 4 were undergoing arteriography to rule out renovascular or aortic disease as a cause for hypertension, 2 had patent ductus arteriosus and 3 had other complex congenital heart disease. Demographics and blood pressure characteristics are shown in Table. Values of $cSBP_{carotid}$ obtained from carotid distension–derived estimates of cSBP (calibrated using MAP_{inv} and DBP_{inv}) were highly correlated with invasive measures, $cSBP_{inv}$ ($r=0.99$; $P<0.0001$; Figure 1A). Bland–Altman analysis demonstrated a small but significant systematic difference which did not vary significantly with $cSBP_{inv}$. The mean $cSBP_{inv}$ was 90 ± 14.9 mmHg, and mean $cSBP_{carotid}$ was 94 ± 13.8 mmHg. The mean difference (ie, aortic to carotid amplification), $cSBP_{carotid}-cSBP_{inv}$ was 3.9 ± 2.5 mmHg (Figure 1B).

Table. Subject Characteristics

Characteristic	Study 1 (Validation Cohort)	Study 2 (Comparison Study)
Number of subjects	9	84
Age, y	10.5 \pm 5.0	13.2 \pm 3.2
Male, n (%)	5 (44)	43 (51.2)
White, n (%)	6 (67)	69 (82)
Black, n (%)	2 (22)	5 (6)
Asian, n (%)	1 (11)	3 (4)
Other, n (%)	...	7 (8)
Height, cm	135.5 \pm 25.4	154.6 \pm 20.3
Weight, kg	35.3 \pm 16.6	53.6 \pm 22.4
BMI, kg/m ²	18.0 \pm 4.0	21.6 \pm 6.1
Controls, n (%)	...	15 (18)
CKD Patients, n (%)	...	56 (67)
Hypertensive patients, n (%)	...	13 (15)
Antihypertensive drugs, n (%)	2 (22)	17 (8)
pSBP, mm Hg	96 \pm 9.4	108 \pm 15.1
pDBP, mm Hg	43 \pm 11.0	59 \pm 10.2
cSBP catheter, mm Hg	90 \pm 14.9	...
cSBP carotid ultrasound, mm Hg	94 \pm 13.8	90 \pm 11.9
cSBP radial tonometry, mm Hg	...	90 \pm 11.7

Values are numbers or means \pm SD. BMI indicates body mass index; CKD, chronic kidney disease; cSBP, central systolic blood pressure; pDBP, peripheral diastolic blood pressure; and pSBP, peripheral systolic blood pressure.

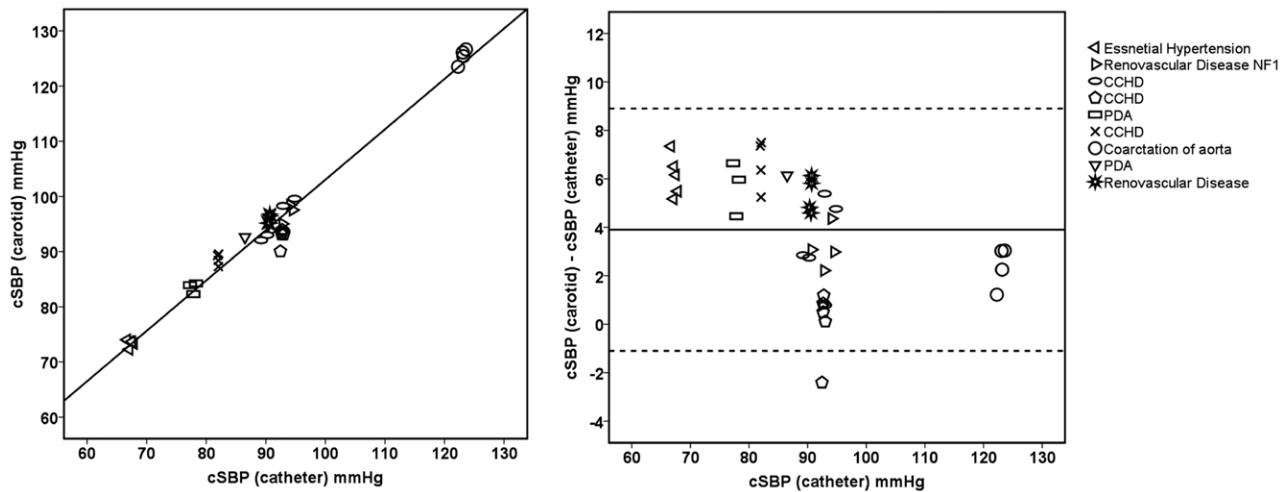


Figure 1. Invasive validation of carotid wall tracking–derived compared with measured aortic central systolic blood pressure (cSBP).

A. Correlation between cSBP measured by invasive catheter and carotid ultrasound ($r=0.99$, $P<0.001$). **B.** The difference between cSBP measured by carotid ultrasound and catheter (mean±SD, 3.9 ± 2.5 mmHg). CCHD indicates complex congenital heart disease; and PDA, patent ductus arteriosus.

Noninvasive Comparison of Radial Tonometry-Derived Versus Carotid Wall Tracking-Derived Estimates of cSBP

Of the 84 children studied, 56 (31 boys) had CKD (stages 1, 2, 3, and 4 of CKD in 10, 21, 20, and 5 respectively), and 14 children with CKD were on antihypertensive medication. Thirteen children (6 boys) had hypertension with normal renal function of whom 3 were taking antihypertensive medication. Fifteen children (6 boys) were healthy control subjects. Characteristics of all subjects are shown in Table. We obtained 3 sequential carotid wall tracking recordings of adequate quality in 71 children, but 3 radial tonometry recordings meeting SphmoCor quality control criterion were obtained in only 52 children. Estimates of

cSBP obtained by radial tonometry and carotid wall tracking were closely correlated ($r=0.95$; $P<0.001$; Figure 2B). There was no significant difference between cSBP of the children on antihypertensive medication ($n=17$) and those without ($n=67$): 88 ± 11.8 mmHg versus 90 ± 11.7 mmHg, respectively ($P=0.43$). Bland–Altman analysis revealed no significant systematic error and no trend for error to vary with mean cSBP. The mean difference $\text{cSBP}_{\text{carotid}} - \text{cSBP}_{\text{RT}}$ was 0.71 ± 3.7 mmHg (95% confidence interval = -1.53 to 1.01). Repeatability of measurements, for both methods, when using the same brachial systolic and diastolic BP for calibration was excellent: the coefficient of variation for repeated measurements was $<2\%$ for both carotid and radial measurements.

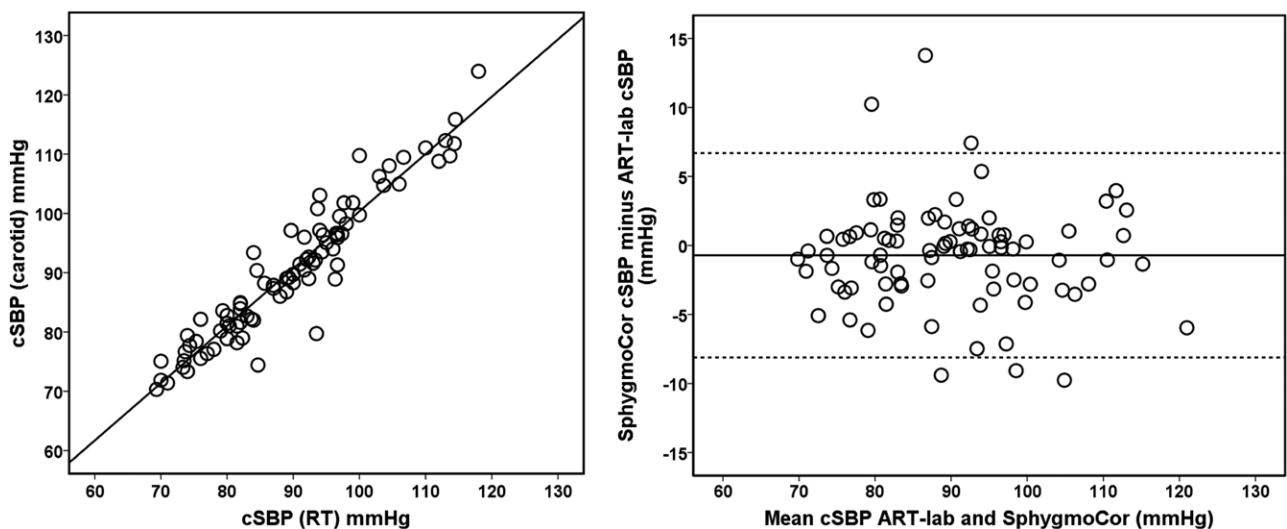


Figure 2. Noninvasive comparison of radial tonometry–derived versus carotid wall tracking–derived estimates of central systolic blood pressure (cSBP). **A.** The correlation between cSBP measured by carotid ultrasound and radial tonometry ($r=0.95$, $P<0.001$). **B.** The difference between cSBP measured by carotid ultrasound and radial tonometry (mean±SD, 0.71 ± 3.7 mmHg). There is no significant difference in the mean cSBP obtained by both devices ($P=0.09$).

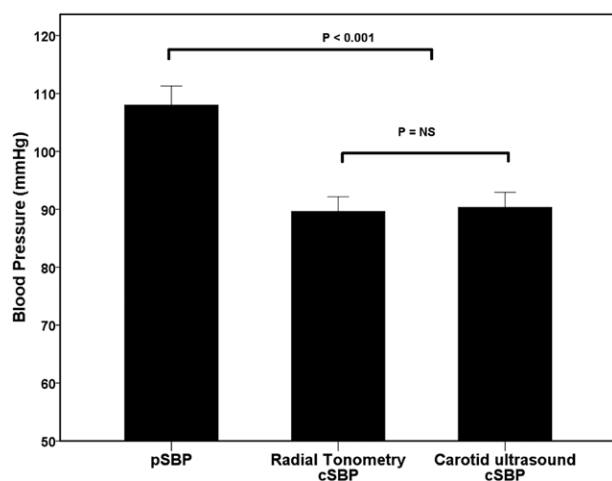


Figure 3. Peripheral-to-central amplification. Mean peripheral systolic blood pressure (pSBP) and central systolic blood pressure (cSBP) measured by radial tonometry and carotid ultrasound. There is no significant difference in cSBP measured by tonometry and carotid ultrasound.

Peripheral to Central Amplification

Values of peripheral and central SBP as measured by both radial tonometry and carotid wall tracking are shown in Figure 3. The mean amplification (peripheral–central SBP) was 18.3 ± 6.6 and 17.7 ± 7.6 mmHg for radial tonometry and carotid wall tracking, respectively.

Discussion

To our knowledge, this is the first study to examine the accuracy with which central aortic systolic pressure can be estimated noninvasively in children. The method that we elected to compare invasive measures, carotid wall tracking, assumes carotid wall distension to be proportional to local intra-arterial carotid pressure and for carotid pressure to approximate aortic root pressure.^{15,16} Theoretically, tonometric measurements obtained at the carotid artery would be expected to perform as well as carotid wall tracking.¹⁰ However, in preliminary studies, we found that high-quality carotid tonometric recordings were more difficult to obtain than ultrasound wall tracking in children. We compared agreement between cSBP estimated from carotid wall tracking with measured cSBP in a heterogeneous group of children in whom central hemodynamics would be expected to vary widely. Despite this, we observed good agreement between estimated and measured central aortic systolic pressures. This suggests that, in most children, assumptions relating to carotid wall distension being linearly related to local intra-arterial pressure and lack of pressure gradient at peak pressure from aorta to carotid are likely to be valid.

We observed a small difference between carotid-derived and measured cSBP with carotid SBP exceeding measured aortic cSBP. This may be because of some aortic-to-carotid amplification of SBP between the 2 measurement sites and could be corrected for by subtracting 3.9 mmHg from the carotid SBP with validation in a further study. It is important

to note that we used invasive measures of mean and diastolic pressures to calibrate the aortic distension waveform to obtain a pressure waveform. This is the usual approach when assessing the accuracy of central systolic pressure determination because it removes the confounding effects of error in peripheral blood pressure determination.^{17,18} However, when the method is applied in practice, noninvasive measurements of peripheral pressures are required, and any inaccuracy in these will influence the accuracy of the derived central aortic systolic pressure.¹⁹

An alternative method (also requiring calibration from peripheral pressure measurements) for assessing central systolic pressure uses radial tonometry and a radial-to-aortic transfer function. We found that radial tonometry was more difficult to perform than carotid ultrasonography in children. The increased success of carotid wall tracking compared with tonometry (as assessed by the greater proportion of children in whom readings of adequate quality could be obtained) suggests this may be the preferred technique in children. However, when high quality recordings with an acceptable SD were used and when the same peripheral blood pressure was used to calibrate both radial artery and carotid artery waveforms, we obtained excellent agreement between estimates of central aortic systolic pressure derived from the 2 techniques. Thus, despite the radial-to-aortic transfer function being derived in adults, these results suggest that it holds to a close approximation in children. Although at first sight this might seem surprising, it is notable that when used to estimate cSBP in adults, the exact form of the transfer function does not seem critical and holds despite hemodynamic perturbations, such as during pacing and vasodilator therapy, which may to some extent mimic the circulatory state in children as compared with adults.^{17,19,20}

Amplification of SBP from the aorta to the upper limb in adults is usually in the order of 10 mmHg but varies with age being greater in younger compared with older adults.⁵ Using an oscillometric device, Elmenhorst et al⁷ reported lower amplification in children and young adults aged 8 to 21 years than we observed (by ≈ 5 mmHg). However, when an oscillometric device was compared with the SphygmoCor, by Stoner et al,²¹ cSBP was, on average, 4.5 mmHg (95% confidence interval 4.0–5.2 mmHg) higher, by the oscillometric method. Thus, discrepancies in amplification may arise from the different measurement techniques.

Results of the present study show that in children, including those with and without hypertension and mild to advanced CKD, amplification is substantial with a mean amplification of ≈ 20 mmHg and thus may be relatively more important than in adults. Although not all studies have shown a closer association of cardiovascular events with central compared with peripheral SBP in adults,²² this may be because of limited sample size or inaccuracies in the measurement of peripheral BP, and target organ damage does seem more closely related to central rather than peripheral BP.⁴

Results from the present study suggest that estimation of central aortic systolic pressure using either carotid wall tracking or radial tonometry will be helpful in determining whether central systolic pressure is equally or more

important than peripheral blood pressure in children compared with adults. However, it should be noted that the absolute accuracy of estimation of central aortic systolic pressure will be dependent on that of the peripheral blood pressure and that several calibration issues remain. These include whether to calibrate from peripheral mean and diastolic pressures or from peripheral systolic and diastolic pressures and if calibrating a radial waveform from a brachial systolic pressure, brachial to radial amplification.²³ Even if there are relatively large errors in determination of peripheral blood pressure, we have previously shown that radial tonometry provides a reasonable estimate of the difference between peripheral and central systolic pressure.¹⁹ Noninvasive estimates of cSBP in children obtained by either carotid wall tracking or radial tonometry should, therefore, be useful in determining (a) factors influencing amplification; (b) whether measurement of central aortic systolic pressure provides incremental value over pSBP when assessing target organ damage; and (c) interventions that have differential effects on central and peripheral systolic pressure.

Perspectives

This study provides data validating noninvasive measurement of central SBP in children. Systolic pressure amplification in children is almost twice the levels of amplification described in adult cohorts and therefore likely to be more clinically relevant. Because of the small sample size of the invasive study, results need to be interpreted with caution and further invasive validation is required. Further work should also investigate the factors determining amplification in children and whether measures of central blood pressure offer incremental value over peripheral blood pressure in the management of children with hypertension and those at risk of cardiovascular disease.

Acknowledgments

We thank the help of research nurses Paula Sofocleous and Jane Boston in study recruitment and facilitation of study investigations.

Sources of Funding

This research was supported by Guy's and St Thomas's Charity, the British Heart Foundation, and the National Institute for Health Research (NIHR) award to the Biomedical Research Centre and Clinical Research Facility at Guys & St Thomas NHS Foundation Trust and King's College London. We acknowledge financial support from the Department of Health via the National Institute for Health Research (NIHR) comprehensive Biomedical Research Centre and Clinical Research Facilities awards to Guy's and St Thomas' NHS Foundation Trust in partnership with King's College London and King's College Hospital NHS Foundation Trust.

Disclosures

P.J. Chowienzyk and King's College London have an interest in Centron Diagnostics, a King's College London spin-out company developing technology for measurement of central blood pressure (not used in the present study).

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Novelty and Significance

What Is New?

- This study measures actual blood pressure close to the heart in children.
- This study validates noninvasive estimates of measurement of blood pressure close to the heart in children.

What Is Relevant?

- Blood pressure measured in the arm differs from that close to the heart, and this difference may be particularly important in children.

- This study will establish whether simple noninvasive methods can be used to measure blood pressure close to the heart in children.

Summary

This study finds that blood pressure close to the heart can be measured accurately using noninvasive devices in children. This study finds a significant difference between blood pressure measured at the arm with that measured close to the heart in children.

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Hypertension. 2015;65:1141-1146; originally published online March 30, 2015;
doi: 10.1161/HYPERTENSIONAHA.115.05196

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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