ORIGINAL RESEARCH

Temporal Trends in Pulse Pressure and Mean Arterial Pressure During the Rise of Pediatric Obesity in US Children

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***Background*—**Somatic growth in childhood is accompanied by substantial remodeling of the aorta. Obesity is associated with increased aortic stiffness and flow and may interfere with aortic remodeling during growth. Wide pulse pressure (PP) indicates mismatch between aortic impedance and pulsatile flow and increases risk for future systolic hypertension and cardiovascular disease (CVD). We hypothesized that the rise of pediatric obesity would be associated with a temporal trend to higher PP.

***Methods and Results*—**We analyzed demographic, anthropometric, and blood pressure (BP) data for 8- to 17-year-old children (N=16 457) from the cross-sectional National Health and Nutrition Examination Surveys (NHANES) for 1976 through 2008. Multivariable adjusted survey regression was used to examine temporal trends in PP and mean arterial pressure (MAP) and the relation to obesity. Across this period, unadjusted PP was higher (0.29 mm Hg/y, 95% CI 0.26 to 0.33 mm Hg/y; $P<0.0001$), while MAP was lower (−0.24 mm Hg/y, 95% CI −0.27 to −0.20 mm Hg/y; $P<0.0001$) across examinations. Adjusting for body mass index partially attenuated the temporal trend for PP by 32% ($P<0.0001$). Obesity amplified the relation between taller height and higher PP (from 0.23 [95% CI 0.19 to 0.28] to 0.27 [95% CI 0.21 to 0.34] mm Hg/cm height in boys and from 0.08 [95% CI 0.04 to 0.13] to 0.22 [95% CI 0.13 to 0.31] mm Hg/cm height in girls; $P<0.01$ for both).

***Conclusions*—**PP has increased during the rise of pediatric obesity. Higher PP may indicate mismatch between aortic diameter, wall stiffness, and flow in obese children during a period of rapid somatic growth when the aorta is already under considerable remodeling stress. **(*J Am Heart Assoc*. 2014;3:e000725 doi: 10.1161/JAHA.113.000725)**

Key Words: blood pressure • child • NHANES • pulse pressure

Excess weight in children during the past 3 decades is associated with increasing prevalence of dyslipidemia, type 2 diabetes mellitus, and hypertension.[1–3] Despite dramatic increases in pediatric excess weight, the National Health and Nutrition Examination Survey (NHANES) 2003–2006 demonstrated that the prevalence of elevated blood pressure (BP), as defined against fixed historic norms, had increased only modestly.[2] At the same time, recent reports demonstrate high proportions of young adults with elevated BP and increasing BP-related cardiovascular disease (CVD) outcomes, suggesting a transition to higher BP and higher risk during late childhood or early adulthood.[4,5]

BP is commonly analyzed as systolic (SBP) and diastolic (DBP) values. However, alternative decomposition into pulse pressure (PP; SBP minus DBP) and mean arterial pressure (MAP; commonly estimated as DBP plus PP/3) equally predict incident CVD events and may provide additional insight into the underlying pathophysiology of high BP.[6] PP is determined by large artery stiffness and flow pulsatility, whereas MAP is determined by small resistance artery function and cardiac output.[6] Wide PP is a precursor of isolated systolic hypertension and predicts incident CVD.[6–10] In a study of urban children, isolated systolic elevation, a form of wide PP, was the most common form of elevated BP in children and was more common in obese children.[11] Because arterial stiffness is a determinant of PP and predicts hypertension, increased PP in children may reflect pathological vascular remodeling and may precipitate further adverse vascular remodeling and incident hypertension.[12–14] Since excess weight in children may cause a mismatch between pulsatile blood flow and aortic size and between cardiac output and peripheral resistance, we hypothesized that the rise in pediatric excess weight would be accompanied by a temporal increase in PP and MAP. The

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This article was handled independently by Pamela N. Peterson, MD, as a guest editor.

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Received December 11, 2013; accepted March 21, 2014.

population-level relation between obesity and PP and MAP in children is not well described. This study examines the temporal trends for PP and MAP in children of the United States from NHANES II (1976–1984) through NHANES 2007–2008, elucidates the contribution of obesity to observed temporal trends, and evaluates the effect of obesity on the sex-specific physiological relations of PP and MAP with height and age.

Methods

NHANES

The NHANES provide cross-sectional data representative of the civilian, noninstitutionalized population of the United States. We retrieved data from the National Center for Health Statistics at the Centers for Disease Control and Prevention for all children 8 to 17 years of age in each survey from NHANES II (1976–1984) through NHANES 2007–2008. Since 1999, the eligible survey sample has been determined by a multistage probability sampling design and includes oversampling of the 12- to 19-year-age range, non-Hispanic blacks, and Mexican Americans.[15] We collected data for sex, age, race/ethnicity, weight, height, waist circumference (WC), heart rate, SBP, and DBP from each survey. Participants with missing data or without at least 2 SBP and DBP measurements were excluded, except for NHANES II, in which only 1 BP value was obtained. On the basis of missing data, we excluded 526 participants from NHANES II, 1668 from NHANES III, 280 from 1999–2000, 331 from 2001–2002, 488 from 2003–2004, 461 from NHANES 2005–2006, and 361 from NHANES 2007–2008. This project was deemed exempt from formal review by the Boston Children's Hospital Institutional Review Board.

Measurements

Auscultatory BP measurements are obtained during the physician examination component of the NHANES visit. In NHANES, the SBP is defined by the pressure where tapping begins (Korotkoff phase 1), while DBP is the pressure where tapping ceases (Korotkoff phase 5). PP was calculated as the difference between SBP and DBP. MAP was calculated as one third of PP added to DBP. Beginning with NHANES III, the examining physicians were trained in a standardized measurement protocol, were provided a full range of BP cuff sizes, and were supported by quality control oversight.[15] For NHANES II, only standard adult and pediatric cuffs were available and no formal oversight process was in place. Subsequently, appropriate BP cuffs were selected to ensure that the bladder length encircled 50% to 80% of the mid-arm circumference. Height was measured using a fixed stadiometer with vertical backboard and movable headboard with participants standing. Weight was measured on a digital scale with participant clothing limited to underwear, a disposable gown, and foam slippers. WC was measured at the level of the pelvic ilium. WC was not measured at NHANES II (1976–1984). Body mass index (BMI) was calculated as kilograms (weight) per meters squared (height). Elevated BP as a category was defined to be above the 95% percentile threshold according to the age, sex, and height referenced normative tables contained in the *Fourth Report on Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents.*[16] To account for smoking, we extracted data on the survey questions HFF1 in NHANES III, SMD410 in subsequent NHANES, and serum cotinine levels. Overall, only 101 participants had valid entries regarding antihypertensive medications and so were included in our analysis without adjustment.

Statistical Analysis

Primary analyses used survey linear regression to model differences in PP over time. Survey weighting was applied according to National Center for Health Statistics guidelines.[17] The primary outcome of interest was PP, with MAP as the secondary outcome of interest. The primary predictor was examination year as calculated by the number of years from midpoint of NHANES II to midpoint of each subsequent survey. Adjustment covariates in the first step included age and sex. Height, heart rate, and race/ethnicity were added on the second step and MAP on the third step to account for the effect of distending pressure on arterial stiffness. Finally, BMI was added as a continuous variable. For MAP, a parallel analysis was performed with examination year as the primary predictor, with age and sex on the first step; height, heart rate, and race/ethnicity on the second step; and continuous BMI on the third step. As a sensitivity analysis in the PP and MAP model sets, we separately examined BMI and WC as categorical obese versus nonobese, as well as continuous measures. BMI obesity was defined as BMI above the age- and sex-specific 95th percentile as published in Centers for Disease Control and Prevention growth charts.[18] WC obesity was defined as greater than the age- and sex-specific 90th percentile.[19] Use of WC helps address cases where high BMI may reflect a difference in lean muscle mass. Given the concerns about BP measurement quality control in NHANES II and the large amount of missing data in NHANES III, sensitivity analyses were performed by including only the NHANES 1999–2008 datasets. In post-hoc analyses, smoking was addressed by additional adjustment for the binary answer to a question on smoking in the home and then for serum cotinine level as a continuous variable.

In secondary analyses, participant data from all the surveys were pooled. Survey regression models examined the association between PP or MAP and chronological age or height. Additional covariates included sex, heart rate, and

race/ethnicity; MAP was also included in PP models. Age–obesity and height–obesity interaction terms were used to identify effect modification of the relation between PP and age or height, respectively, by the presence of dichotomous BMI obesity status. To maintain consistency with a significant examination year–sex interaction term in the MAP temporal trend, pooled-sex and sex-specific analyses are reported across all model results. Additionally, we analyzed the effect of race by including a race–NHANES year interaction term. Central tendencies are reported as mean with SEM. SAS 9.2 (IBM) was used for statistical analyses. *P* values <0.05 were deemed significant.

Results

Sample Characteristics

Sample characteristics are detailed in Table 1. The proportion of children with obesity (defined by BMI) more than tripled between NHANES II and NHANES 2007–2008. Average height increased and heart rate fell modestly. While the proportion of non-Hispanic blacks remained stable, proportions of Mexican Americans more than tripled, whereas those of non-Hispanic whites fell across the serial surveys. Correlations between relevant variables are listed in Table 2.

Temporal Trends in BP and Obesity

During the study period, unadjusted PP was progressively higher with time, particularly since 1999 (Figure 1, Table 3). In contrast, MAP was progressively lower, although the reduction was less marked from 1999 to 2008 (Table 4). The PP and MAP time trends persisted in multivariable-adjusted models (Tables 3 and 4). The opposing trends in PP and MAP resulted in flat SBP over the entire study period (−0.03 mm Hg/y, 95% CI 0.08 to 0.01 mm Hg/y; *P*=0.16), with a slight increase after 1999 (0.18 mm Hg/y, 95% CI 0.02 to 0.35 mm Hg/y; *P*=0.03) (Figure 2). Unadjusted sex-specific

Table 1. Sample Characteristics for Children 8 to 17 Years of Age

NHANES	1976–1984 (NHANES II)	1988–1994 (NHANES III)	1999–2000	2001–2002	2003–2004	2005–2006	2007–2008
N examined	3084	3374	2298	2380	1909	1991	1421
N weighted, millions	37.5	27.7	16.5	20.6	33.0	34.6	34.9
Age, y	12.8±0.04	12.1±0.08	12.6±0.1	12.6±0.09	12.9±0.14	12.9±0.07	12.8±0.12
Girls, %	49.1	49.3	49	49.5	51.1	49.9	49.6
Non-Hispanic white, %	70.2	68.3	56.6	63.6	63.4	60.7	60.1
Non-Hispanic black, %	13.8	14.5	15.6	13.7	14.5	14.6	14
Hispanic, %	7.1	8.3	21.6	16.5	17	16.3	19.9
Other race/ethnicity, %	8.9	9	6.2	6.2	5.2	8.5	6
Height, cm	154.8±0.3	154.2±0.4	155.4±0.5	155.7±0.4	157.4±0.7	156.9±0.6	156.9±0.6
Weight, kg	48.4±0.3	49.8±0.6	53±0.6	53.1±0.5	55.6±0.9	54.6±0.8	55.4±0.8
BMI, kg/m^2	19.6±0.1	20.4±0.2	21.3±0.2	21.3±0.2	21.9±0.3	21.6±0.2	21.9±0.2
BMI >95th percentile, %	6	12	17	16	19	18	21
Waist circumference, cm	n.a.	70.8±0.5	74.5±0.5	74.7±0.4	76.7±0.7	75.9±0.6	76.4±0.6
Waist circumference >90th percentile, %	n.a.	12	18	17	23	19	22
Heart rate, bpm	83±0.3	79±0.7	78±0.7	79±0.5	80±0.4	80±0.6	80±0.4
Systolic BP, mm Hg	109±0.6	104±0.4	106±0.3	106±0.4	107±0.5	108±0.5	107±0.6
Diastolic BP, mm Hg	69±0.4	58±0.3	62±0.4	60±0.4	58±0.4	59±0.6	59±0.5
Hypertension, %	5.9	0.9	0.7	0.8	1.6	1.7	1.8
Mean arterial pressure, mm Hg	82±0.5	73±0.3	77±0.3	75±0.3	75±0.4	75±0.5	75±0.5
Pulse pressure, mm Hg	40±0.4	46±0.4	45±0.3	46±0.7	49±0.6	49±0.6	48±0.6
PP >50 mm Hg, %	14	34	29	33	42	43	41
Elevated BP with PP >50 mm Hg, %	64	95	99	100	100	98	93

Data are given as mean±SEM or as proportion. Waist circumference was not measured in 1976–1984 (NHANES II). BMI indicates body mass index; BP, blood pressure; NHANES, National Health and Nutrition Examination Surveys; PP, pulse pressure.

Table 2. Correlation Matrix for Pulse Pressure and Mean Arterial Pressure

	Age	Female	Race/Ethnicity	Height	Heart Rate	Body Mass Index	MAP
PP	0.10	−0.14	−0.04	0.17	−0.08	0.26	−0.26
MAP	0.34	−0.05	0.06	0.36	0.05	0.23	—

Values listed are Pearson correlation coefficients. *P* values for all <0.0001. PP indicates pulse pressure; MAP, mean arterial pressure.

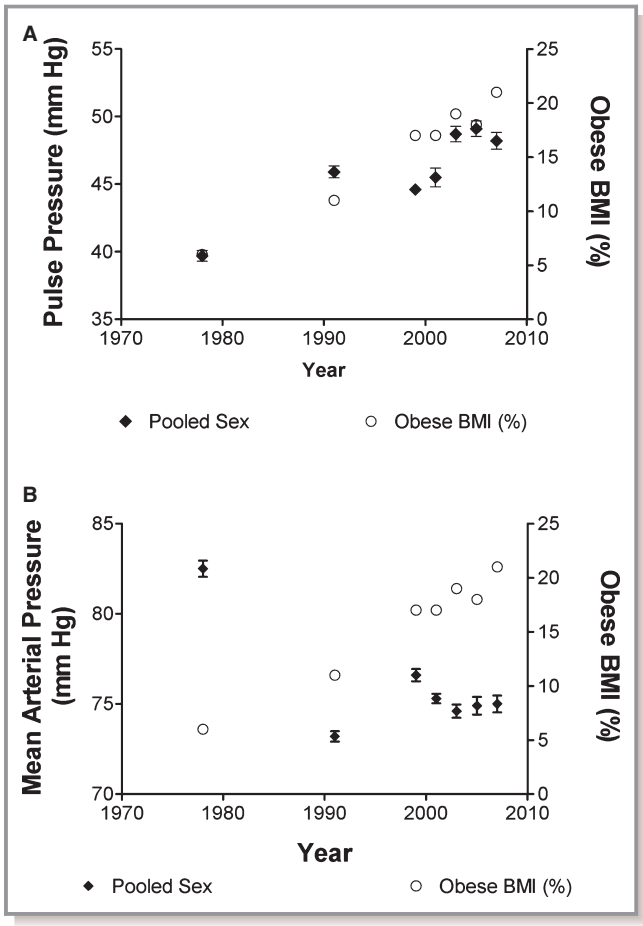

Figure 1. Temporal trends in pooled sex PP, MAP (diamonds), and obesity prevalence (open circles) in children. Left *y*-axes are (A) PP and (B) MAP in millimeters mercury, and the right *y*-axis is the proportion with obese BMI. Values are plotted against the midpoint of each NHANES along the *x*-axis. BMI indicates body mass index; MAP, mean arterial pressure; NHANES, National Health and Nutrition Examination Surveys; PP, pulse pressure.

PP and MAP trends are shown in Figure 3. Fully adjusted models showed no sex difference in PP trends (−0.04, 95% CI −0.09 to 0.01; *P*=0.13), but MAP did have a significant sex interaction (0.09, 95% CI 0.06 to 0.12; *P*<0.0001). Of children with elevated BP as defined by the *Fourth Report on Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*, 81% had PP wider than 50 mm Hg (Table 1).

Greater BMI was associated strongly with higher PP (0.66 mm Hg per 1 kg/m^2, 95% CI 0.59 to 0.73 mm Hg per 1 kg/m^2; *P*<0.0001) and higher MAP (0.41 mm Hg per 1 kg/m^2, 95% CI 0.37 to 0.46 mm Hg per 1 kg/m^2; *P*<0.0001). PP and MAP relations with BMI were comparable after exclusion of NHANES II and III (data not shown). Adjusting the PP×time model for BMI attenuated the temporal trend by 31% in girls and 29% in boys, although a significant residual temporal trend persisted after all adjustments (Table 3). On the other hand, adjustment for BMI steepened the falling trend in MAP by 11% in girls and 7% in boys over the entire study period. The PP and MAP temporal trends were not substantially affected by further adjustment for active or passive smoking. Race/ethnicity did not appear to modify the temporal trends (interaction term *P* value 0.5 for PP and 0.3 for MAP). The use of WC instead of BMI yielded similar results (fully adjusted PP model r^2 for continuous BMI 0.21, and for continuous WC, 0.22).

The Effects of Obesity on PP and MAP Relations With Height and Age

In multivariable-adjusted models, PP was higher with greater height in girls and boys, although the relation was more pronounced in boys (Table 5 and Figure 4). The PP×height relation was augmented comparably in boys and girls who were obese (based on BMI). MAP was comparably higher with greater height in girls and boys (Table 5, Figure 5). In obese children, the relation between MAP and height was diminished because of relatively higher MAP in shorter obese children. There was no relation between age and PP in obese girls and a marginal inverse trend in nonobese girls. In boys, PP was higher with age and the relation was augmented by obesity. MAP was higher with age in girls and boys, although the relation between MAP and age was diminished because of relatively higher MAP at an earlier age in obese children.

Discussion

Consistent with our hypothesis regarding the effect of excess weight on aortic function during childhood, PP has increased substantially during the past 3 decades in parallel with the increasing prevalence of childhood obesity. A substantial proportion of the temporal trend in PP is attributable to

Table 3. Adjusted Differences in Pulse Pressure per Examination Year

	Model r^2	Pooled Sex	Boys	Girls
All NHANES				
Age-sex	0.09	0.29	0.34	0.25
		(0.26 to 0.33)	(0.30 to 0.38)	(0.20 to 0.29)
Multivariable	0.10	0.28	0.32	0.24
		(0.25 to 0.32)	(0.28 to 0.37)	(0.19 to 0.29)
Multivariable+MAP	0.16	0.19	0.21	0.16
		(0.14 to 0.23)	(0.16 to 0.26)	(0.11 to 0.22)
Multivariable+MAP+BMI	0.21	0.13	0.15	0.11
		(0.09 to 0.18)	(0.10 to 0.20)	(0.06 to 0.16)
1999–2008				
Age-sex	0.05	0.47	0.46	0.48
		(0.28 to 0.66)	(0.24 to 0.67)	(0.21 to 0.75)
Multivariable	0.06	0.47	0.44	0.49
		(0.28 to 0.66)	(0.23 to 0.66)	(0.22 to 0.75)
Multivariable+MAP	0.16	0.37	0.31	0.42
		(0.17 to 0.56)	(0.09 to 0.53)	(0.16 to 0.56)
Multivariable+MAP+BMI	0.23	0.33	0.27	0.39
		(0.15 to 0.51)	(0.07 to 0.47)	(0.15 to 0.64)

Regression coefficients with 95% CIs in parentheses indicate mm Hg change in pulse pressure per year. "All NHANES" indicates regression model results from NHANES 1976–2008 examinations; "1999–2008," regression model results from 1999–2008 examinations; model r^2, cumulative proportion of variance in PP attributable to all variables included at each step; model 1, pooled model was adjusted for age and sex (sex-specific models were adjusted only for age); model 2, multivariable adjustment included age, sex, height, heart rate, and race/ethnicity; model 3, multivariable+MAP indicates the addition of MAP to model 2 variables; model 4, multivariable+MAP+BMI indicates the addition of BMI to variables in model 3. $P<0.0001$ for all cells in "All NHANES." $P\leq0.01$ for all cells in "1999–2008." PP indicates pulse pressure; NHANES, National Health and Nutrition Examination Surveys; MAP, mean arterial pressure; BMI, body mass index.

Table 4. Adjusted Differences in Mean Arterial Pressure per Examination Year

	Model r^2	Pooled Sex	Boys	Girls
All NHANES				
Age-sex	0.19	−0.24	−0.28	−0.20
		(−0.27 to −0.20)	(−0.31 to −0.24)	(−0.24 to −0.16)
Multivariable	0.23	−0.24	−0.28	−0.19
		(−0.27 to −0.20)	(−0.32 to −0.25)	(−0.23 to −0.15)
Multivariable+BMI	0.24	−0.26	−0.30	−0.21
		(−0.29 to −0.22)	(−0.34 to −0.26)	(−0.25 to −0.17)
1999–2008				
Age-sex	0.12	−0.17	−0.21	−0.12*
		(−0.30 to −0.04)	(−0.35 to −0.08)	(−0.30 to 0.06)
Multivariable	0.16	−0.18	−0.25	−0.12*
		(−0.31 to −0.05)	(−0.38 to −0.11)	(−0.29 to 0.05)
Multivariable+BMI	0.17	−0.19	−0.25	−0.13*
		(−0.32 to −0.06)	(−0.39 to −0.12)	(−0.30 to 0.04)

Regression coefficients with 95% CIs in parentheses indicate mm Hg change in MAP per year. "All NHANES" indicates regression model results from NHANES 1976–2008 examinations; "1999–2008," regression model results from 1999–2008 examinations; model r^2, proportion of variance in MAP over time accounted for by variables added at each step; model 1, pooled model was adjusted for age and sex (sex-specific models were adjusted only for age); model 2, multivariable adjustment included age, sex, height, heart rate, and race/ethnicity; model 3, multivariable+BMI indicates the addition of BMI added to variables in model 2. $P<0.0001$ for all cells in "All NHANES." $P\leq0.01$ for all cells in "1999–2008" except where indicated *. MAP indicates mean arterial pressure; NHANES, National Health and Nutrition Examination Surveys; BMI, body mass index.
*$P>0.1$.

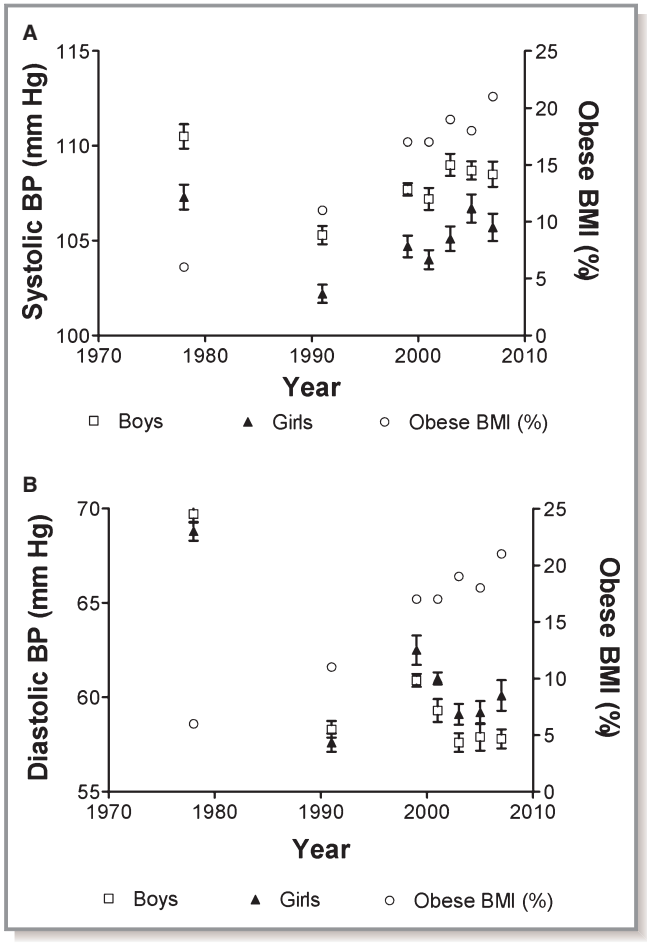

Figure 2. Sex-specific temporal trends in (A) SBP, (B) DBP, and obesity are plotted against the midpoint year of each NHANES period. Separate curves are plotted for boys (open squares), girls (solid triangles), and obesity (open circles) for SBP or DBP on the left *y*-axis and proportion obese on the right *y*-axis. BMI indicates body mass index; DBP, diastolic blood pressure; NHANES, National Health and Nutrition Examination Surveys; SBP, systolic blood pressure.

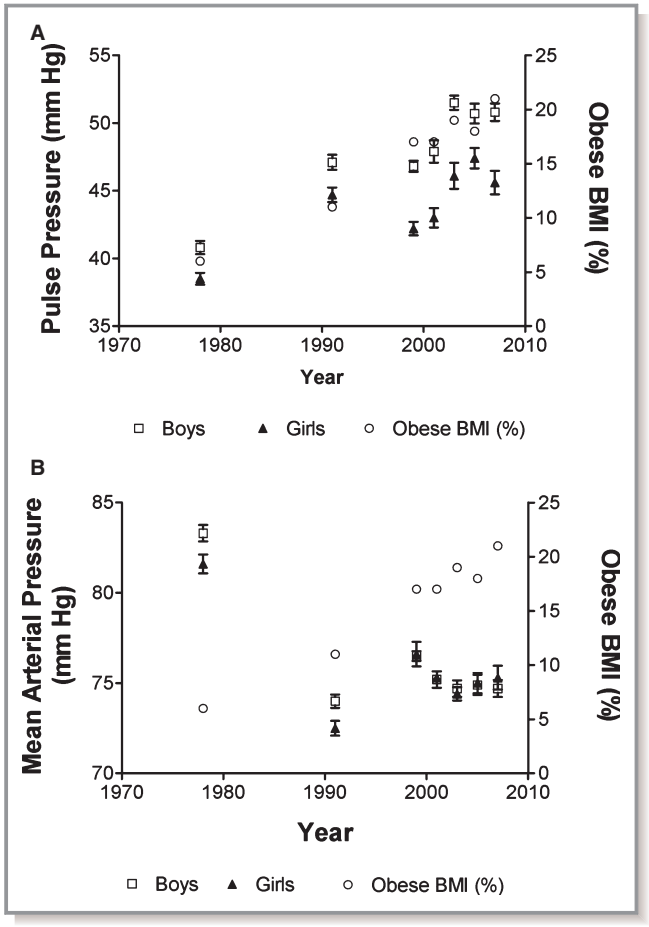

Figure 3. Sex-specific temporal trends in PP (A), MAP (B), and obesity are plotted against the midpoint year of each NHANES period. Separate curves are plotted for boys (open squares), girls (solid triangles), and obesity (open circles) for PP or MAP on the left *y*-axis and proportion obese on the right *y*-axis. BMI indicates body mass index; MAP, mean arterial pressure; NHANES, National Health and Nutrition Examination Surveys; PP, pulse pressure.

obesity, suggesting either that common factors contributed to a parallel increase in obesity and PP or that the increase in obesity contributed to the increase in PP. Obesity amplified the relation between height and PP in both sexes. Obesity augmented the relation between PP and age in boys but not in girls. Wider PP was very common in children with elevated BP. In light of recent data showing that higher PP in a normotensive individual predicts future hypertension,[14] our present observations suggest that the pediatric obesity epidemic may increase the burden of systolic hypertension through wider PP.[14]

Obese children have increased blood volume, larger stroke volume, and higher steady and pulsatile flow, which increases PP.[20] Large arteries accommodate higher ambient flow by remodeling to a larger diameter.[21–24] During childhood, the aorta remodels to accommodate somatic growth. After the first few years of life, when elastic fiber production is active, subsequent aortic lumen enlargement requires extracellular matrix remodeling around a fixed content of elastic fibers, which increases load on elastin and, hence, may transfer load from elastin to much stiffer collagen.[21,25,26] A larger diameter reduces impedance to pulsatile flow and helps maintain PP in a physiological range but also amplifies mean and pulsatile tension on the aortic wall. Increased wall tension can lead to increased wall stiffness through elastin fragmentation and deposition of stiffer matrix components.[21] Therefore, higher PP likely represents a combination of greater aortic wall stiffness and higher flow that has exceeded capacity for outward aortic remodeling.[27–29] Previous work shows the consequence of repeated cycles of wide PP is, in turn, more arterial stiffness and implies that central adiposity is a key determinant.[9,10]

Table 5. Association Between Height or Age and Pulse Pressure or Mean Arterial Pressure: Effect Modification by Obesity

	PP		MAP	
	Boys	Girls	Boys	Girls
Height, mm Hg/cm				
Nonobese BMI	0.23*	0.08†	0.12*	0.14*
	(0.19 to 0.28)	(0.04 to 0.13)	(0.09 to 0.14)	(0.11 to 0.17)
Obese BMI	0.27*	0.22*	0.07‡	0.05
	(0.21 to 0.34)	(0.13 to 0.31)	(0.02 to 0.11)	(−0.02 to 0.12)
Age, mm Hg/y				
Nonobese BMI	0.64*	−0.20§	0.73*	0.76*
	(0.42 to 0.88)	(−0.40 to −0.01)	(0.55 to 0.91)	(0.64 to 0.87)
Obese BMI	0.90*	0.29	0.48†	0.55*
	(0.56 to 1.24)	(−0.09 to 0.68)	(0.21 to 0.76)	(0.32 to 0.77)

Regression coefficients with 95% CIs in parentheses indicate mm Hg increase or decrease in PP or MAP per centimeter increase in height or per year of age. Obese BMI is defined as BMI >95% referenced to age and sex. PP model is sex specific and adjusted for heart rate, race/ethnicity, MAP, and age or height as appropriate. MAP model is sex specific and adjusted for heart rate, race/ethnicity, and age or height as appropriate. The height× or age×BMI interaction term was ≤0.01 for PP and MAP. Three-way interaction terms for height or age with obesity and sex were not significant for all model sets. PP indicates pulse pressure; MAP, mean arterial pressure; BMI, body mass index.
*P<0.0001, †P<0.001, ‡P=0.004, §P=0.04.

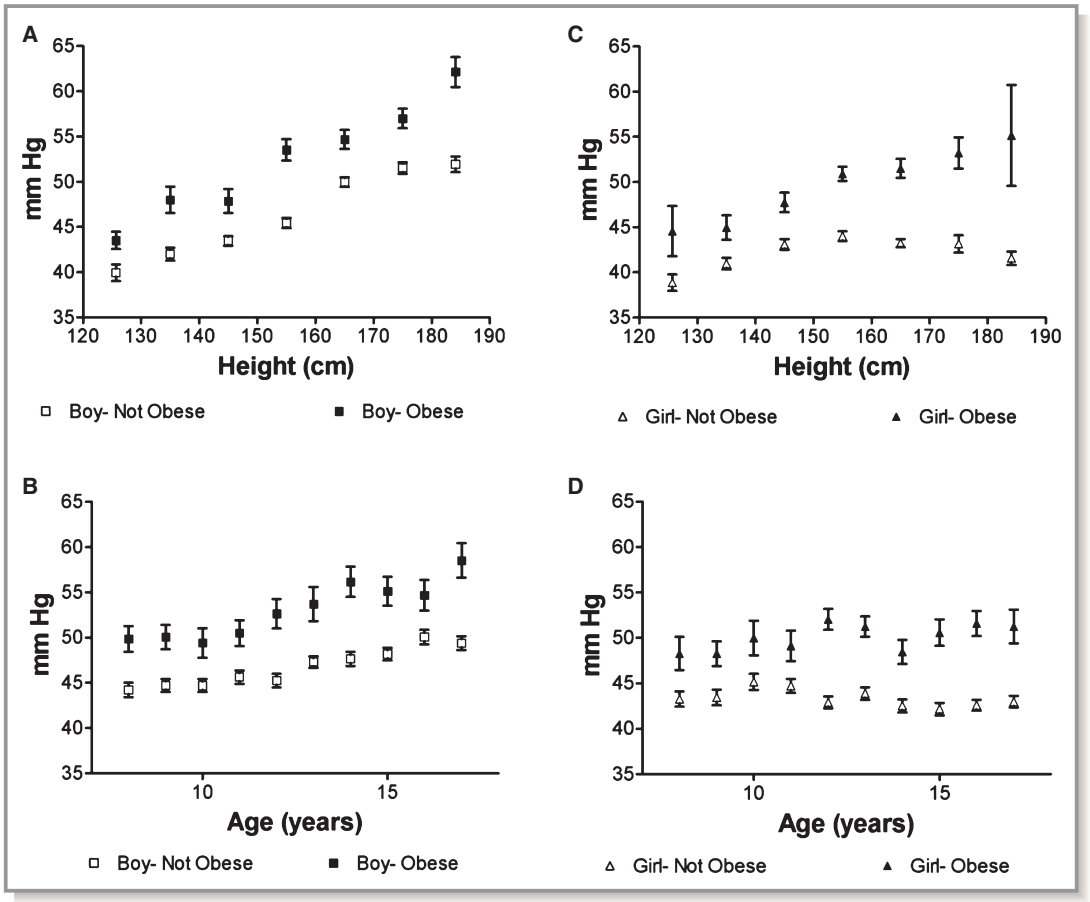

Figure 4. The sex-specific relations between pulse pressure (PP) and height or age for boys (A and B) and girls (C and D). PP in millimeters mercury is plotted against height in 10-cm increments or age in years for nonobese boys (open squares), obese boys (filled squares), nonobese girls (open triangles), and obese girls (filled triangles).

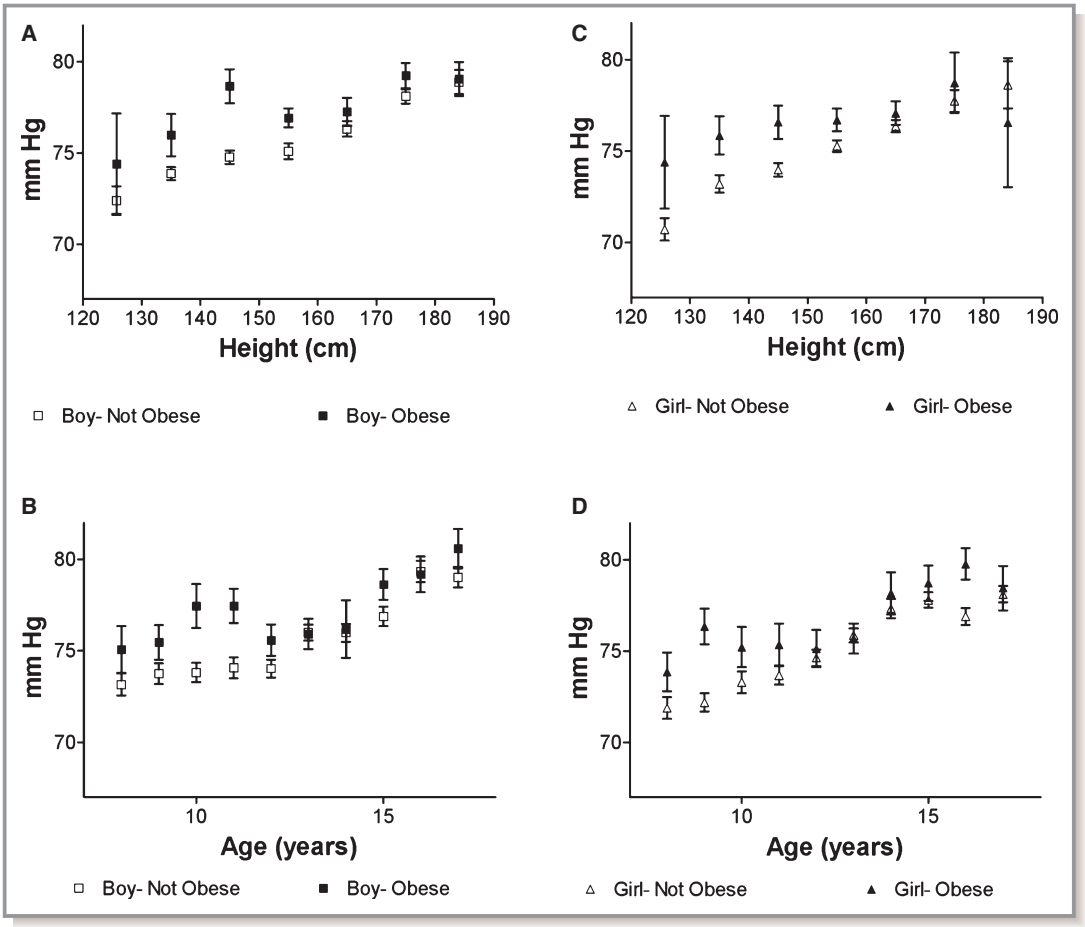

Figure 5. The sex-specific relations between mean arterial pressure (MAP) and height or age for boys (A and B) and girls (C and D) stratified by obesity status. MAP in millimeters mercury is plotted against height in 10 cm increments or age in years for not obese boys (open squares), obese boys (filled squares), not obese girls (open triangles), and obese girls (filled triangles).

Obesity amplified the relation between PP and height, suggesting that a marked increase in pulsatile flow in the face of the combination of rapid somatic growth and excess weight may have overwhelmed the capacity of the aorta to remodel, leading to an increase in pressure pulsatility. Alternatively, obesity may interfere with matching between aortic diameter and flow, possibly because of stiffening of the aortic wall or an adverse effect on endothelial function that limits transduction of the flow stimulus that drives adaptive remodeling.[24,27]

Obesity modestly amplified the relation between PP and age in boys but not in girls. A lower PP slope with age in girls and less PP accentuation with obesity during growth and maturation may be consistent with more effective compensatory remodeling in girls, presumably because of sex-related differences in somatic growth during adolescence. The present observations extend sex-specific relations of pulsatile load with age and height to pediatric age groups.[23,30] PP in young adult women is lower than that in young adult men, but after 50 years of age, PP accelerates in women to meet and exceed PP in men.[13] The roots of the sex difference in our analyses are unclear. Puberty-related hormonal status could play a role as menarche appears to be occurring at earlier ages,[31,32] but NHANES did not capture pubertal status at each examination.

The trends in MAP are complex. Despite the expected and observed association between higher BMI and higher MAP, MAP has decreased over the study period; therefore, obesity cannot account for the MAP trend. In both sexes, obesity attenuated the relations between height or age and MAP. In theory, countervailing trends in pressure pulsatility versus small artery resistance could occur if increased cross-sectional arterial area were developed in growing, developing children to dissipate the excess pulsatile energy. Angiogenic growth factors are associated with pulsatile and steady state parameters in adults.[33] Additionally, the change from 4th to 5th Korotkoff sound and initiation of quality controls from NHANES II to NHANES III may have contributed to the decline in DBP and MAP between those examinations.[34] However, a very modest downward trend in MAP persisted

after excluding NHANES II from the analysis. Our analysis does not support a contribution from temporal trends in smoking.[35–38]

Opposite temporal trends in PP and MAP extend the results of several recent reports in pediatric and adult populations of stable or decreasing SBP and DBP despite increasing obesity and contradict another report suggesting a modest increase in elevated BP prevalence.[39–45] In light of the excess risk associated with higher PP at any given SBP in adults, the PP trend may signal higher risk for future hypertension and CVD end points as these children transition into adulthood. Recent reports of a 19% prevalence of elevated BP in a large cohort of 25- to 34-year-old persons underscore the possibility that children represented in previous NHANES examinations are beginning to experience adverse consequences of elevated PP.[4] Other work highlights a temporal increase in stroke hospitalization in 15- to 34-year-olds, more of whom have hypertension.[5] In adults, incident stroke risk is higher in those individuals with elevated PP.[7,8,46] Previous work in younger adults that minimized the importance of PP on CVD risk may not be applicable to modern children and adolescents because the effects of persistent exposure to higher obesity-related PP during somatic growth have not been studied.[46–48]

Limitations

The NHANES datasets are cross-sectional and, therefore, do not permit causal inferences regarding longitudinal changes in BP within individuals and prevent an analysis of the effects of age of onset or duration of exposure to obesity. However, the NHANES are nationally representative and thus uniquely suited to describe temporal trends in US children. Also, obesity does track moderately through childhood.[49–51] We avoid the ecological fallacy by using survey regression on individual-level data that inherently account for distribution differences within populations as opposed to modeling central measures. We considered the effect of inappropriate cuff sizes as previously enumerated[34] by performing a sensitivity analysis that included only those participants at each NHANES year with BP measured using appropriate cuff sizes and found similar results for MAP and PP. We tested cycle-specific artifacts, like Korotkoff 4 versus Korotkoff 5 for DBP or end-digit preferences as heterogeneity in the BMI relation to PP or MAP.[52] In sensitivity analyses using all participants pooled, we found no effect modification by examination cycle of the relation between BMI and PP. There was an interaction for MAP, underscoring that after exclusion of NHANES II and III, the negative MAP trend persisted only in boys (results not shown). Overall, the consistency in results under a variety of sensitivity analyses supports the validity of our findings.

Conclusion

During the period of rising obesity in US children from 1976 to 2008, PP has increased. Battling obesity and elucidating mechanistic links between obesity and aortic function may offer an opportunity to prevent the potentially severe adverse sequelae of prevalent elevated pressure pulsatility, including future hypertension and consequent CVD.

Sources of Funding

This work was supported through National Institutes of Health/National Heart, Lung, and Blood Institute grants T32 HL007572 and K23 HL111335 (Dr Zachariah).

Disclosures

Dr Mitchell is owner of Cardiovascular Engineering Inc, a company that designs and manufactures devices that measure vascular stiffness. The remaining authors have no conflicts of interest with regard to this manuscript.

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