Long-Term Excessive Body Weight and Adult Left Ventricular Hypertrophy Are Linked Through Later-Life Body Size and Blood Pressure

The Bogalusa Heart Study

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Rationale: **Childhood adiposity is associated with cardiac structure in later life, but little is known regarding to what extent childhood body weight affects adult left ventricular geometric patterns through adult body size and blood pressure (BP).**

Objective: **Determine quantitatively the mediation effect of adult body weight and BP on the association of childhood body mass index (BMI) with adult left ventricular (LV) hypertrophy.**

Methods and Results: **This longitudinal study consisted of 710 adults, aged 26 to 48 years, who had been examined for BMI and BP measured ≥4× during childhood and ≥2× during adulthood, with a mean follow-up period of 28.0 years. After adjusting for age, race, and sex, adult BMI had a significant mediation effect (76.4%; $P<0.01$) on the childhood BMI–adult LV mass index association. The mediation effects of adult systolic BP (15.2%), long-term burden (12.1%), and increasing trends of systolic BP (7.9%) were all significant ($P<0.01$). Furthermore, these mediators also had significant mediation effects on the association of childhood BMI with adult LV hypertrophy, eccentric hypertrophy, and concentric hypertrophy. Importantly, the mediation effects of adult BMI were all significantly stronger than those of adult systolic BP on LV mass index, LV hypertrophy, and LV remodeling patterns ($P<0.01$). Additionally, the mediation effect of systolic BP on concentric hypertrophy was significantly stronger than that on eccentric hypertrophy ($P<0.01$).**

Conclusions: **These findings suggest that increased childhood BMI has long-term adverse impact on subclinical changes in adult cardiac structure, and early life excessive body weight and adult LV hypertrophy are linked through later life excessive body weight and elevated BP. (*Circ Res*. 2017;120:1614-1621. DOI: 10.1161/CIRCRESAHA.116.310421.)**

Key Words: blood pressure ■ body weight ■ left ventricular remodeling ■ longitudinal study ■ mediation effect

Left ventricular (LV) hypertrophy (LVH), an increase in LV mass (LVM), is an independent predictor of cardiovascular events, such as heart failure and cardiovascular mortality.[1–3] It has been well documented that obesity and hypertension are the most important determinants of LVH in the general population.[4–6] Extensive observations have indicated that adiposity is one of the major predictors of LVH, especially eccentric LVH.[4,7] Further, elevated blood pressure (BP) plays a driving role in the development of concentric LVH through chronic hemodynamic overload and increased central pressure.[8]

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Obesity early in life is a risk factor for adult hypertension and cardiovascular disease.[9–12] It is well established that childhood adiposity is associated with higher LVM in children and predicts increased adult LVM.[10–14] The Bogalusa Heart Study has reported that early life obesity and elevated BP have adverse impact on LVH and LV remodeling.[7,11,14] It is well known that childhood adiposity tracks into adulthood, and increased adult body mass index (BMI) is strongly associated with hypertension and leads to cardiovascular disease.[15–17]

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Novelty and Significance

What Is Known?

- Childhood obesity is associated with cardiac hypertrophy in later life.
- Obesity causes eccentric cardiac hypertrophy with a normal heart wall thickness.
- Childhood obesity and the risk of developing a large heart size are linked through increased adult body weight.

What New Information Does This Article Contribute?

- The relationship between childhood body weight and adult heart size is largely dependent on increased adult body weight and blood pressure as well as their life-long burden.
- Childhood body weight imparts its effects on adult heart size largely through adult body weight than through adult blood pressure.
- Excessive body weight during childhood is strongly associated with eccentric cardiac enlargement in adulthood.

Despite extensive studies on the childhood obesity–adult heart size association, little is known regarding the magnitude of this relationship. We found that 76.4%–81.3% of the effect of childhood body weight on adult cardiac mass is mediated through increased body weight in adulthood. The mediation effect of adult body weight is more important than that of adult blood pressure. Moreover, childhood excessive body weight is strongly associated with eccentric cardiac enlargement in adults. However, the effect of childhood body weight on concentric cardiac hypertrophy in adults is mainly through blood pressure in adults. The quantification of the mediation effects of adult body weight and blood pressure would facilitate the development of novel prevention and intervention strategies for controlling the important predictors and mediators beginning in childhood to reduce the risk of cardiovascular disease in adult life.

Nonstandard Abbreviation and Acronyms

AUC	area under the curve
BMI	body mass index
BP	blood pressure
SBP	systolic blood pressure
DBP	diastolic blood pressure
LVH	left ventricular hypertrophy
EH	eccentric hypertrophy
CH	concentric hypertrophy
LVMI	left ventricular mass index
RWT	relative wall thickness

Existing evidence suggests that increased adult BMI may play an important role in mediating the risk of developing LVH associated with childhood obesity.[18,19] Although the concept has been generally accepted that early life obesity and adult LVH are linked through later life obesity and hypertension, the degree of the mediation effect of adult BMI and BP, especially the long-term measures of BMI and BP from childhood to adulthood, on the childhood BMI–adult LVH association has never been reported. In the current study, we aimed to determine quantitatively the mediation effect of adult body weight and BP levels on the association of childhood BMI, with adult LVH and LV geometric remodeling patterns using a longitudinal cohort enrolled in the Bogalusa Heart Study.

Methods

The methods are described in detail in the Online Data Supplement.

Study Cohort

The current longitudinal study cohort consisted of 710 black and white adult subjects, aged 26 to 48 years, who had been examined for LV dimensions in adulthood during 2004 to 2010 and BMI and BP ≥6× (at least 4× in childhood and at least 2× in adulthood). The mean follow-up period was 28.0 years. Standardized protocols were used by trained examiners across all surveys since 1973.

Echocardiographic LV Structure Measurements

To take body size into account, LVM was indexed for body height ($m^{2.7}$) as LV mass index (LVMI). LV relative wall thickness (RWT) was calculated as septal wall thickness plus posterior wall thickness divided by LV end-diastolic diameter. The presence of LVH was defined by LVMI>46.7 g/$m^{2.7}$ in women and >49.2 g/$m^{2.7}$ in men; LV geometry was considered concentric when RWT was >0.42. Four patterns of LV geometry were defined: (1) normal LV geometry (normal RWT with no LVH), (2) concentric remodeling (increased RWT but no LVH), (3) eccentric hypertrophy (EH; normal RWT with LVH), and (4) concentric hypertrophy (CH; increased RWT with LVH).

Statistical Methods

Long-term burden and trends of BMI and BP were measured as the area under the curve (AUC). The AUC of childhood BMI was calculated using 4 to 9 measurements during childhood. Long-term AUC measures of BMI, systolic BP (SBP), and diastolic BP (DBP) were calculated using 6 to 16 measurements from childhood to adulthood. General causal mediation analysis models were performed using linear and logistic regression models for LVMI and LVH geometries, respectively, adjusting for adulthood age, race, and sex. In the mediation models, the predictor variables were AUCs of childhood BMI or long-term BMI from childhood to adulthood; the mediator variables were adult BMI, adult BP, or their respective AUCs from childhood to adulthood; the outcome variables were LVMI, LVH, EH, and CH in separate models.

Results

Table 1 summarizes the study variables with respect to childhood AUC values, long-term AUC values, and adulthood values by race and sex. There were some race and sex differences in childhood AUC values and relatively greater race and sex differences in AUC values from childhood to adulthood. In adulthood, BMI, SBP, and DBP showed significant race (blacks>whites) and sex differences (males>females), except for race difference in BMI among males. Males had significantly higher values of LVM than females; black women had higher values of LVM and LVMI than white women. Black versus white subjects had a higher prevalence of EH (15.7% versus 9.5%; $P<0.01$) and CH (8.0% versus 3.3%; $P<0.05$), but concentric remodeling did not show a significant black–white difference (11.9% versus 11.6%; $P=0.90$).

Table 2 presents total effect of BMI on adult LVMI and LV geometry in linear and logistic regression analyses, respectively, adjusted for adult age, race, and sex. Adult LVMI was consistently associated with childhood BMI AUC (standardized regression coefficient, β=0.40; $P<0.01$), total BMI AUC (β=0.48; $P<0.01$),

Table 1. Characteristics (Mean±SD) of Study Variables by Race and Sex

Characteristic	Whites (n=447)		Blacks (n=263)		*P* for Race Difference	
	Males (n=202)	Females (n=245)	Males (n=99)	Females (n=164)	Males	Females
Childhood AUC*						
Average age, y	12.7 (2.3)	12.3 (2.2)	12.9 (2.2)	12.8 (2.0)	0.576	0.013
BMI, kg/m^2	19.6 (3.5)	19.0 (3.2)	19.5 (3.7)	20.3 (4.0)	0.686	0.004
SBP, mm Hg	105.9 (7.6)†	103.9 (6.6)	106.2 (7.5)	104.8 (6.9)	0.927	0.885
DBP, mm Hg	63.9 (5.4)‡	65.0 (5.2)	64.1 (5.3)‡	65.5 (4.9)	0.969	0.545
AUC§						
Average age, y	20.1 (3.3)	19.9 (3.2)	20.0 (3.6)	20.3 (3.1)	0.679	0.133
Total AUC of BMI, kg/m^2	24.3 (4.2)‡	23.2 (4.4)	24.2 (4.9)	25.6 (5.6)	0.846	<0.001
Total AUC of SBP, mm Hg	112.8 (7.4)‡	107.2 (6.5)	115.7 (7.5)‡	111.1 (8.0)	<0.001	<0.001
Total AUC of DBP, mm Hg	71.8 (5.4)‡	69.6 (4.5)	72.9 (5.7)†	71.5 (5.4)	0.044	<0.001
Incremental AUC of BMI, kg/m^2	7.3 (2.7)‡	6.4 (3.4)	7.2 (2.9)‡	8.3 (3.7)	0.645	<0.001
Incremental AUC of SBP, mm Hg	14.0 (5.0)‡	9.8 (5.4)	18.1 (6.2)‡	14.2 (6.2)	<0.001	<0.001
Incremental AUC of DBP, mm Hg	12.0 (3.0)‡	10.0 (3.8)	12.4 (3.7)†	11.3 (3.8)	0.318	<0.001
Adulthood (Last examination)						
Age, y	37.2 (4.2)	36.5 (4.2)	37.1 (4.7)	36.9 (4.3)	0.847	0.392
BMI, kg/m^2	28.8 (5.3)	28.0 (7.0)	29.2 (7.0)†	31.4 (8.5)	0.556	<0.001
SBP, mm Hg	118.0 (11.5)‡	110.7 (12.3)	126.9 (14.8)‡	120.4 (17.0)	<0.001	<0.001
DBP, mm Hg	79.3 (7.9)‡	74.6 (8.4)	84.2 (10.4)‡	80.1 (10.9)	<0.001	<0.001
LVM, g	177.9 (50.2)‡	128.9 (40.8)	182.3 (55.0)‡	143.2 (49.1)	0.465	0.002
LVMI, g/m$^{2.7}$	37.8 (10.2)‡	34.0 (10.8)	38.9 (11.9)	38.2 (13.1)	0.382	<0.001
RWT	0.35 (0.07)	0.34 (0.08)	0.35 (0.07)	0.35 (0.07)	0.972	0.060

AUC indicates area under the curve; BMI, body mass index; DBP, diastolic blood pressure; LVM, left ventricular mass; LVMI, left ventricular mass index; RWT, left ventricular relative wall thickness; and SBP, systolic blood pressure.

*Childhood AUCs calculated using ≥4 measurements during childhood.

Sex difference within racial groups: †P<0.05; ‡P<0.01.

§AUCs calculated using ≥6 measurements from childhood to adulthood.

and incremental BMI AUC (β=0.39; P<0.01). In logistic regression models, odds ratios (ORs) of childhood BMI AUC (OR, 2.15), total BMI AUC (OR, 2.71), and incremental BMI AUC (OR, 2.29) for LVH were all significant (P<0.01). Similarly, these 3 measures were all significantly associated with adult EH and CH (P<0.01). The total effect, β (95% CI), of childhood, total, and incremental BMI AUCs on adult LVM indexed for body surface area (g/m^2) was 0.16 (0.09–0.24; P<0.01), 0.19 (0.12–0.26; P<0.01), and 0.15 (0.08–0.22; P<0.01), respectively.

The total effects of childhood, total, and incremental BMI AUCs (βs and ORs) were all significant in whites and blacks; the association parameters did not differ significantly between race groups except for the association between childhood BMI AUC and LVMI (P=0.03; Online Table I). The total effects of the 3 BMI AUCs were all significant, except for the association of childhood and incremental BMI AUCs with CH in males; the association parameters did not differ significantly between sex groups (Online Table II).

Figure 1 presents covariates-adjusted adult LVMI according to childhood BMI and adulthood BMI (Figure 1, left panel) or SBP (Figure 1, right panel) status (low and high, defined as below and above the median, respectively). Individuals with higher values of BMI or SBP in adulthood had significantly higher LVMI compared with those in the low–low group. Higher values of childhood BMI with higher adult BMI or SBP were associated with the highest adult LVMI (P<0.01). The differences in LVMI in other pair-wise comparisons were all significant, except the BMI-high and the SBP-low group versus BMI-low and SBP-high group (P=0.33).

Figure 2 shows the mediation effect of adult BMI and SBP on the childhood BMI–adult LVMI association, adjusting for adulthood age, race, and sex. The total effect of childhood BMI on adult LVMI measured as standardized regression coefficient (β_{Tot}=0.40; P<0.01) was estimated without adult BMI in the model. The total indirect effect (β_{Ind}=0.31; P<0.01) through adult BMI defined as the product of indirect effect 1 (β_1) and indirect effect 2 (β_2) was significant (Figure 2A). Likewise, the total indirect effect (β_{Ind}=0.06; P<0.01) through adult SBP was also significant (Figure 2B). The mediation effect of adult BMI on the childhood BMI–adult LVMI association was significantly stronger than that of adult SBP (76.4% versus 15.2%; P<0.01 for difference). Net mediation effects of adult BMI and adult SBP independent of each other were both reduced from 76.4% to 67.5% (decreased by 11.6%) for adult BMI adjusted

Table 2. Total Effect of BMI on Adult LVM Index and LVH Geometry in Linear and Logistic Regression Analyses, Adjusted for Covariates* in the Model

Dependent Variable	Independent Variable		
	AUC of Childhood BMI†	Total AUC of BMI‡	Incremental AUC of BMI§
LVMI (β) (n=710)	0.40‖ (0.34–0.47)	0.48‖ (0.42–0.54)	0.39‖ (0.33–0.45)
LVH (OR) (control:LVH=608:102)	2.15‖ (1.76–2.65)	2.71‖ (2.19–3.40)	2.29‖ (1.86–2.85)
EH (OR)¶ (control:EH=537:74)	2.25‖ (1.79–2.86)	2.67‖ (2.11–3.44)	2.25‖ (1.77–2.90)
CH (OR)¶ (control:CH=537:28)	1.88‖ (1.34–2.62)	2.36‖ (1.69–3.36)	2.08‖ (1.52–2.89)

β indicates standardized regression coefficient (95% CI); AUC, area under the curve; BMI, body mass index; CH, concentric LVH; CI, confidence interval; EH, eccentric LVH; LVH, left ventricular hypertrophy; LVM, left ventricular mass; LVMI, left ventricular mass index; and OR, odds ratio (95% CI).

*Covariates included adult age, race, and sex in all models.

†Childhood AUC calculated using BMI measured 4–9 times during childhood was adjusted for childhood average age and then Z-transformed.

‡Total AUC calculated using BMI measured ≥6 times from childhood to adulthood was adjusted for childhood-to-adulthood average age and then Z-transformed.

§Incremental AUC of BMI calculated using BMI measured ≥6 times from childhood to adulthood was adjusted for childhood-to-adulthood average age and first measure of BMI in childhood and then Z-transformed.

‖β, different from 0: $P<0.01$; OR, different from 1: $P<0.01$.

¶Concentric remodeling (n=71) was not included. The control group had 537 subjects with normal LV geometry.

for adult SBP and from 15.2% to 9.3% (decreased by 38.8%) for adult SBP adjusted for adult BMI. The net mediation effects of adult BMI and adult SBP were 78.9% and 7.9%, respectively, adjusted for childhood SBP. The mediation effect using LVM indexed for body surface area (g/m^2) was 47.9% for adult BMI and 29.0% for adult SBP. These mediation effects on the LVMI (g/m^2) were substantially changed, compared with 76.4% and 15.2% on the LVMI (g/m$^{2.7}$) in Figure 2.

Figure 3 shows the mediation effects of total and incremental SBP AUCs on the total BMI AUC–adult LVMI and incremental BMI AUC–adult LVMI associations, respectively, adjusting for adulthood age, race, and sex. The total effects on LVMI were significant for total BMI AUC (β_{Tot}=0.48; $P<0.01$) and incremental BMI AUC (β_{Tot}=0.39; $P<0.01$). The mediation effect of total SBP AUC on the BMI–LVMI association was estimated at 12.1%, with a significant total indirect effect of 0.06 (Figure 3A). Likewise, the mediation effect of incremental SBP AUC on the BMI–LVMI association was estimated at 7.9%, with a significant total indirect effect of 0.03 (Figure 3B). Net mediation effects of the long-term AUC measures of BMI and SBP from childhood to adulthood were not estimated because the last measurement of adult BMI or SBP was included in the calculation of total and incremental AUC values. The mediation effect using LVM indexed for body surface area (g/m^2) was 36.8% for total SBP AUC and 26.3% for incremental SBP AUC. These mediation effects on the LVMI (g/m^2) were significantly increased, compared with 12.1% and 7.9% on the LVMI (g/m$^{2.7}$) in Figure 3. The mediation effects of long-term measures of DBP on the BMI–adult LVMI association in Online Figure I were substantially similar to those with SBP as a mediator.

Table 3 presents the results of mediation analyses with LVH geometry as the outcome in association with BMI and SBP, adjusted for adulthood age, race, and sex. Adult BMI and SBP had significant mediation effects on the association of childhood and long-term BMI values with adult LVH and LV remodeling patterns. The mediation effect of adult BMI on the association of childhood BMI with adult LVH was significantly stronger than that of adult SBP (81.3% versus 22.2%; $P<0.01$ for difference). Similarly, the mediation effect of adult BMI was stronger than that of adult SBP on the association of childhood BMI with EH (80.3% versus 20.0%; $P<0.01$ for

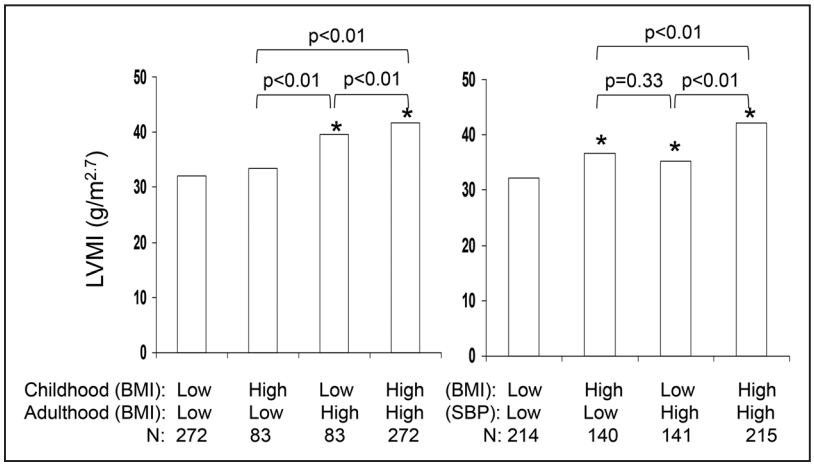

Figure 1. Covariates-adjusted mean values of adult LVMI by childhood and adulthood BMI and SBP status. Covariates included adult age, race, and sex. BMI indicates body mass index; LVMI, left ventricular mass index; and SBP, systolic blood pressure. *$P<0.01$ vs low-low group.

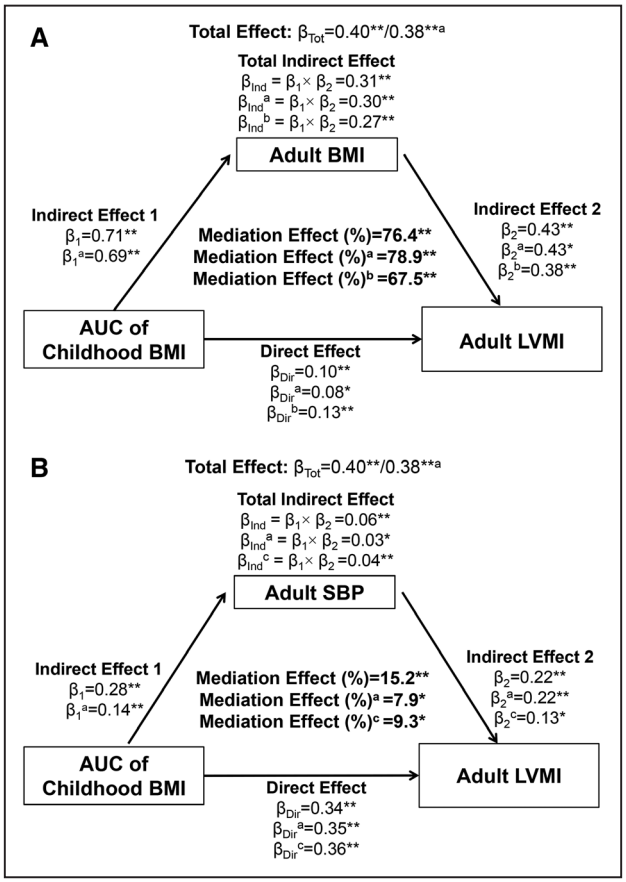

Figure 2. Mediation effect of adult BMI and SBP on the childhood BMI–Adult LVMI association. **A**, Mediation effect of adult BMI. **B**, Mediation effect of adult SBP. *P<0.05 and **P<0.01. [a]Total and net mediation effect of adult BMI and SBP after additional adjustment for childhood SBP. [b]Net mediation effect of adult BMI after adjustment for adult SBP. [c]Net mediation effect of adult SBP after adjustment for adult BMI. β indicates standardized regression coefficient; β_1, indirect effect 1; β_2, indirect effect 2; β_{Dir}, direct effect; β_{Ind}, total indirect effect; β_{Tot}, total effect; AUC, area under the curve; BMI, body mass index; LVMI, left ventricular mass index; and SBP, systolic blood pressure.

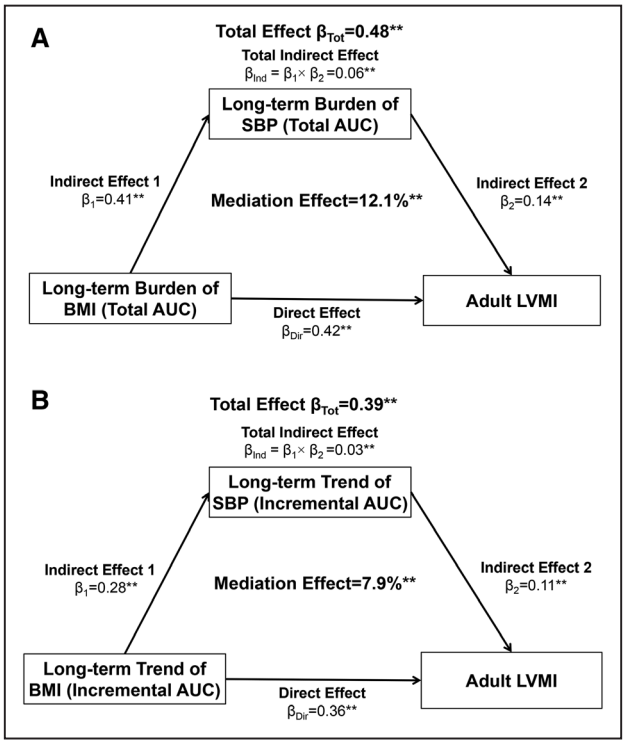

Figure 3. Mediation effect of long-term burden of SBP on the association between long-term burden of BMI and adult LVMI. **A**, Mediation effect of total SBP AUC. **B**, Mediation effect of incremental SBP AUC. β indicates standardized regression coefficient; β_1, indirect effect 1; β_2, indirect effect 2; β_{Dir}, direct effect; β_{Ind}, total indirect effect; β_{Tot}, total effect; AUC, area under the curve; BMI, body mass index; LVMI, left ventricular mass index; and SBP, systolic blood pressure. *P<0.05, **P<0.01.

difference); however, such a difference was not noted for CH (80.0% versus 28.1%; P=0.317 for difference) because the 2 β_2s (0.72 versus 0.69) were close. Of note, the mediation effect of adult SBP on CH was stronger than that on EH in the models with childhood BMI AUC (28.1% versus 20.0%; P<0.01 for difference), total BMI AUC (32.2% versus 14.3%; P<0.01 for difference), and incremental BMI AUC (28.3% versus 11.6%; P<0.01 for difference) as predictors. Net mediation effects of adult BMI and adult SBP on LVH, EH, and CH independent of each other were all reduced. The adjustment for adult BMI resulted in the largest change from 20.0% to 13.2% (decreased by 34.0%) in the mediation effect of adult SBP on the childhood BMI–EH association; the adjustment for adult BMI resulted in the smallest change from 28.1% to 27.0% (decreased by 3.9%) in the mediation effect of adult SBP on the childhood BMI–CH association. As mentioned earlier, the net mediation effects of the long-term AUC measures of BMI and SBP from childhood to adulthood could not be estimated. Additional adjustment for childhood SBP did not result in substantial changes in the net mediation effect of adult BMI on the BMI–LV geometry associations, but considerably reduced the net mediation effect of adult SBP by ≈50%.

Online Table III shows the results of mediation analyses with DBP measures as mediators, adjusted for adulthood age, race, and sex. The mediation effects of adult DBP and DBP AUCs on the association of childhood BMI AUCs with adult LVH geometries were substantially similar to those of adult SBP. Further, the mediation effect of adult DBP on CH was significantly stronger than that on EH (P<0.01 for difference), with childhood (24.2% versus 16.8%), total (24.7% versus 17.8%), and incremental BMI AUCs (20.9% versus 9.9%). The net mediation effects of adult DBP, adjusted for adult BMI, were substantially similar to those of adult SBP. The adjustment for adult BMI resulted in the largest change from 17.3% to 9.3% (decreased by 46.2%) in the mediation effect of adult DBP on the childhood BMI–EH association; the adjustment for adult BMI resulted in the smallest change from 23.8% to 22.2% (decreased by 6.7%) in the mediation effect of adult DBP on the childhood BMI–CH association.

Online Table IV presents mediation analyses, with LVMI and LVH as the outcome in association with BMI, SBP, and DBP by race and sex groups. Adult BMI showed greater mediation effects in whites than in blacks; but the mediation effects of SBP and DBP did not show consistent differences between whites and blacks. The mediation effects of adult BMI, SBP, and DBP and their respective AUC values were consistently greater in females than in males.

Table 3. Mediation Analysis With LVH Geometry as the Outcome in Association With BMI and SBP

	Indirect Effect			Direct Effect (β_{Dir})	Total Effect (β_{Tot})	Mediation Effect, %	Mediation Effect, %*	Mediation Effect, %†
	β_1	β_2	β_{Ind}					
LVH (control:LVH=608:102)								
Childhood BMI AUC→adult BMI→LVH	0.71‡	0.88‡	0.62‡	0.14	0.77‡	81.3‡	68.8‡	83.1%‡
Childhood BMI AUC→adult SBP→LVH	0.28‡	0.60‡	0.17‡	0.60‡	0.77‡	22.2‡	17.1‡	11.5%‡
Total BMI AUC→total SBP AUC→LVH	0.41‡	0.46‡	0.19‡	0.81‡	0.99‡	19.2‡		
Increm BMI AUC→Increm SBP AUC→LVH	0.28‡	0.46‡	0.13‡	0.70‡	0.83‡	15.5‡		
EH (control:CH=537:74)§								
Childhood BMI AUC→adult BMI→EH	0.72‡	0.90‡	0.65‡	0.16	0.81‡	80.3‡	67.9‡	81%‡
Childhood BMI AUC→adult SBP→EH	0.30‡	0.54‡	0.16‡	0.65‡	0.81‡	20.0‡	13.2‡	11.1%
Total BMI AUC→total SBP AUC→EH	0.42‡	0.34‡	0.14‖	0.84‡	0.98‡	14.3‖		
Increm BMI AUC→Increm SBP AUC→EH	0.28‡	0.34‡	0.09‖	0.72‡	0.81‡	11.6‖		
CH (control:CH=537:28)§								
Childhood BMI AUC→adult BMI→CH	0.70‡	0.72‡	0.51‡	0.13	0.63‡	80.0‡	71.4‡	89.7%‖
Childhood BMI AUC→adult SBP→CH	0.26‡	0.69‡	0.18‡	0.45‖	0.63‡	28.1‡	27.0‡	14.8%‖
Total BMI AUC→total SBP AUC→CH	0.37‡	0.75‡	0.28‡	0.58‡	0.86‡	32.2‡		
Increm BMI AUC→Increm SBP AUC→CH	0.27‡	0.78‡	0.21‡	0.53‡	0.73‡	28.3‡		

β indicates standardized regression coefficient; β_1, indirect effect 1; β_2, indirect effect 2; β_{Dir}, direct effect; β_{Ind}, total indirect effect; β_{Tot}, total effect; BMI, body mass index; AUC, area under the curve; CH, concentric LVH; EH, eccentric LVH; Increm AUC, incremental AUC; LVH, left ventricular hypertrophy; and SBP, systolic blood pressure.

*Net mediation effect of adult BMI independent of adult SBP, and net mediation effect of adult SBP independent of adult BMI.

†Net mediation effect of adult BMI and SBP after additional adjustment for childhood SBP.

‡$P<0.01$.

§Concentric remodeling (n=71) was not included. The control group had 537 subjects with normal LV geometry.

‖$P<0.05$.

Discussion

Obesity and hypertension are the most important risk factors related to cardiac enlargement in both children and adults.[7,11,20,21] The Bogalusa Heart Study reported that long-term cumulative burden of overweight/obesity and elevated BP since early life had adverse impact on increased adult LVM and LV geometric remodeling patterns.[7] It is well known that childhood adiposity tracks into adulthood.[15,16,18] Although it is generally accepted that childhood adiposity affects LVM through adult BMI and BP connection, the degree of the mediation effect of later life excessive body weight and elevated BP has never been reported, especially by using the long-term BMI and BP measured from childhood to adulthood. In the current study, we quantified the mediation effects of adult BMI and BP and their long-term measures and found that the childhood BMI–adult LVH association was significantly mediated by adult BMI and BP and their long-term values. Further, we noted that the mediation effect of adult BMI was stronger than that of adult BP on the association of childhood BMI with adult LV geometry patterns, especially adult EH. On the other hand, the mediation effects of adult BP and AUC values on adult CH were stronger than those on adult EH. These findings suggest that long-term influence of increased BMI from early life on subclinical changes in cardiac structure is mediated through later life increased BMI and elevated BP.

Previous studies have shown that early life adiposity was significantly associated with excessive cardiac growth in children and adults.[7,11,13,14,22] The longitudinal observation from the Bogalusa Heart Study has indicated that increased childhood BMI significantly predicts adult LVH and LV geometric remodeling patterns, especially EH.[7,13] The current study found that childhood excessive body weight was linked to increased adult cardiac mass predominantly through adult increased BMI, with a mediation effect of 76.4%, whereas the path through adult elevated SBP accounted for only 15.2%. Of interest, the adjustment for adult BMI showed a substantially greater decrease in the mediation effect of adult SBP on the association of childhood BMI with EH than that with CH (decreased by 34.0% versus 3.9%). These observations provided additional, stronger evidence to support previous findings from our[7,13] and other[4] studies that adiposity is more strongly associated with EH than with CH. Despite consistent existing observations, the pathological mechanisms underlying the link between childhood adiposity and increased LVM and LV geometric patterns in later life need to be further delineated.

It is well recognized that childhood obesity measures persist into adulthood, and adult obesity is strongly associated with cardiovascular disease.[15–17] The tracking correlation between childhood and adulthood BMI suggests that childhood obesity might affect cardiovascular disease risk through adult obesity connection. Juonala et al[18] reported that overweight or obese children who were obese as adults had increased risks of type 2 diabetes mellitus, hypertension, dyslipidemia, and carotid artery atherosclerosis. Despite the strong belief in the

adult obesity connection, the degree of the mediation effect through adult body weight is largely unknown. The quantitative mediation analyses of the current study indicated that the childhood BMI–adult LVH association was significantly mediated by adult increased BMI and long-term values. Our analyses of LV remodeling patterns showed that increased childhood BMI had an adverse effect on adult LVH types, which was largely mediated through adult BMI levels, with a mediation effect of 80.3% for EH and 80.0% for CH. The present study provides strong evidence that the impact of increased childhood BMI on adult LVM and LVH involves an indirect effect, with adult BMI as a mediator located in the pathway from childhood BMI to adult LVH. On the other hand, despite a significant direct effect (0.10) of childhood BMI on adult LVMI in Figure 1, the direct effect of childhood BMI on adult LVH (0.14), EH (0.16), and CH (0.13) shown in Table 3 was not significant after adjustment for adult BMI in the present study. There are studies also showing that the association between childhood BMI and adult cardiovascular risk became not significant after adjustment for adult obesity.[18,23] Further investigation is needed to confirm these findings in studies with a larger number of subjects.

Studies have shown that adiposity affects heart size through hemodynamic, metabolic, and inflammatory alterations, leading to LV enlargement and cardiac remodeling.[24,25] The Framingham Heart Study reported that obesity accounted for ≈26% of cases of hypertension and ≈20% of cases of coronary heart disease.[26] Clinical and epidemiological studies have consistently demonstrated the role of elevated BP in the development of LVH and concentric LV remodeling through chronic hemodynamic overload and increased central pressure.[8] As childhood adiposity is highly correlated with increased risk of hypertension,[18,27] elevated adult BP is generally considered to mediate the association of childhood adiposity with increased adult LVM and LVH. However, it was unclear to what extent childhood obesity affects LVH through adult BP connection. In the present study, we found that adult BP and long-term BP values had a significant mediation effect on the childhood BMI–adult LVH association, and adult SBP showed a significantly stronger mediation effect on CH (28.1%–32.2%) than on EH (11.6%–20.0%) as shown in Table 3. The findings from the current and previous studies[7,8,28,29] on the stronger association between elevated BP and CH point to the importance of BP control for the development of CH, which is considered to carry higher risk for cardiovascular events.[2,30]

This community-based longitudinal cohort provides a unique opportunity to examine the mediation effects of BMI and BP in terms of both adult values and cumulative burden. There were, however, a few limitations in this study. The forced values of 140/90 mm Hg assigned to the measured SBP/DBP for hypertensive patients under treatment would result in some bias in the association and mediation analyses. Therefore, we repeated the analyses by using +10/5 mm Hg to the measured SBP/DBP values and model adjustment for BP treatment. The association and mediation parameters did not change substantially. LVH can be reversed by long-term antihypertensive treatment. However, such an effect cannot be assessed without the LVM progression data in this study.

In summary, we demonstrated that BMI and BP, measured in adulthood and as life-long burden and trends (AUCs), had a significant mediation effect on the childhood BMI–adult LVH association. In particular, the mediation effect of adult BMI on the association of childhood BMI with adult LVM and LV remodeling patterns was stronger than that of adult BP. In addition, the mediation effect of adult BP on CH was stronger than that on EH using childhood BMI and cumulative BMI as predictors. The novelty of this study is that we quantified the degree of the mediation effect of adult BMI and BP on the association between childhood BMI and adult cardiac structure changes. These findings suggest that long-term influence of increased BMI since early life has adverse impact on subclinical changes in cardiac structure, and childhood excessive body weight and adult LVH are linked through increased BMI and elevated BP in later life. The quantification of the mediation effects of adult BMI and BP may facilitate the development of novel prevention and intervention strategies for controlling the important predictors and mediators beginning in childhood to reduce the risk of cardiovascular disease in adult life.

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H. Zhang, T. Zhang, and W. Chen generated the hypothesis, directed implementation, and wrote the article. S. Li and W. Shen contributed to analytic strategy, statistical analyses, and editing the article. Y. Guo and C. Fernandez contributed to data collection and edited the article. E. Harville, L.A. Bazzano, E.M. Urbina, and J. He supervised the field activities and data collection or edited the article.

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Disclosures

None.

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Long-Term Excessive Body Weight and Adult Left Ventricular Hypertrophy Are Linked Through Later-Life Body Size and Blood Pressure: The Bogalusa Heart Study

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Supplement Materials

Detailed Methods

Study cohort

The Bogalusa Heart Study, a series of long-term studies in a semi-rural biracial (65% white and 35% black) community in Bogalusa, Louisiana, was founded by Dr. Gerald Berenson in 1973. This study focuses on the early natural history of cardiovascular disease since childhood.[1] In the community of Bogalusa, 9 cross-sectional surveys of children aged 4-19 years and 11 cross-sectional surveys of adults aged 20-50 years who had been previously examined as children were conducted between 1973 and 2010. Linking these repeated cross-sectional surveys conducted every 2-3 years has resulted in serial observations from childhood to adulthood. The current longitudinal study cohort consisted of 710 adult subjects (447 whites and 263 blacks; 42.4% males; age range=26-48 years; mean age=37.1 years at follow-up) who had been examined for LV dimensions in adulthood during 2004 -2010 and body mass index (BMI) and blood pressure (BP) 6 or more times (at least 4 times in childhood and at least 2 times in adulthood). The mean follow-up period was 28.0 years.

All subjects in this study gave informed consent at each examination, and for those under 19 years of age, consent of a parent/guardian was obtained. Study protocols were approved by the Institutional Review Board of the Tulane University Health Sciences Center.

General examinations

Standardized protocols were used by trained examiners across all surveys since 1973.[1] BMI (weight in kilograms divided by the square of the height in meters) was used as a measure of adiposity. BP levels were measured between 8:00 AM and 10:00 AM on the right arm in a relaxed, sitting position by 2 trained observers (3 replicates each). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) was recorded using a mercury sphygmomanometer. The fourth Korotkoff phase was used for DBP in children and the fifth Korotkoff phase was used for adults.[2] The mean values of the 6 readings were used for analysis. For hypertensive patients (n=96) who were under treatment and had SBP/DBP<140/90 mmHg, forced values (140/90 mmHg) were assigned for measured SBP/DBP.

Echocardiographic LV structure measurements

LV dimensions were assessed by 2-dimensional guided M-mode echocardiography with 2.25- and 3.5-MHz transducers according to American Society of Echocardiography recommendations.[3] Parasternal long- and short-axis views were used for measuring LV end-diastolic and end-systolic measurements in duplicate, and the mean was calculated. LVM was calculated from a necropsy-validated formula on the basis of a thick-wall prolate ellipsoidal geometry.[4] To take body size into account, LVM was indexed for body height ($m^{2.7}$) as LV mass index (LVMI). LV relative wall thickness (RWT) was calculated as septal wall thickness plus posterior wall thickness divided by LV end-diastolic diameter.[5] The presence of LVH was defined by LVMI>46.7 $g/m^{2.7}$ in women and >49.2$g/m^{2.7}$ in men; LV geometry was considered concentric when RWT was >0.42.[6] Four patterns of LV geometry were defined: 1) normal LV geometry (normal RWT with no LVH, n=537), 2) concentric remodeling (CR, increased RWT but no LVH, n=71), 3) eccentric hypertrophy (EH, normal RWT with LVH, n=74), and 4) concentric hypertrophy (CH, increased RWT with LVH, n=28).[5-8] For comparison, LVM was also indexed for body surface area (g/m^2) calculated using the formula

proposed by Mosteller.[9]

Statistical methods

Long-term burden and trends of BMI and BP were measured as the area under the curve (AUC) which was calculated using statistical models we previously described.[10-12] Growth curves of BMI and BP measured repeatedly multiple times from childhood to adulthood were constructed using a random-effects model by SAS proc MIXED (SAS Institute Inc., Cary, North Carolina). The mixed model incorporates fixed and random effects and allows the intercept, linear and nonlinear parameters to vary from individual to individual. The random effect coefficients represent the difference between the fixed effect parameters and the observed values for each individual. This model also allows for repeated measurements and different numbers of unequally spaced observations across individuals.[13] The mixed linear model computes maximum likelihood estimates of curve parameters, generating 710 different sets of curve parameters for all subjects of the study cohort. The model selection was based on the Akaike's Information Criterion (AIC). The most parsimonious model was selected based on p-values of the independent variable (age) at the significance level of 0.05. Age and its higher-order terms were included one by one for model building. The higher-order terms of age were not included in the model if they were not significant, or made lower-order terms not significant, or did not improve the goodness-of-fit of the model based on AIC values. Age was centered to the mean age (20.1 years) to remove the collinearity of age with its higher-order terms. The term age^2 was divided by 10 and age^3 by 20 to improve the model fitting.[14] A quadratic curve was fitted for BMI, and a cubic curve for SBP and DBP in race-sex groups. As shown in **Online Figures II and III**, using BMI and systolic BP as examples, respectively, the AUCs were calculated as the integral of the curve parameters during the follow-up period in each subject. Since individuals had different follow-up periods, the AUC values were divided by the number of follow-up years. The AUC measures in **Online Figures II and III** have advantages over other longitudinal analysis models in that they measure both long-term burden and trends. Total AUC (a+b) can be considered a measure of a long-term cumulative burden; incremental AUC (a), determined by within-subject variability, represents a combination of linear and nonlinear longitudinal trends. We used these AUC measures in our previous studies.[10-12] The AUC of childhood BMI and BP was calculated using 4-9 measurements during childhood. Long-term AUC measures of BMI and BP were calculated using 6-16 measurements from childhood to adulthood.

Multivariable linear and logistic regression analyses were performed for adult LVMI and LVH, respectively, to examine the association with childhood BMI and long-term BMI, adjusted for adulthood age, race, and sex. For assessing the total effect of childhood BMI on adult LV geometry, EH and CH were analyzed in separate logistic regression models using subjects with normal geometry as the control group. Prior to regression analyses, childhood and adulthood values as well as total and incremental AUC values were adjusted for age by regression residual analyses and then standardized with Z-transformation (mean=0, SD=1) by race-sex groups to avoid collinearity of childhood and adulthood ages in the same model. In addition, for analyses of incremental AUCs, baseline values of BMI and BP were included in the model for adjustment to control the regression-to-the-mean bias.

General causal mediation analysis models were constructed as previously proposed by VanderWeele and Sobel.[15,16] Linear and logistic regression models were used to estimate standardized regression coefficients (βs) for LVMI and LVH geometries, respectively, adjusting for adulthood age, race and sex. In the mediation models (**Online Figure IV**), the predictor variables (X) were AUCs of childhood BMI or long-term BMI from childhood to adulthood; the mediator variables (M) were adult BMI, adult BP, or their respective AUCs from

childhood to adulthood; the outcome variables (Y) were LVMI, LVH, EH and CH in separate models. Four steps of the mediation analysis were involved in the calculation of the mediating effect:

Step 1: Showing that the predictor variable determines the outcome (Model $Y=\beta_{Tot}X$) (β_{Tot}=total effect).

Step 2: Showing that the predictor variable affects the mediator (Model $M=\beta_1X$) (β_1=indirect effect 1).

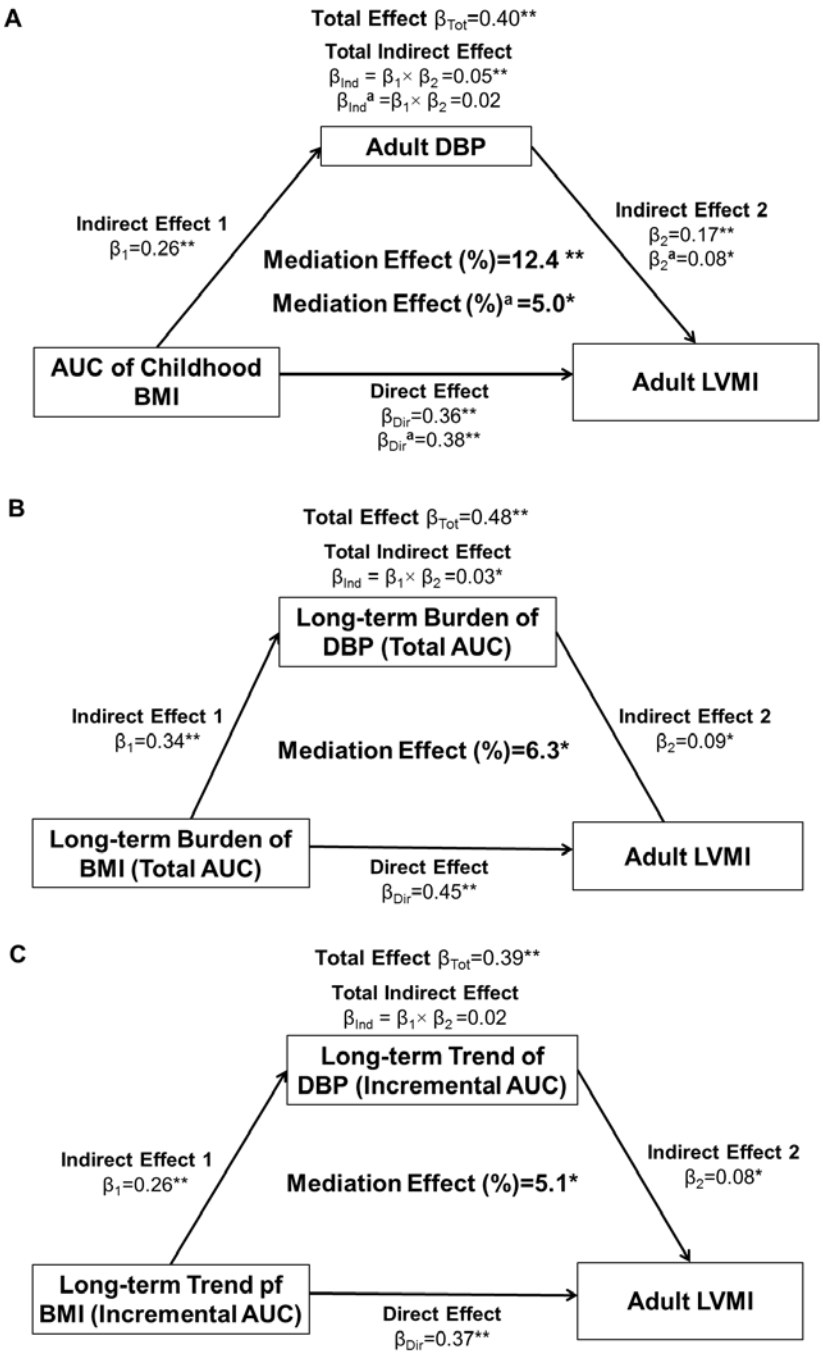
Step 3: Showing that the mediator determines the outcome controlling for the predictor (Model $Y=\beta_2M + \beta_{Dir}X$) ($\beta_2$=indirect effect 2, β_{Dir}=direct effect).

Step 4: Calculating the proportion of mediation effect (%) by $(\beta_1\times\beta_2 / \beta_{Tot}) \times 100\%$.

In mediation analyses, testing the significance of the mediation effect is equivalent to testing the null hypothesis H_0: $\beta_2=0$ versus the alternative hypothesis H_a: $\beta_2\neq0$, by using the procedures of R package *mediation*.[17]

The significance of the difference between two standardized regression coefficients (βs) derived from the standardized variables (Z-scores) was tested using Fisher's Z-test as described in our previous study.[18] Net mediation effects of the last measurement of adult BMI and BP independent of each other were estimated by including adult BP or BMI as an additional covariate in the model for adjustment. The net mediation effects of the long-term AUC measures of BMI and BP from childhood to adulthood were not estimated because the last measurement of adult BP or BMI was included in the growth curve construction and calculation of the long-term AUC values (total and incremental AUCs). In addition, the net mediation effects of adult BMI and adult BP were also estimated by including childhood SBP as a covariate in the model for additional adjustment.

The power of the mediation analysis was calculated using Vittinghoff's method[19] by R package *PowerMediation*. In the mediation analysis in **Online Figure IV**, the power is totally dependent on the power to detect the indirect effect 2 (β_2) in Step 3. The sample size of 263 blacks, 447 whites and 710 in total achieved 80% power to detect a β_2 of 0.177, 0.135 and 0.107, respectively, with the correlation between M and Y of 0.20 at a significance level of 0.05. The sample size of 565 for CH analyses and 611 for EH analyses achieved 80% power to detect a β_2 of 0.128 and 0.116, respectively.

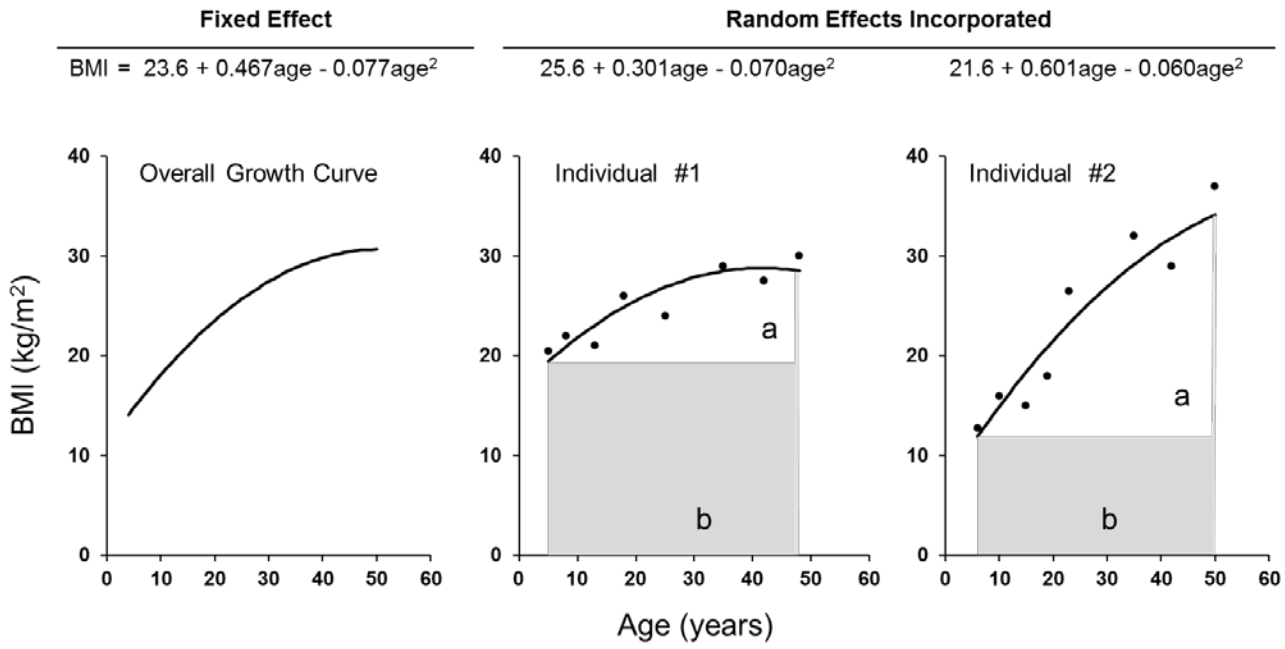


Online Figure I. Mediation effect of DBP on BMI-LVMI association.

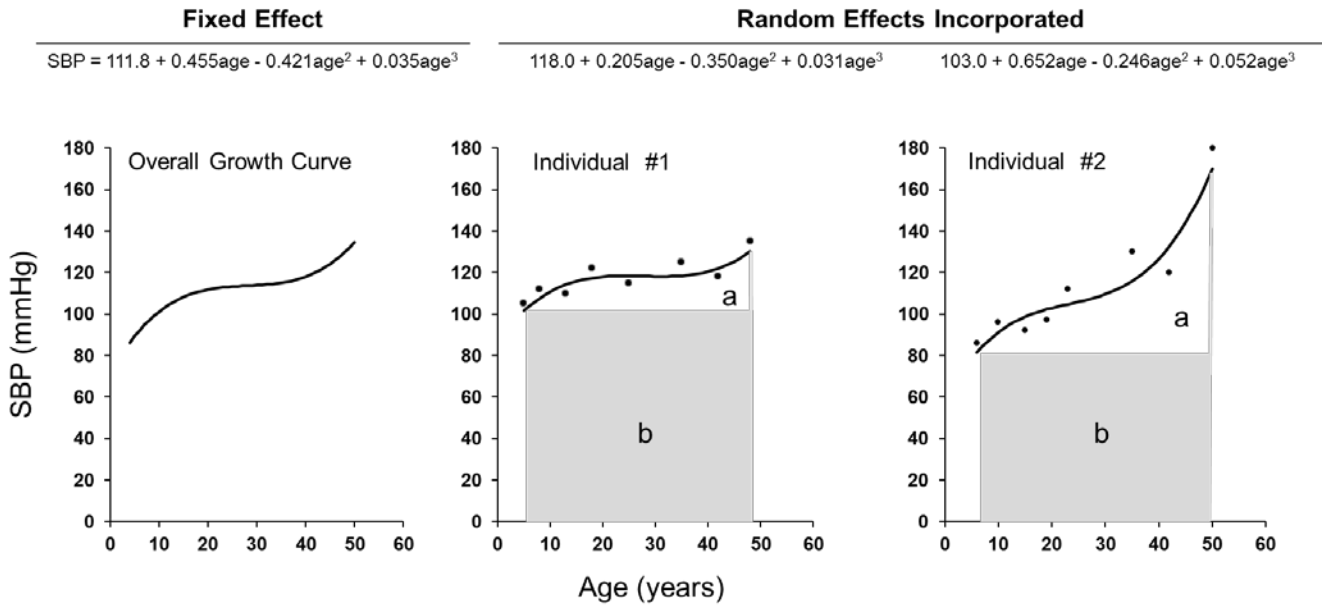
β=standardized regression coefficient; β_1=indirect effect 1; β_2=indirect effect 2; β_{ind}=total indirect effect; β_{dir}=direct effect; β_{tot}=total effect; BMI=body mass index; DBP=diastolic blood pressure; AUC=area under the curve; LVMI=left ventricular mass index

* p<0.05, ** p<0.01

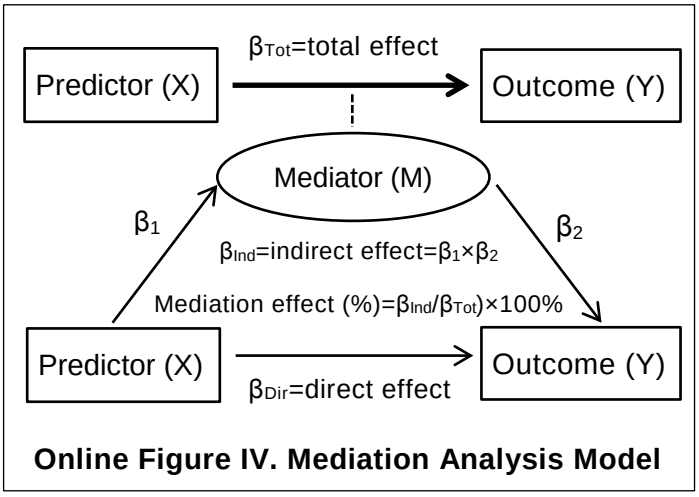
a, net mediation effect of adult DBP after adjustment for adult BMI



Online Figure II. Area Under the Curve (AUC) of Body Mass Index (BMI) and Two Examples. a=incremental AUC; b=baseline AUC



Online Figure III. Area Under the Curve (AUC) of Systolic Blood Pressure (SBP) and Two Examples. a=incremental AUC; b=baseline AUC



Online Figure IV. Mediation Analysis Model

Online Table I. Total effect of BMI on adult LVM index and LVH geometry in linear and logistic regression analyses by race, adjusted for covariates[a] in the model

Dependent Variable		Independent Variable		
		AUC of Childhood BMI[b]	Total AUC of BMI[c]	Incremental AUC of BMI[d]
LVMI (β)	Whites (n=447)	0.35** (0.26~0.43)	0.46** (0.38~0.55)	0.41** (0.32~0.49)
	Blacks (n=263)	0.50** (0.40~0.60)	0.56** (0.46~0.65)	0.41** (0.31~0.52)
	P for race difference	0.033	0.161	0.971
LVH (OR)	Whites (n=398 vs.49)	1.93** (1.48~2.52)	2.62** (1.95~3.51)	2.28** (1.71~3.04)
	Blacks (n=210 vs.53)	2.49** (1.80~3.43)	2.96** (2.09~4.19)	2.49** (1.75~3.54)
	P for race difference	0.270	0.621	0.809
EH (OR)[e]	Whites (n=352 vs.37)	2.03** (1.49~2.77)	2.55** (1.84~3.53)	2.23** (1.61~3.08)
	Blacks (n=185 vs.37)	2.52** (1.77~3.59)	2.95** (2.01~4.34)	2.43** (1.62~3.67)
	P for race difference	0.355	0.512	0.857
CH (OR)[e]	Whites (n=352 vs.12)	1.90** (1.22~2.97)	2.47** (1.51~4.02)	2.01** (1.26~3.20)
	Blacks (n=185 vs.16)	1.87* (1.13~3.09)	2.39** (1.43~3.98)	2.41** (1.45~4.02)
	P for race difference	0.955	0.944	0.599

BMI=body mass index; AUC=area under the curve; LVMI=left ventricular mass index; LVH=left ventricular hypertrophy; EH=eccentric LVH; CH=concentric LVH

β=standardized regression coefficient (95% CI); OR=odds ratio (95% CI)
β different from 0: ** p<0.01
OR different from 1: * p<0.05; ** p<0.01

a, Covariates included adult age, and sex in all models.
b, Childhood AUC calculated using BMI measured 4 or more times during childhood was adjusted for childhood average age and then Z-transformed
c, Total AUC calculated using BMI measured 6 or more times from childhood to adulthood was adjusted for childhood-to-adulthood average age and then Z-transformed.
d, Incremental AUC of BMI calculated using BMI measured 6 or more times from childhood to adulthood was adjusted for childhood-to-adulthood average age and first measure of BMI in childhood and then Z-transformed.
e, Concentric remodeling (n=71) was not included. The control group had 537 subjects with normal LVM.

Online Table II. Total effect of BMI on adult LVM index and LVH geometry in linear and logistic regression analyses by sex, adjusted for covariates[a] in the model

Dependent Variable		Independent Variable		
		AUC of Childhood BMI[b]	Total AUC of BMI[c]	Incremental AUC of BMI[d]
LVMI (β)	Males (n=301)	0.38** (0.28~0.48)	0.43** (0.33~0.53)	0.34** (0.23~0.45)
	Females (n=409)	0.42** (0.33~0.51)	0.55** (0.47~0.63)	0.46** (0.37~0.55)
	P for sex difference	0.627	0.073	0.061
LVH (OR)	Males (n=260 vs 41)	2.34** (1.69~3.22)	2.79** (1.97~3.95)	2.30** (1.60~3.30)
	Females (n=348 vs 61)	2.02** (1.56~2.62)	2.73** (2.04~3.66)	2.44** (1.83~3.25)
	P for sex difference	0.478	0.854	0.607
EH (OR)[e]	Males (n=218 vs 39)	2.30** (1.64~3.23)	2.68** (1.87~3.83)	2.37** (1.64~3.44)
	Females (n=319 vs 35)	2.18** (1.59~2.99)	2.75** (1.95~3.88)	2.29** (1.61~3.25)
	P for sex difference	0.921	0.937	0.934
CH (OR)[e]	Males (n=218 vs 2)	20.4 (0.79~524.5)	4.84* (1.12~21.0)	0.98 (0.25~3.87)
	Females(n=319 vs 26)	1.70** (1.19~2.41)	2.30** (1.60~3.31)	2.32** (1.62~3.32)
	P for sex difference	0.071	0.333	0.315

BMI=body mass index; AUC=area under the curve; LVMI=left ventricular mass index; LVH=left ventricular hypertrophy; EH=eccentric LVH; CH=concentric LVH

β=standardized regression coefficient (95% CI); OR=odds ratio (95% CI)
β different from 0: ** p<0.01
OR different from 1: * p<0.05; ** p<0.01

a, Covariates included adult age, and race in all models.
b, Childhood AUC calculated using BMI measured 4 or more times during childhood was adjusted for childhood average age and then Z-transformed
c, Total AUC calculated using BMI measured 6 or more times from childhood to adulthood was adjusted for childhood-to-adulthood average age and then Z-transformed.
d, Incremental AUC of BMI calculated using BMI measured 6 or more times from childhood to adulthood was adjusted for childhood-to-adulthood average age and first measure of BMI in childhood and then Z-transformed.
e, Concentric remodeling (n=71) was not included.

Online Table III. Mediation analysis with LVH geometry as the outcome in association with DBP

	Indirect Effect			Direct Effect (β_{Dir})	Total Effect (β_{Tot})	Mediation Effect (%)	Mediation Effect (%)[a]
	β_1	β_2	β_{Ind}				
LVH							
Childhood BMI AUC→Adult DBP →LVH	0.26**	0.54**	0.14**	0.63**	0.77**	18.2**	13.0*
Total BMI AUC→total DBP AUC →LVH	0.34**	0.58**	0.20**	0.79**	0.99**	20.2**	
Increm BMI AUC→Increm DBP AUC →LVH	0.26**	0.40**	0.11**	0.72**	0.83**	13.3**	
EH							
Childhood BMI AUC→Adult DBP →EH	0.29**	0.47**	0.14*	0.67**	0.81**	17.3**	9.3*
Total BMI AUC→total DBP AUC →EH	0.35**	0.50**	0.18**	0.81**	0.98**	18.4**	
Increm BMI AUC→Increm DBP AUC →EH	0.28**	0.29*	0.08	0.73**	0.81**	9.9	
CH							
Childhood BMI AUC→Adult DBP →CH	0.26**	0.59*	0.15*	0.48**	0.63**	23.8*	22.2*
Total BMI AUC→total DBP AUC →CH	0.30**	0.70*	0.21*	0.65**	0.86**	24.4*	
Increm BMI AUC→Increm DBP AUC →CH	0.25**	0.60*	0.15*	0.58**	0.73**	20.5*	

effect; β_{Dir}=direct effect; β_{Tot}=total effect;
BMI=body mass index; DBP=diastolic blood pressure; AUC=area under the curve;
increm AUC=incremental AUC; LVH=left ventricular hypertrophy; EH=eccentric LVH; CH=concentric LVH

β=standardized regression coefficient; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=total indirect * $p<0.05$; ** $p<0.01$

a, Net mediation effect of adult DBP independent of adult BMI

Online Table IV. Mediation effect (%) of BMI, SBP and DBP on LVMI and LVH as the outcomes by race and sex groups

	White (n=447)	Black (n=263)	Males (n=301)	Females (n=409)
Childhood BMI AUC→ Adult BMI→LVMI	91.8**	62.8**	73.5**	79.9**
Childhood BMI AUC→ Adult SBP→LVMI	13.3**	16.6**	9.8**	18.9**
Total BMI AUC→ Total SBP AUC→LVMI	10.5**	13.4**	9.5	13.1**
Increm BMI AUC→ Increm SBP AUC→LVMI	6.3**	8.3**	1.3	12.2**
Childhood BMI AUC→ Adult DBP→LVMI	12.4**	8.3*	5.1	14.4**
Total BMI AUC→ Total DBP AUC→LVMI	7.0*	4.6	3.0	7.8**
Increm BMI AUC→ Increm DBP AUC→LVMI	3.3	5.9*	1.7	9.3**
Childhood BMI AUC→ Adult BMI→LVH	86.5**	74.3**	78.2**	82.7**
Childhood BMI AUC→ Adult SBP→LVH	19.5**	24.7**	13.5**	29.6**
Total BMI AUC→ Total SBP AUC→LVH	18.4**	20.8**	13.4	24.3**
Increm BMI AUC→ Increm SBP AUC→LVH	19.4**	10.3**	7.6	21.9**
Childhood BMI AUC→ Adult DBP→LVH	20.5**	14.4**	9.7**	24.2**
Total BMI AUC→ Total DBP AUC→LVH	22.6**	16.6*	14.5	23.7**
Increm BMI AUC→ Increm DBP AUC→LVH	13.8*	8.8**	3.5	19.2**

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; AUC=area under the curve; Increm AUC=incremental AUC; LVMI=left ventricular mass index; LVH=left ventricular hypertrophy

* $p<0.05$; ** $p<0.01$

Supplemental References for Detailed Methods

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