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Assessment of vascular function in low socioeconomic status preschool children: a pilot study

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Abstract

Elevated brachial blood pressure (BP) in childhood tracks into adulthood. Central BP and measures of arterial stiffness, such as aortic augmentation index (AIx) and pulse wave velocity (PWV), have been associated with future cardiovascular disease. This pilot study assessed the feasibility of noninvasively measuring these parameters in preschool children and explored factors that may be associated with elevated BP in this age group. Brachial BP was measured using an electronic oscillometric unit (Dinamap PRO 100) and defined as elevated when systolic BP (SBP) and/or diastolic BP (DBP) was the 90th percentile for age, gender, and height. Central BP, AIx, and PWV were measured using applanation tonometry (SphygmoCor). C-reactive protein (CRP) was measured in serum samples. Sixteen African-American preschool children were recruited (4.4 ± 0.8 years, 69% males), 6 (38%) of whom had an elevated brachial BP (110 ± 10/69 ± 4 vs. 96 ± 8/55 ± 6 mm Hg, Cohen's d = 2.2). Children with elevated brachial BP had higher central SBP (d = 1.6) and DBP (d = 1.96) (97 ± 6/68 ± 4 vs. 85 ± 8/57 ± 6 mm Hg), AIx (d = 0.88) (31 ± 8 vs. 18 ± 16%, standardized to heart rate), and CRP (3.1 [2.3–6.3] vs. 0.1 [0.1–0.3] mg/dL, d = 2). There was no significant difference in PWV between groups (d = 0.26). CRP and SBP (Spearman r = 0.70), DBP (r = 0.68), central SBP (r = 0.58), and central DBP (r = 0.71) were positively correlated. Wide confidence intervals for the estimated effect sizes indicated a large degree of uncertainty about all estimates due to the small sample size. Noninvasive assessment of central BP and arterial stiffness is feasible in preschool children. Vascular inflammation may be an important factor that influences BP at an early age. Further studies in pre-school children are needed to elucidate mechanisms of early onset hypertension.

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Keywords

Aortic stiffness; hypertension; vascular inflammation

Worldwide, more than 1 billion people have hypertension (HTN), which is estimated to account for 7.1 million deaths annually.¹ In the United States (US), over 80 million adults and an estimated 2–3 million children have HTN, an important risk factor for cardiovascular disease (CVD), the leading cause of death worldwide.² Given current trends, it is projected that an additional 27 million US adults will develop HTN by 2030.³ There is increasing evidence that CVD risk factors, including HTN, appear in childhood and track to adulthood.^{4–6} Therefore, it is important to identify children at high risk of developing CVD later in life in order to introduce preventive interventions at an early time point.

Elevations in noninvasive measures of vascular function, including arterial stiffness indexed by aortic pulse wave velocity (PWV), aortic augmentation index (AIX), and central blood pressure (BP), are associated with premature CVD in adults.⁵ It is now widely recognized that vascular inflammation, which can be assessed by serum C-reactive protein (CRP) levels, is an important contributor to vascular health and has been associated with the development of CVD and CVD events in individuals without clinically apparent disease.⁷

Few studies have assessed vascular function in children. Lurbe et al⁸ evaluated PWV in 8- to 18-year-old children and adolescents and demonstrated a progressive increase in PWV with increasing BP. Although BP elevations may be evident in preschool children,⁹ very few studies have assessed vascular function in this age group. Further, we lack data on factors that influence BP and vascular function at an early age.

The principal aim of the current study is to assess the feasibility of noninvasively measuring central BP, AIX, and PWV in 3- to 5-year-old preschool children. A secondary aim is to explore factors that may be associated with elevated brachial and central BP and aortic stiffness in this age group.

Methods

Study Participants

We conducted a pilot study in low socioeconomic status (SES) preschool children recruited from urban Head Start/Early Head Start (HS/EHS) programs Birmingham, Alabama. The HS/EHS program, sponsored by the US Department of Health and Human Services, provides comprehensive early childhood education, health, nutrition, and parental involvement services to low-income children and their families.¹⁰

Inclusion criteria included the following: (1) enrollment in an HS/EHS program; (2) age 3–5 years at time of study; (3) parental informed consent; and (4) ability to understand instructions, speak, and understand English. Important exclusion criteria included the following: (1) febrile illness, (2) known congenital heart disease, (3) reported chronic disease or recent viral illness by the child or his/her caregiver, and (4) any visible signs of

viral illness. The study was approved by the UAB Institutional Review Board and was conducted according to institutional guidelines.

Demographics, Height, Weight, and Waist Circumference

Age, gender, race, and existing medical conditions of the participants were assessed based on parental responses to a standardized demographic questionnaire. Height was measured in inches using a portable stadiometer, and weight was measured in pounds and ounces by a digital scale according to a standard protocol.¹¹ Body mass index (BMI) was calculated based on the formula $BMI = \text{body weight in kilograms} / \text{body height in meters squared}$. BMI percentile for age, gender, and height was calculated based on the CDC growth charts.¹² Children with a BMI ≥ 85 th percentile were considered overweight.

BP Measurement

BP was measured using an electronic oscillometric unit (Dinamap PRO 100) according to the protocol developed by the National High BP Education Program Working Group on Hypertension Control in Children and Adolescents.¹³ Each child rested for 5 minutes in the seated position, while an age-appropriate children's book was read to her/him prior to and during BP measurements. BP was measured twice, one minute apart. The mean of the two systolic (SBP) and the diastolic (DBP) brachial BPs was used to classify children as being normotensive (SBP and/or DBP $<$ the 90th percentile for age, gender, and height) or having elevated BP (SBP and/or DBP $\geq$ 90th percentile).¹³ We then calculated form factor, an indicator of pulse wave shape, $FF = (MAP - DBP) / \text{pulse pressure (mean arterial pressure [MAP])}$.¹⁴

Laboratory Evaluation

Blood samples were collected by fingerstick (<0.5 mL). Serum was separated, aliquoted, and stored in a -80°C freezer to avoid multiple freeze-thaw cycles. A commercial high-sensitivity CRP ELISA kit (GenWay Biotech, San Diego, CA, USA) that has a coefficient of variation of 5% at a mean CRP of 0.004 mg/L was used to measure circulating CRP as an indicator of vascular inflammation. All specimens were measured in duplicate.

Pulse Wave Analysis and PWV Assessment

In addition to the operator, two nurses and the caregiver (mother for the majority of the children) were present in the room throughout the assessment. The nurses read an age-appropriate book to the child before and during the procedure. The study procedure was demonstrated on a doll in front of the children immediately before starting, and the child was given a chance to apply the tonometer on the doll. This was followed by tonometer application on the child's arm so that he/she would not be alarmed when the assessment was done. The assessment did not start until the child was comfortable, and the questions of the child and caregiver were answered.

Aortic PWV was calculated from measurements of common carotid and femoral artery waveforms using an automated applanation tonometry-based device (SphygmoCor system-AtCor Medical, Sydney, NSW, Australia). All measurements were performed by a single operator (L.G.) who was trained on using this device and had extensive experience in

performing these measurements in adults. Electrocardiogram-gated pulse waveforms were obtained sequentially over the common carotid and femoral arteries. The carotid-femoral PWV was calculated from measurements of pulse transit time and the distance traveled between the two recording sites $PWV = \text{distance (meters [m])} / \text{transit time (seconds [s])}$.¹⁵ The carotid-femoral distance was estimated by subtracting the distance between the carotid location and the sternal notch from the distance between the sternal notch and the femoral site. A minimum of 10 consecutive pressure waveforms were used for calculation of the mean PWV.¹⁵ Higher values represent greater arterial stiffness. Measurements for PWV were repeated 1–2 times as long as the child was cooperative. We were able to get two PWV measurements for 50% of the children and included the measurement that had the better operator index.

Central artery waveforms were obtained with the same device and derived from the radial artery waveform and pressure using a transfer function validated previously during catheterization studies.¹⁶ In addition to central aortic BPs (aortic SBP, DBP MAP, and form factor), the AIx was calculated as the difference between the first and second systolic peaks of the ascending aortic waveform expressed as a percentage of the central pulse pressure (the difference between central SBP and DBP) and was then standardized to a heart rate of 75 beats/min (AIx75).¹⁵ The point at which the central aortic pressure becomes augmented by wave reflection was recognized by a computer program, and the degree of increase expressed as the AIx, which is quantified as a percentage of the aortic pulse pressure.¹⁵ Higher percentage values represent greater arterial stiffness. We were able to obtain AIx on all children (with an average operator index = 90%). We repeated the measurement two times and included the AIx with better operator index.

Statistical Analysis

Demographics and clinical characteristics were summarized using descriptive statistics. Continuous values were expressed as mean $\pm$ standard deviation (except for CRP which was presented as median and interquartile range since its distribution was highly skewed) and compared between groups using the effect size *d*, that is, the standardized mean difference (or mean rank difference). The magnitudes of the observed *d* effect sizes were interpreted using Cohen's guidelines¹⁷: small ~ 0.2 , medium ~ 0.5 , and large ~ 0.8 . Discrete variables were presented as frequencies and percentages and compared between groups using *d*-equivalent effect sizes.¹⁸ Spearman correlations (effect size *r*) were used to estimate bivariate associations among continuous variables. The magnitudes of the observed *r* effect sizes were interpreted using Cohen's guidelines¹⁷: small ~ 0.1 , medium ~ 0.3 , and large ~ 0.5 . To measure the uncertainty about the sample estimates of effect sizes, simultaneous confidence intervals (CI) for all effects sizes were constructed using a false discovery rate approach.¹⁹ The false discovery rate was set at a 10% level. Noncentral *t*-distributions were used for estimating the confidence intervals about the *d* effect sizes, and Fisher's *Z* transformation was used for estimating the confidence intervals about the *r* effect sizes. To estimate intrasubject consistency of measurements for AIx, AI75, and PWV, we calculated the intraclass correlation coefficient and considered values > 0.8 as excellent. We also estimated intrasubject reliability of these measurements by calculating the average of the within-subject standard deviations, which depicts the magnitude of the typical deviation

from the average of the measurements within a subject. The analyses were carried out with SPSS Statistics version 17 (SPSS, Inc, Chicago, IL, USA) and R version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study Participants

We recruited 16 African-American preschool children from HS/EHS programs in Birmingham, Alabama, into this pilot study. Table 1 shows baseline characteristics of the cohort as a whole and of the normotensive and elevated BP subgroups. The average age overall was 4.4 ± 0.7 years, with more boys (69%) than girls; 19% of all study participants were overweight.

Study Procedure Feasibility

BP and vascular function were successfully obtained on all children attempted for this study. The children and the caregivers did not have any major concerns during the procedures and none of the children or caregivers refused to proceed with the assessment. Significant attention was provided to calm the children prior to obtaining the measurements as described in the methods. The procedure, including the time used to calm the child and demonstrate the assessment, took 15–30 minutes. Most children remained calm throughout the assessment. For two children, a 10-minute break was needed before resuming the assessment to calm them when they became restless.

Intrasubject Variability

The intrasubject correlation coefficients for AIx, AIx75, and PWV were 0.97, 0.96, and 0.98, respectively, which are considered excellent. The intrasubject variabilities for AIx, AIx75, and PWV were 2.03%, 3.31%, and 0.16 m/s, respectively.

BP Measurements

In the cohort as a whole, the mean brachial SBP was 101 ± 11 mm Hg and brachial DBP was 60 ± 9 mm Hg, corresponding to a percentile SBP of 65 ± 30 and DBP of 69 ± 25 by age, gender, and height. Central measurements obtained using the Sphygmocor device showed a mean aortic SBP of 89 ± 9 mm Hg, DBP of 61 ± 8 mm Hg, AIx of $18 \pm 13\%$, AIx75 of $23 \pm 16\%$, and PWV of 5.2 ± 1.4 m/s. The mean circulating serum CRP level was 0.3 (0.1 – 3.0) mg/L.

Children With Elevated BP

Of the 16 children, 6 (38%) had elevated brachial BP readings (SBP and/or DBP 90th percentile). Both brachial ($110 \pm 10/69 \pm 4$ vs. $96 \pm 8/55 \pm 6$ mm Hg) and central ($97 \pm 6/68 \pm 4$ vs. $85 \pm 8/57 \pm 6$ mm Hg) SBP and DBP readings were higher in these children compared to those with normal BP readings (Table 1). Medium-sized differences in age, gender, weight, height, and small differences in BMI and birth weight were observed between the normotensive and elevated BP groups (Table 1). Compared to those with normotensive BP readings, children with elevated BP had higher AIx and AIx75, but PWV

was comparable between the groups (Table 1). Serum CRP (3.1 [2.3–6.3] vs. 0.1 [0.1–0.3] mg/dL) was higher in children with elevated BP readings. Figure 1 shows examples of vascular function measurements (shown in Table 2) in two 5-year-old African-American girls, one with normal BP and the other with elevated BP.

Factors Associated With BP and Vascular Function

BP and vascular function data according to gender and BMI (categorized around the 50th percentile) are shown in Tables 3 and 4, respectively. In terms of gender differences (Table 3), large effect sizes were observed in brachial pulse pressure (higher in boys than in girls) and central SBP (higher in girls than in boys). Medium-sized differences were observed in brachial DBP, brachial MAP, central DBP, and central MAP in boys vs. girls. A large effect size was observed in PWV categorized around the 50th percentile of BMI (lower among children with BMI < 50th percentile). Medium-sized differences were seen in brachial MAP, brachial PP, and central DBP in those with BMI < 50th percentile vs. ≥ 50th percentile (Table 4).

Serum CRP was strongly correlated with SBP (Spearman $r = 0.70$, 90% CI: 0.05–0.93) and DBP ($r = 0.68$, 90% CI: 0.02–0.93) percentiles and with central SBP ($r = 0.58$, 90% CI: –0.12 to 0.9) and DBP ($r = 0.71$, 90% CI: 0.05–0.94). CRP was moderately correlated with AIx ($r = 0.40$, 90% CI: –0.33 to 0.83) and weakly with AIx75 ($r = 0.25$, 90% CI: –0.43 to 0.75) and PWV ($r = -0.2$, 90% CI: –0.69 to 0.41).

BMI was not correlated with SBP percentile ($r = -0.05$, 90% CI: –0.6 to 0.54), DBP percentile ($r = -0.18$, 90% CI: –0.7 to 0.47), central aortic SBP ($r = 0.01$, 90% CI: –0.56 to 0.57), central aortic DBP ($r = 0.17$, 90% CI: –0.47 to 0.69), AIx ($r = -0.17$, 90% CI: –0.69 to 0.47), or AIx75 ($r = -0.13$, 90% CI: –0.66 to 0.49) and was only weakly correlated with PWV ($r = -0.27$, 90% CI: –0.75 to 0.4). Similarly, birth weight did not correlate with BP or any of the vascular parameters (data not shown).

Discussion

In this pilot study: (1) we demonstrated the feasibility of noninvasively measuring vascular function in preschool children aged 3–5 years with excellent intrasubject variability. (2) We showed that children with elevated brachial BP readings had higher central BP and higher AIx and AIx75 values than children with normal brachial BP, but PWV was comparable in the two groups. (3) Serum CRP, a measure of vascular inflammation, was higher in children with elevated BP and was more strongly correlated with brachial and aortic BPs than with vascular stiffness. (4) We found no strong correlation between BMI or birth weight and BP or vascular function. However, due to the inherent uncertainty about estimates computed from small samples, all of the aforementioned results should be interpreted with caution.

We evaluated vascular function and central BP measurements on preschool children using applanation tonometry. To our knowledge, this is the first study to use the Sphygmo-Cor system on children 3–5 years of age. In addition to demonstrating the feasibility of performing these measurements in this age group, we found that children with elevated peripheral BP had higher central BP and higher indices of vascular stiffness (AIx and AIx75,

Table 1). In contrast, PWV was similar in children with normal BP and those with elevated BP (small effect size, $d = 0.26$). PWV measurements in our study were largely consistent with those obtained in previous studies that evaluated older children.^{20,21} Studies of larger cohorts are needed to evaluate the reproducibility of using applanation tonometry to assess vascular stiffness in preschool children and to assess the long-term implications of these measurements for vascular health.

In our pilot study, 38% of preschool children had elevated brachial BPs. Although BP elevation in this age group has not been extensively studied, the proportion of preschoolers with elevated BP has ranged from 7.7% to over 30% in prior reports.^{9,22,23} It is possible that elevated BP in our study may not indicate HTN since our measurements were performed on only one occasion and the current definition of HTN in children requires BP elevation in three distinct encounters.⁶ However, there is mounting evidence that BP elevation in children, even on a single encounter, predicts the development of HTN and CVD in adulthood.^{4–6,24,25} In the Cardiovascular Risk in Young Finns Study, SBP in childhood, adolescence, and early adulthood (3–24 years, $N = 1927$) was correlated with that in middle age (30–45 years, Pearson $r = 0.35$).²⁵ In the younger children (3–9 years) from that study, an elevated BP in childhood, even on a single occasion, predicted HTN in adulthood with no statistical improvement when additional BP measurements were included.²⁵ Although not diagnostic of HTN, an elevation of BP on a single encounter in childhood may have implications for vascular health later in life and offer a window on interventions at an earlier age, a time when lifestyle interventions may have the greatest impact (ie, primordial prevention).^{25,26}

A secondary aim of our study was to explore factors in childhood that may be associated with elevated BP. We found no strong association between BP and age (by design our cohort included a narrow age range), gender, weight, height, BMI, or birth weight. Factors known to influence BP in older children include obesity, gender, birth weight, SES, and inflammation.^{27–29} Some studies have reported that arterial stiffness may be related to gender, obesity, and birth weight.^{30,31} However, these associations with vascular stiffness have not been uniform across studies,^{24,31} with some being dependent on the ages of the children studied.³⁰ Further study of vascular function in younger/pre-school children is needed in order to fully appreciate the lifetime trajectory of BP and development of vascular dysfunction.

Circulating CRP is a measure of vascular inflammation and an independent marker of CVD risk and has been associated with BP and HTN in adults in large epidemiological studies.⁷ To our knowledge, our study is the first to assess CRP, arterial stiffness, and BP in preschool age children. We found that serum CRP was higher in preschool children with elevated BP compared to those with normal BP and that the level of CRP correlated with brachial and aortic SBP and DBP. This finding is consistent with the concept that vascular inflammation contributes to the initiation, progression, and maintenance of BP elevation and resultant CVD.^{7,32}

Strengths of the current pilot study include its prospective design, the reliability of measurement of BP and vascular function, and the young age of the participants. The main

limitation of the study is the small sample size. Thus, the wide confidence intervals for the estimated quantities and relationships indicated a large degree of uncertainty about all estimates, as expected in small pilot studies. Also, our study population included only African-American children of low SES, thus limiting the generalizability of the findings. Thus, our findings should be interpreted with caution and considered hypothesis generating rather than definitive. Further studies with larger cohorts of preschool children of different races and SES backgrounds are needed. Assessment of vascular function in this age group is technically demanding and limited by child cooperation, and development of newer techniques is needed to facilitate future vascular studies in young children. For example, Milne et al³³ recently validated a central assessment of BP by radiofrequency ultrasound wall tracking of the carotid artery. While we tried to exclude children with illness, we cannot be certain that the elevated CRP levels were not due to subclinical disease.

In this study, we demonstrated the feasibility of noninvasively assessing central BP and arterial stiffness in preschool children and found elevated BP in a substantial proportion of this cohort. Further, brachial and central BPs were strongly correlated with vascular inflammation. Larger studies in young children are needed to confirm the association of vascular inflammation with BP in order to identify a cohort at risk for future development of CVD and pave the way for interventions at an early age.

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Figure 1.

Examples of vascular function studies in two preschool children. (A) Vascular function studies of a 5-year-old girl with normal BP with values presented in Table 2. (B) Vascular function studies of another 5-year-old girl with hypertensive BP with values presented in Table 2. The characteristics of the two girls, their BPs, and the results of their vascular function studies are shown. Note that the AIx of the girl with elevated BP (B) is larger than

that of the girl with normal BP (A), while the PWVs of the two girls are similar. AIx, augmentation index; BP, blood pressure; PWV, pulse wave velocity.

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Table 1

Demographics, vascular function, and laboratory tests in children with normal vs. elevated blood pressure

Characteristic	All (n = 16)	Normotensive (n = 10) (90th Percentile)	Elevated BP (n = 6) (<90th Percentile)	Effect Size D (90% Simultaneous CI)
Age (y)	4.4 ± 0.7	4.6 ± 0.7	4.2 ± 0.8	0.54 (−0.82 to 1.87)
Males (%)	11 (69)	80	50	0.58 (−0.8 to 1.94)
Weight (lbs)	40 ± 8	41 ± 6	38 ± 11	0.45 (−0.87 to 1.76)
Height (in)	42 ± 3	43 ± 2	41 ± 4	0.67 (−0.75 to 2.06)
Body mass index (kg/m ²)	15.6 ± 1.2	15.5 ± 0.9	15.6 ± 1.7	0.07 (−1.14 to 1.28)
Overweight (%)	3 (19)	10	33	0.35 (−0.93 to 1.62)
Birth weight (lbs)*	6.5 ± 1.6	6.4 ± 1.8	6.6 ± 1.3	0.17 (−1.06 to 1.39)
Brachial measurements				
Brachial SBP (mm Hg)	101 ± 11	96 ± 8	110 ± 10	1.73 (−0.04 to 3.48)
Brachial DBP (mm Hg)	60 ± 9	55 ± 6	69 ± 4	2.21 (0.25–4.18)
Brachial MAP (mm Hg)	75 ± 8	71 ± 6	84 ± 4	2.21 (0.25–4.18)
Brachial PP (mm Hg)	41 ± 7	41 ± 6	42 ± 10	0.21 (−1.02 to 1.44)
Brachial form factor	0.37 ± 0.12	0.38 ± 0.10	0.36 ± 0.15	0.2 (−1.04 to 1.42)
Central aortic measurements				
Aortic SBP (mm Hg)	89 ± 9	85 ± 8	97 ± 7	1.6 (−0.13 to 3.29)
Aortic DBP (mm Hg)	61 ± 8	57 ± 6	68 ± 4	1.96 (0.08–3.83)
Aortic MAP (mm Hg)	76 ± 9	71 ± 7	84 ± 4	2.14 (0.2–4.07)
Aortic PP (mm Hg)	28 ± 4	27 ± 4	28 ± 5	0.21 (−1.02 to 1.44)
Aortic form factor	0.53 ± 0.11	0.51 ± 0.07	0.57 ± 0.16	0.48 (−0.85 to 1.8)
AIx (%)	18 ± 13	14 ± 14	24 ± 7	0.86 (−0.6 to 2.3)
AIx75 (%)	23 ± 16	18 ± 18	31 ± 8	0.88 (−0.59 to 2.32)
PWV (m/s)	5.2 ± 1.4	5.3 ± 1.4	4.9 ± 1.4	0.26 (−1 to 1.5)
Laboratories				
CRP (mg/L)	0.3 (0.1, 3.0)	0.1 (0.1, 0.3)	3.1 (2.3, 6.3)	2.02 (0.12–3.92)

AIx, augmentation index; AIx75, augmentation index at standardized heart rate of 75 beats per minute; BP, blood pressure; CI, confidence interval; CRP, C-reactive protein; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity; SBP, systolic blood pressure.

Effect size d = standardized mean (or mean rank) difference, small ~0.2, medium ~0.5, large ~0.8. Large effect sizes in bold. Simultaneous confidence intervals estimated using a false discovery rate approach.

* Birth weight was not available on two of our children: one normotensive and one with elevated BP.

Table 2

Vascular function results for child A and B

	Patient A (Normotensive)	Patient B (Elevated Blood Pressure)
Age (y)	5	5
BMI (kg/m ²)	15	14
Brachial SBP/DBP (mm Hg)	90/47	103/63
Brachial BP percentile	<90th	>90th
Central SBP/DBP (mm Hg)	72/49	95/65
AIx (%)	−4	31
AI75 (%)	8	30
PWV (m/s)	7.9 ± 3.4 (37% SD)	7.2 ± 2.2 (28% SD)

AIx, augmentation index; AI75, AIx standardized at heart rate of 75 beats/min; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; PWV, pulse wave velocity; SBP, systolic blood pressure; SD, standard deviation.

Table 3

Gender comparison in characteristics and vascular function measures

Characteristic	Girls (n = 5)	Boys (n = 11)	Effect Size
			D (90% Simultaneous CI)
Age (y)	3.6 ± 0.5	4.8 ± 0.5	2.21 (0.2–4.23)
Weight (lbs)	31 ± 4	44 ± 6	2.21 (0.2–4.23)
Height (in)	38 ± 2	44 ± 2	2.21 (0.2–4.23)
Body mass index (kg/m ²)	14.9 ± 1.0	15.9 ± 1.3	0.82 (–0.68 to 2.29)
Birth weight (lbs)*	6.1 ± 1.2	6.6 ± 1.7	0.31 (–1.01 to 1.61)
Brachial SBP (mm Hg)	100 ± 7	102 ± 13	0.2 (–1.08 to 1.49)
Brachial DBP (mm Hg)	63 ± 5	59 ± 10	0.53 (–0.88 to 1.92)
Brachial MAP (mm Hg)	79 ± 6	74 ± 9	0.58 (–0.86 to 2)
Brachial PP (mm Hg)	36 ± 6	43 ± 7	1.07 (–0.57 to 2.69)
Brachial form factor	0.42 ± 0.04	0.35 ± 0.14	0.83 (–0.67 to 2.31)
Aortic SBP (mm Hg)	93 ± 4	87 ± 11	0.93 (–0.6 to 2.44)
Aortic DBP (mm Hg)	65 ± 6	59 ± 8	0.82 (–0.68 to 2.29)
Aortic MAP (mm Hg)	79 ± 6	75 ± 10	0.55 (–0.86 to 1.95)
Aortic PP (mm Hg)	28 ± 5	27 ± 4	0.08 (–1.19 to 1.34)
Aortic form factor	0.48 ± 0.07	0.56 ± 0.11	0.87 (–0.65 to 2.37)
AIx (%)	19 ± 19	18 ± 10	0.1 (–1.17 to 1.36)
AIx75 (%)	24 ± 26	22 ± 11	0.16 (–1.12 to 1.43)
PWV (m/s)	4.8 ± 1.5	5.3 ± 1.4	0.3 (–1.02 to 1.61)
CRP (mg/L)	0.4 (0.2, 3.0)	0.3 (0.1, 3.1)	0.22 (–1.07 to 1.5)

AIx, augmentation index; AIx75, augmentation index at standardized heart rate of 75 beats per minute; BP, blood pressure; CI, confidence interval; CRP, C-reactive protein; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity; SBP, systolic blood pressure.

Effect size d = standardized mean (or mean rank) difference, small ~0.2, medium ~0.5, large ~0.8. Large effect sizes in bold. Simultaneous confidence intervals estimated using a false discovery rate approach.

* Birth weight was not available on two of our children: one normotensive and one with elevated BP.

Table 4

Differences in characteristics and vascular function according to classification over the 50th percentile of BMI

Characteristic	BMI <50th Percentile (n = 8)	BMI 50th Percentile (n = 8)	Effect Size D (90% Simultaneous CI)
Age (y)	4.1 ± 0.8	4.7 ± 0.7	0.86 (−0.56 to 2.26)
Males (%)	50	88	0.6 (−0.74 to 1.92)
Weight (lbs)	35 ± 6	45 ± 6	1.78 (0.02 to 3.52)
Height (in)	41 ± 3	44 ± 3	1.03 (−0.49 to 2.52)
Body mass index (kg/m²)	14.5 ± 0.5	16.6 ± 0.8	2.21 (0.29 to 4.14)
Birth weight (lbs) *	6.2 ± 0.9	6.7 ± 0.7	0.3 (−0.93 to 1.51)
Brachial SBP (mm Hg)	99 ± 10	103 ± 13	0.4 (−0.87 to 1.65)
Brachial DBP (mm Hg)	60 ± 10	60 ± 8	0.11 (−1.06 to 1.29)
Brachial MAP (mm Hg)	74 ± 8	77 ± 9	0.49 (−0.8 to 1.76)
Brachial PP (mm Hg)	39 ± 6	43 ± 8	0.54 (−0.77 to 1.84)
Brachial form factor	0.35 ± 0.13	0.39 ± 0.11	0.4 (−0.88 to 1.66)
Aortic SBP (mm Hg)	88 ± 10	90 ± 10	0.27 (−0.95 to 1.49)
Aortic DBP (mm Hg)	60 ± 8	62 ± 8	0.34 (−0.9 to 1.57)
Aortic MAP	74 ± 8	78 ± 9	0.57 (−0.78 to 1.91)
Aortic PP	28 ± 5	28 ± 4	0 (−0.82 to 0.82)
Aortic form factor	0.49 ± 0.07	0.58 ± 0.12	0.81 (−0.6 to 2.21)
AIx (%)	16 ± 16	21 ± 8	0.4 (−0.87 to 1.65)
AIx75 (%)	20 ± 20	26 ± 12	0.38 (−0.88 to 1.63)
PWV (m/s)	5.9 ± 1.7	4.5 ± 0.7	0.92 (−0.51 to 2.33)
CRP (mg/L)	0.3 (0.1, 2.3)	0.4 (0.1, 3.1)	0.06 (−1.11 to 1.22)

AIx, augmentation index; AIx75, augmentation index at standardized heart rate of 75 beats per minute; BP, blood pressure; CI, confidence interval; CRP, C-reactive protein; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; PWV, pulse wave velocity; SBP, systolic blood pressure.

Effect size d = standardized mean (or mean rank) difference, small ~0.2, medium ~0.5, large ~0.8. Large effect sizes in bold. Simultaneous confidence intervals estimated using a false discovery rate approach.

* Birth weight was not available on two of our children: one normotensive and one with elevated BP.