Journal of the American Heart Association

ORIGINAL RESEARCH

Impact of Long-Term Burden of Body Mass Index and Blood Pressure From Childhood on Adult Left Ventricular Structure and Function

Yang Liu, MD, MS; Yinkun Yan, MD, PhD; Tingbo Jiang, MD, PhD; Shengxu Li, MD, PhD; Yajun Guo, MD; Camilo Fernandez, MD; Rupert Barshop, MPH; Lydia Bazzano, MD, PhD; Jiang He, MD, PhD; Wei Chen, MD, PhD

BACKGROUND: Data are limited regarding the relationship between the life-course burden of risk factors and adult cardiac function. This study sought to examine the impact of long-term burden of body mass index (BMI) and blood pressure (BP) levels on changes in adult left ventricular (LV) structure and function in a community-based cohort.

METHODS AND RESULTS: The longitudinal study cohort consisted of 1108 adult patients (726 White; 41.9% men; mean age, 48.2 years in the last survey) who had been examined 4 to 16 times for BMI and BP and echocardiographic LV structure and function in adulthood, with a mean follow-up period of 38.8 years. The area under the curve was used as a measure of long-term burden of BMI and BP. Adult LV mass index was significantly associated with childhood and adulthood BMI and systolic BP (SBP), and their area under the curve values (β=0.07–0.37; $P<0.05$ for all). Adult LV ejection fraction was negatively associated with childhood BMI (β=−0.08), adult BMI (β=−0.07) and BMI area under the curve (β=−0.07) ($P<0.05$ for all); the effects of SBP measures were not significant. Adult E/A ratio was negatively associated with adulthood SBP (β=−0.13; $P<0.01$) and total area under the curve of SBP (β=−0.13; $P<0.01$). E/e′ ratio was positively associated with BMI and SBP measures. The effects of diastolic BP measures were substantially similar to those of SBP measures. Participants with LV hypertrophy, eccentric hypertrophy, and concentric hypertrophy had significantly lower LV ejection fraction and higher E/e′ ratio.

CONCLUSIONS: These observations provide strong evidence that early-life adiposity and BP levels and their life-course cumulative burdens are associated with subclinical changes in adult LV structure and function in the general population.

Key Words: blood pressure ■ body mass index ■ cardiac function ■ left ventricular hypertrophy ■ longitudinal study

Left ventricular (LV) hypertrophy (LVH) manifested as enlarged chamber and thickened walls, often accompanied by abnormal cardiac function, is an independent predictor of adverse cardiovascular events such as heart failure, ischemic heart disease, and sudden cardiac arrest.[1–3] It has been demonstrated that traditional cardiovascular risk factors are closely related to the development of LVH. Among them, obesity and hypertension are considered the most harmful determinants of LVH in the general population.[4–6] Substantial evidence from epidemiologic studies suggests the adverse effects of obesity on cardiac structure and function.[7,8] During this process, hypertension plays a key role through chronic hemodynamic burden and central pressure overload.[9] Despite preponderant evidence for the association of obesity and hypertension with LVH, the impact of increased body mass index (BMI) and elevated blood pressure

Correspondence to: Wei Chen, MD, PhD, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Room 1504G, New Orleans, LA 70112. E-mail: wchen1@tulane.edu

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.016405

For Sources of Funding and Disclosures, see pages 7 and 8.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This study provides new findings and insights into the research area of the early origins of subclinical changes in cardiac structure and function.

What Are the Clinical Implications?

- These observations have implications for developing novel prevention and intervention strategies for controlling body weight and blood pressure levels beginning in childhood to reduce the risk of cardiovascular disease in later life.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis Risk in Communities Study
ASE	American Society of Echocardiography
AUC	area under the curve
BHS	Bogalusa Heart Study
BMI	body mass index
BP	blood pressure
CARDIA	Coronary Artery Risk Development in Young Adults
CH	concentric hypertrophy
CHS	Cardiovascular Health Study
DBP	diastolic blood pressure
E/A ratio	early to late peak diastolic mitral flow velocity ratio
E/e′ ratio	ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity
EH	eccentric hypertrophy
FHS	Framingham Heart Study
LV	left ventricular
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy
LVM	left ventricular mass
LVMI	left ventricular mass index
RWT	relative wall thickness
SBP	systolic blood pressure

(BP) in early life and their long-term cumulative burden on cardiac function is unclear.

It is well known that cardiovascular disease begins in early life.[10,11] Many previous studies have shown that early-life cardiovascular risk factors are associated with LVH and LV geometric patterns.[12–15] The BHS (Bogalusa Heart Study) has previously shown that BMI and BP measured from childhood are predictors for the development of LVH.[8,12–15] Data are, however, limited on their long-lasting influence on subclinical changes in cardiac systolic and diastolic function.[3,7] The present study was designed to examine the impact of BMI and BP measured in early life and their life-course burden since childhood on alterations in adult LV structure and function utilizing a longitudinal cohort from the BHS.

METHODS

The data that support the findings of the present study are available from the corresponding authors on reasonable request.

Study Cohort

The BHS, a series of long-term epidemiologic studies in a semirural 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 and risk factors of cardiovascular disease from childhood.[16] Nine cross-sectional surveys of children aged 4 to 19 years and 12 cross-sectional surveys of adults aged 20 to 57 years who had been previously examined as children were conducted between 1973 and 2016. These repeated cross-sectional surveys have resulted in serial observations from childhood to adulthood. The present longitudinal study cohort consisted of 1108 adult patients (726 Whites and 382 Blacks; 41.9% men; mean age, 48.2 years in the last survey). These participants were examined 4 to 16 times for BMI and BP (at least 2 times in childhood and at least 2 times in adulthood) from 1973 to 2016, and echocardiographic measurements of LV structure and function were performed in the last adult survey during 2013 to 2016. The mean follow-up period of BMI and BP was 38.8 years from the first childhood to the last adult survey.

All adult patients gave informed consent for each survey. For those younger than 18 years, 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 staff members in all surveys since 1973.[16] Height and weight were measured in duplicate, and the mean values were used for analysis. BMI was calculated as weight in kilograms divided by height in meters squared. Systolic BP (SBP) and diastolic BP (DBP) were obtained using a mercury sphygmomanometer

on the right arm of patients sitting in a relaxed position by 2 trained observers (3 times each) between 8 AM and 10 AM. The mean values of the 6 readings were used for analysis of BP. For patients with hypertension (n=388) who were under antihypertensive treatment and had SBP/DBP <140/90 mm Hg, forced values (140/90 mm Hg) were assigned for measured SBP/DBP.

Echocardiographic LV Structure and Function Measurements

LV structure and function were assessed by 2-dimensional guided M-mode, Doppler and tissue Doppler echocardiography measurements with 2.25- and 3.5-MHz transducers according to American Society of Echocardiography (ASE) recommendations.[17] Parasternal long- and short-axis views were collected for measuring LV end-diastolic and end-systolic measurements in duplicate, and the mean was calculated.

LV mass (LVM) was calculated from a necropsy-validated formula on the basis of a thick-wall prolate ellipsoidal geometry.[18] To take body size into account, LVM was indexed for body height ($m^{2.7}$) as LVM index (LVMI). LV relative wall thickness (RWT) was calculated as septal wall thickness plus posterior wall thickness divided by LV end-diastolic diameter.[19] 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.[20] 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).[19–22]

LV systolic function was evaluated by LV ejection fraction (LVEF), which was calculated using the modified Simpson rule from LV end-diastolic volume and LV end-systolic volume obtained from the apical 4-chamber view based on ASE recommendations.[23] LV diastolic function was evaluated using E/A and E/e′ ratios, which were measured by pulsed-wave Doppler and pulsed-wave tissue Doppler imaging. Peak velocities of the early phase (E) and late phase (A) at the level of mitral valve leaflet tips were assessed by pulsed-wave Doppler and the E/A ratio was calculated. Using tissue Doppler imaging, early peak diastolic mitral annular velocity (e′) was measured from the average of the septal and lateral tissue velocities in the apical 4-chamber view. The E/e′ ratio was calculated as an index of LV filling pressures.[24]

Statistical Analysis

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.[25–27] In short, growth curves of BMI and BP measured multiple times from childhood to adulthood were constructed using a random-effects model by SAS proc MIXED (SAS Institute Inc.). Quadratic curves were fitted for BMI and cubic curves for SBP and DBP in race-sex groups. As shown in Figure 1, using a White man as an example, the AUCs were calculated as the integral of the curve parameters during the follow-up period for each participant. Since participants

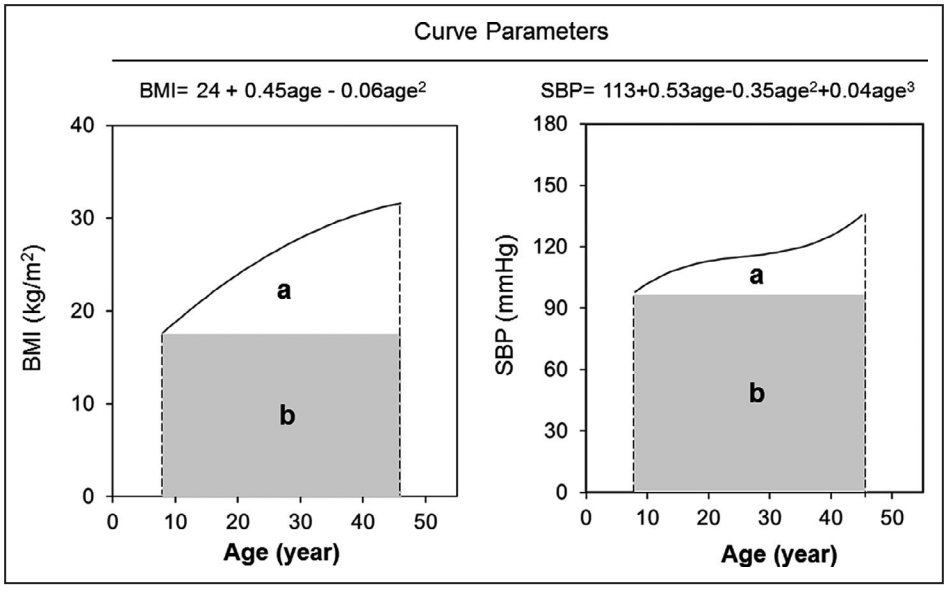

Figure 1. Illustration of the area under the curve (AUC) of body mass index (BMI) and systolic blood pressure (SBP) using a White male as an example.
a=incremental AUC; b=baseline AUC; a+b=total AUC

had different lengths of follow-up, the AUC values were divided by the number of follow-up years. The AUC measures have advantages over other conventional longitudinal analysis models in that they measure both long-term burden and trends. Total AUC can be considered a measure of a long-term cumulative burden of BMI and BP.

Multivariable linear regression analyses were performed to examine the associations of LVMI, LVEF, E/A ratio, and E/e′ ratio with BMI and BP measures, adjusted for age, race, sex, heart rate, smoking, and alcohol drinking. In the association analyses, childhood values (first measurement), adulthood values (last measurement), and total AUC values were analyzed in separate regression models. Before regression analyses, childhood and adulthood values, as well as total AUC values of BMI and BP, were adjusted for corresponding age (or average 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. For LV geometry analyses, LVH, concentric remodeling, EH, and CH were separately analyzed using normal LVM as a control group. Differences in the regression coefficients between races were tested for significance in interaction regression models by including the race-predictor interaction terms in the model.

RESULTS

Table 1 summarizes the characteristics of study variables in childhood, adulthood, and long-term measures of BMI and BP by race and sex. There were no significant differences in childhood BMI, SBP, and DBP between race and sex groups, except for DBP between White and Black males. Adult BMI showed significant race differences in women and sex differences in Blacks; Black women had the highest prevalence of obesity among the 4 groups. Adult SBP and DBP showed significant race differences in both men and women and sex differences in Whites. Race differences in total AUC of BMI, SBP and DBP were significant except for males. Adult LV structure measures, including LVM, LVMI, and RWT, had significant race (Black>White) and sex (men>women) differences. Males had significantly lower values of LVEF than females in Blacks and Whites; Black males had lower values of LVEF than White males. There were significant race and sex differences in E/e′ ratio.

Table 2 presents linear regression analyses of adult LVMI, LVEF, E/A ratio, and E/e′ ratio on BMI and SBP measures, adjusting for age, race, sex, heart rate, smoking, and alcohol drinking. Adult LVMI was significantly associated with BMI and SBP measures, with BMI showing bigger effect size than SBP in all 3 models. Childhood BMI, adulthood BMI, and AUC of BMI were significantly and negatively associated with LVEF, but SBP measures were not. Adulthood SBP and AUC of SBP were significantly and negatively associated with E/A ratio, but BMI measures were not. All BMI and SBP measures were significantly and positively associated with E/e′ ratio. Race differences in standardized regression coefficients of BMI and SBP on LV structural and functional measures were tested for significance, adjusting for covariates (Table S1). The effect of BMI did not differ significantly in all 12 models between Blacks and Whites. The race differences in the effect of SBP were significant in 6 of the 12 models. The effects of DBP measures were substantially similar to those of SBP measures (Table S2).

Figure 2 shows prevalence of LVH and remodeling patterns by race and sex. Blacks versus Whites had a significantly higher prevalence of LVH (32.5% versus 10.7%, respectively; $P<0.001$), concentric remodeling (27.5% versus 22.9%, respectively; $P<0.001$), EH (5.8% versus 3.9%, respectively; $P=0.002$), and CH (26.7% versus 6.9%, respectively; $P<0.001$). Males had significantly higher prevalence of concentric remodeling (31.2% versus 19.6%; $P<0.001$) than females.

Table 3 presents covariate-adjusted mean values of LV function measures by LVH and remodeling patterns. Compared with normal LVM, participants with LVH, EH, and CH had significantly lower LVEF and higher E/e′ ratio. E/A ratio did not differ significantly between LVH groups.

DISCUSSION

It is incontestable that obesity and hypertension are the most important risk factors related to LVH.[4–6] Previous studies have shown that higher levels of childhood BMI and BP significantly predict adult LVH.[28–30] The BHS has reported that long-term cumulative burden of excessive adiposity and elevated BP from childhood was significantly associated with LVH and LV geometric remodeling patterns.[8,12–15] However, the impact of obesity measures and BP in early life and their long-term cumulative burden on adult cardiac function has not been examined in previous studies. In addition, the changes in cardiac function measures in relation to LV geometry remodeling patterns have not been reported. Based on the longitudinal database we previously reported,[8,12–15] we took advantage of the most recent adult survey in 2013 to 2016 of the BHS to examine adult cardiac structure and function changes in relation to longitudinal BMI and BP in the current study. We found that the influence of BMI and BP levels on subclinical changes in midlife adult cardiac structure and function began in early life. Childhood

Table 1. Characteristics of Study Participants by Race and Sex

Characteristic	White		Black		*P* for Race Difference		Total
	Male (n=319)	Female (n=407)	Male (n=145)	Female (n=237)	Male	Female	
Childhood (first examination)							
Age, y	9.8 (3.5)	9.4 (3.3)	9.2 (3.2)	9.1 (3.2)	0.101	0.219	9.4 (3.3)
BMI, kg/m^2	17.5 (3.4)	17.6 (3.5)	17.2 (3.1)	17.4 (3.7)	0.706	0.859	17.5 (3.5)
SBP, mm Hg	100.2 (9.4)	99.0 (10.0)	99.7 (9.8)	98.1 (10.8)	0.734	0.604	99.2 (9.9)
DBP, mm Hg	60.4 (8.4)	60.9 (8.6)	62.0 (7.8)	60.8 (9.0)	0.003	0.565	60.9 (8.6)
Adulthood (last examination)							
Age, y	49.0 (4.9)	48.0 (5.2)*	47.6 (5.8)	47.6 (5.4)	0.005	0.343	48.2 (5.3)
BMI, kg/m^2	30.6 (6.1)	30.3 (7.5)	31.0 (8.6)	34.7 (8.8)*	0.799	<0.001	31.4 (7.8)
Obesity, No. (%)	150 (47.0)	182 (44.7)	66 (45.5)	170 (71.7)*	0.763	<0.001	568 (51.3)
SBP, mm Hg	131.3 (15.5)	125.0 (17.6)*	136.7 (15.7)	136.0 (19.4)	<0.001	<0.001	130.7 (17.8)
DBP, mm Hg	83.9 (11.7)	80.5 (12.6)*	87.5 (12.5)	87.7 (12.7)	<0.001	<0.001	60.9 (8.6)
AUC measures							
Average age, y	25.0 (5.5)	24.8 (5.3)	23.4 (5.6)	23.7 (5.2)	0.004	0.014	24.4 (5.4)
Total AUC of BMI	26.2 (4.6)	25.6 (5.8)	26.3 (5.8)	28.1 (6.7)*	0.720	<0.001	26.4 (5.7)
Total AUC of SBP	116.3 (7.7)	110.3 (7.9)*	120.9 (9.3)	116.4 (9.5)*	<0.001	<0.001	114.7 (9.2)
Total AUC of DBP	75.0 (5.9)	72.1 (5.5)*	76.8 (7.3)	75.5 (6.5)	<0.001	<0.001	74.3 (6.3)
Adulthood (last examination)							
Smokers, No. (%)	90 (28.2)	105 (25.8)	71 (49.0)	58 (24.5)*	<0.001	0.709	32.4 (29.2)
Drinkers, No. (%)	158 (49.5)	147 (36.1)*	48 (33.1)	46 (19.4)*	0.001	<0.001	399 (36.0)
HR, beats per min	69.3 (11.3)	73.4 (10.7)*	71.4 (11.3)	72.3 (12.2)	0.061	0.185	71.7 (11.4)
LVM, g	172.1 (46.6)	132.7 (45.1)*	212.3 (73.6)	158.6 (43.6)*	<0.001	<0.001	160.0 (56.2)
LVMI, g/m$^{2.7}$	36.7 (9.8)	36.0 (12.9)	46.0 (15.3)	42.5 (11.4)*	<0.001	<0.001	38.9 (12.7)
RWT, cm	0.42 (0.07)	0.40 (0.07)*	0.46 (0.09)	0.44 (0.09)*	<0.001	<0.001	0.421 (0.08)
LVEF, %	0.64 (0.04)	0.65 (0.04)*	0.61 (0.07)	0.64 (0.05)*	<0.001	0.355	0.64 (0.05)
E/A ratio	1.18 (0.32)	1.18 (0.34)	1.15 (0.36)	1.13 (0.36)	0.110	0.054	1.17 (0.34)
E/e′ ratio	6.38 (1.64)	6.62 (1.73)*	6.67 (2.16)	7.55 (2.31)*	0.029	<0.001	6.76 (1.95)

Data are expressed as mean (SD) unless otherwise indicated. AUC indicates area under the curve; DBP, diastolic blood pressure; E/A ratio, early to late peak diastolic mitral flow velocity ratio; E/e′ ratio, ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity; HR, heart rate; LVM, left ventricular mass; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; RWT, relative wall thickness; and SBP, systolic blood pressure.

Sex difference within racial groups: *P<0.05.

Obesity was defined as body mass index (BMI) ≥30 kg/m^2.

BMI, adult BMI, and the long-term cumulative burden were more closely related to LVH compared with respective BP measures. More importantly, BMI measures but not BP were inversely associated with adult cardiac systolic function measured as LVEF. Both BMI and BP measures were significantly and positively associated with diastolic function measured as E/e′ ratio. Participants with LVH, EH, and CH had significantly lower LVEF and higher E/e′ ratio compared with the normal LVM group. These observations provide strong evidence for the early-life origin of the impact of higher levels of BMI and BP on subclinical alterations in LV structure and function.

The harmful effect of obesity on LV contractility was previously reported. In the Olmsted County Heart Function Study, Ammar et al[31] found that BMI was associated with LV diastolic dysfunction measured as E/A ratio and deceleration time, but the correlation between BMI and LVEF was not significant in adults aged 45 to 96 years. Prospective longitudinal data from the CARDIA (Coronary Artery Risk Development in Young Adults) study[7] demonstrated that greater BMI was associated with higher cardiac structural indices, lower longitudinal myocardial deformation, lower E/A ratio, and higher E/e′ ratio, but was not significantly associated with LVEF in young adulthood and middle age. Participants in the present study cohort were relatively younger, and childhood BMI, adulthood BMI, and long-term BMI were found to be inversely and significantly correlated with LVEF. The inconsistent associations in this study and previous studies suggest that the relationship between obesity and subclinical changes in LV systolic function might vary by age periods.

Table 2. Standardized Regression Coefficients of BMI and SBP on LV Structure and Function Measures, Adjusting for Age, Race, Sex, Heart Rate, Smoking, and Alcohol Drinking

	Dependent Variable							
	LVMI		LVEF		E/A Ratio		E/e′ Ratio	
Independent Variable	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value	β (SE)	*P* Value
Model 1								
Childhood BMI*	0.25 (0.03)	<0.001	−0.08 (0.03)	0.017	0.01 (0.03)	0.857	0.10 (0.03)	0.002
Childhood SBP*	0.07 (0.03)	0.028	0.02 (0.03)	0.564	−0.04 (0.03)	0.217	0.12 (0.03)	<0.001
Model 2								
Adulthood BMI†	0.37 (0.03)	<0.001	−0.07 (0.03)	0.023	−0.05 (0.03)	0.063	0.19 (0.03)	<0.001
Adulthood SBP†	0.21 (0.03)	<0.001	0.01 (0.03)	0.701	−0.13 (0.03)	<0.001	0.26 (0.03)	<0.001
Model 3								
Total AUC of BMI‡	0.36 (0.03)	<0.001	−0.07 (0.03)	0.044	0.002 (0.03)	0.954	0.16 (0.03)	<0.001
Total AUC of SBP‡	0.19 (0.03)	<0.001	−0.05 (0.03)	0.089	−0.13 (0.03)	<0.001	0.19 (0.03)	<0.001

AUC indicates area under the curve; β, standardized regression coefficient; BMI, body mass index; E/A ratio, early to late peak diastolic mitral flow velocity ratio; E/e′ ratio, ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity; LV, left ventricular; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; SBP, systolic blood pressure; and SE, standard error.

*Adjusted for childhood age and then *Z*-transformed (mean, 0; SD, 1).

†*Z*-transformed (mean, 0; SD, 1).

‡Adjusted for average age and then *Z*-transformed (mean, 0; SD, 1).

Clinical and epidemiological studies have documented the role of hypertension in the development of LVH through chronic hemodynamic overload and increased central pressure.[5,8,9,15] The current study found that childhood BP, adulthood BP, and the lifelong burden of BP levels all significantly predicted midlife LVH and LV geometric patterns, with adjustment for BMI. In addition, these BP measures were all significantly and positively associated with cardiac diastolic function measured as E/e` ratio, but not with systolic function measured as LVEF. These observations are consistent with other large population studies.[32,33] Elevated BP levels were not correlated with LVEF in the CARDIA study.[32] In the FHS (Framingham Heart

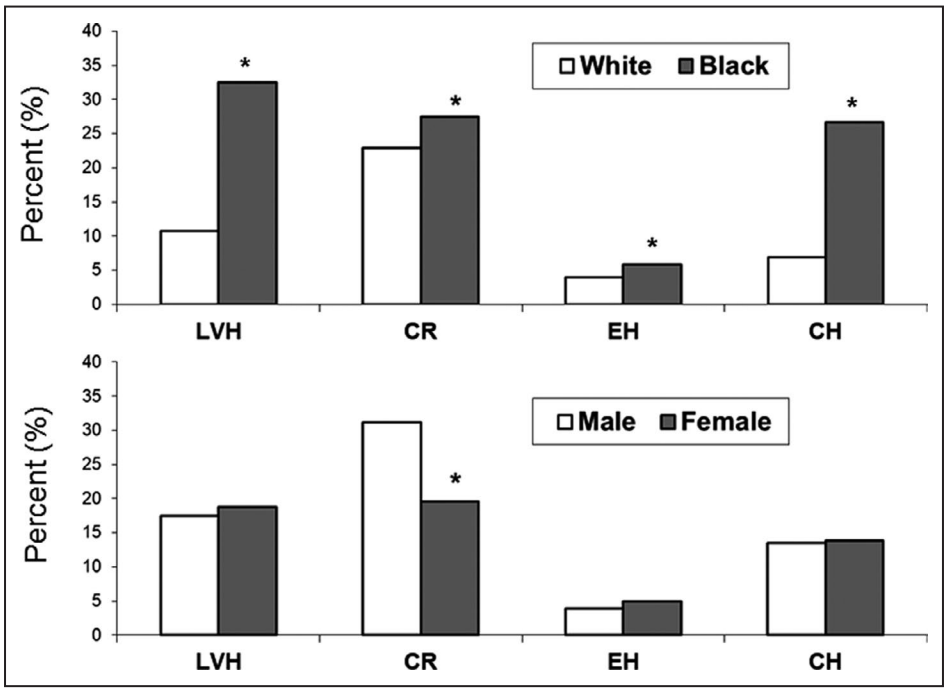

Figure 2. Prevalence of left ventricular hypertrophy (LVH) and geometric remodeling patterns by race and sex.

*P<0.001 for group difference. CH indicates concentric hypertrophy; CR, concentric remodeling; and EH, eccentric hypertrophy.

Table 3. Covariate-Adjusted LV Function Measures by LVH and Remodeling Patterns

	LV Functional Measures		
	LVEF	E/A Ratio	E/e′ Ratio
LVH (n=202)	0.623	1.195	7.680
Normal LVM (n=635)	0.641	1.157	6.493
P value	<0.001	0.199	<0.001
CR (n=271)	0.643	1.158	6.557
Normal LVM (n=635)	0.641	1.189	6.383
P value	0.548	0.174	0.133
EH (n=50)	0.604	1.232	7.885
Normal LVM (n=635)	0.642	1.208	6.369
P value	<0.001	0.616	<0.001
CH (n=152)	0.628	1.144	7.499
Normal LVM (n=635)	0.642	1.196	6.477
P value	0.005	0.118	<0.001

CH indicates concentric hypertrophy; CR, concentric remodeling; EH, eccentric hypertrophy; E/A ratio, early to late peak diastolic mitral flow velocity ratio; E/e′ ratio, ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity; LV, left ventricular; LVH, left ventricular hypertrophy; LVEF, left ventricular ejection fraction; and LVM, left ventricular mass.

Covariates included age, race, sex, heart rate, smoking, alcohol drinking, body mass index, and systolic blood pressure.

Study), Kaess et al[33] found that BP was related to diastolic function measured as E/e` but not to systolic function measured as LV fractional shortening. These findings indicate that the influence of hypertension on diastolic function occurs earlier than its influence on systolic function in the general population.

E/e` ratio and E/A ratio are the most commonly used indices of cardiac diastolic function. The relationship between a higher E/e` ratio and severity of diastolic dysfunction is linear. However, E/A ratio declines in the early stages of impaired diastolic function and then goes up during the development of heart failure.[34,35] We found that LVH, EH, and CH groups had significantly lower LVEF and higher E/e′ ratio compared with the normal LVM group. CHS (Cardiovascular Health Study)[3] reported that increased LVM was a risk factor for the development of a depressed LVEF. Fox et al[36] found that EH was related to systolic dysfunction, and CH was related to diastolic dysfunction in the Jackson cohort of ARIC (Atherosclerosis Risk in Communities Study). Compared with the normal LVM group, the EH group showed greater differences in LVEF and E/e′ ratio than the CH group in the present study cohort. It appears that EH is more important for reduced cardiac function. Further studies are needed to confirm the findings in this regard.

This community-based longitudinal cohort provides a unique opportunity to examine the impact of obesity and elevated BP from childhood on adult LV structure and function. There were a few limitations in this study. First, patients with hypertension taking pharmacological treatment represent a subgroup that would be expected to have the highest BP levels without treatment; the forced values of 140/90 mm Hg assigned to the measured SBP/DBP for these patients with hypertension would result in some bias in the association analyses. In particular, this adjustment method of BP would amplify the bias by comparing the effect of BMI with BP. Second, LVH and LV function can be reversed by long-term antihypertensive treatment. However, this effect cannot be assessed without the progression data of LV measurements in this study. Third, Bogalusa is a semirural biracial (65% White and 35% Black) community. Adult obesity (51.3%) is more prevalent in Bogalusa than in other areas. Generalizing the findings of the current study to other populations should be done cautiously.

CONCLUSIONS

We demonstrated that the impact of increased levels of BMI and BP and their life-long burden measures on cardiac structure and function began in early life, and BMI measures were more closely related to LVH compared with BP measures. Furthermore, BMI measures were inversely associated with adult cardiac systolic function measured as LVEF, whereas BP measures were more strongly associated with diastolic function measured as E/e′ ratio compared with BMI. Participants with LVH, EH, and CH have worse systolic and diastolic function than the normal LVM group. These observations provide strong evidence for the long-lasting influence of adiposity and BP levels on subclinical changes in cardiac structure and function in asymptomatic adults in the general population.

ARTICLE INFORMATION

Received February 26, 2020; accepted June 2, 2020.

Affiliations

From the Department of Cardiology, The First Affiliated Hospital of Soochow University, Suzhou, China (Y.L., T.J.), Department of Epidemiology, Tulane University, School of Public Health and Tropical Medicine, New Orleans, LA (Y.L., Y.Y., Y.G., C.F., R.B., L.B., J.H., W.C.); Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China (Y.Y.); and Children's Minnesota Research Institute, Children's Hospitals and Clinics of Minnesota, Minneapolis, MN (S.L.).

Acknowledgments

The BHS is a joint effort of many investigators and staff members whose contribution is gratefully acknowledged. Author contributions: Y.L., Y.Y., and W.C. generated the hypothesis, performed statistical analyses, and wrote the article. T.J., S.L., Y.G., C.F., R.B., L.B., J.H., and W.C. contributed to field activities, data collection, analytic strategy, and article editing.

Sources of Funding

This study was supported by grants R01HL121230 from the National Heart, Lung, and Blood Institute; R03AG060619 from the National Institute on Aging; and P20GM109036 from the National Institute of General Medical Sciences of the National Institutes of Health. Liu was supported by a research training grant (D43TW009107) from the Fogarty International Center of the National Institutes of Health, Bethesda, Maryland.

Disclosures

None.

Supplementary Materials

Tables S1–S2.

REFERENCES

1. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med*. 1990;322:1561–1566.
2. Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann Intern Med*. 1991;114:345–352.
3. Drazner MH, Rame JE, Marino EK, Gottdiener JS, Kitzman DW, Gardin JM, Manolio TA, Dries DL, Siscovick DS. Increased left ventricular mass is a risk factor for the development of a depressed left ventricular ejection fraction within five years: the Cardiovascular Health Study. *J Am Coll Cardiol*. 2004;43:2207–2215.
4. Cuspidi C, Rescaldani M, Sala C, Grassi G. Left-ventricular hypertrophy and obesity: a systematic review and meta-analysis of echocardiographic studies. *J Hypertens*. 2014;32:16–25.
5. Cuspidi C, Sala C, Negri F, Mancia G, Morganti A. Prevalence of left-ventricular hypertrophy in hypertension: an updated review of echocardiographic studies. *J Hum Hypertens*. 2012;26:343–349.
6. Lauer MS, Anderson KM, Levy D. Separate and joint influences of obesity and mild hypertension on left ventricular mass and geometry: the Framingham Heart Study. *J Am Coll Cardiol*. 1992;19:130–134.
7. Kishi S, Armstrong AC, Gidding SS, Colangelo LA, Venkatesh BA, Jacobs DR, Carr JJ, Terry JG, Liu K, Goff DC, et al. Association of obesity in early adulthood and middle age with incipient left ventricular dysfunction and structural remodeling: the CARDIA study (Coronary Artery Risk Development in Young Adults). *JACC Heart Failure*. 2014;2:500–508.
8. Lai CC, Sun D, Cen R, Wang J, Li S, Fernandez-Alonso C, Chen W, Srinivasan SR, Berenson GS. Impact of long-term burden of excessive adiposity and elevated blood pressure from childhood on adulthood left ventricular remodeling patterns: the Bogalusa Heart Study. *J Am Coll Cardiol*. 2014;64:1580–1587.
9. Lorell BH, Carabello BA. Left ventricular hypertrophy: pathogenesis, detection, and prognosis. *Circulation*. 2000;102:470–479.
10. Dwyer T, Sun C, Magnussen CG, Raitakari OT, Schork NJ, Venn A, Burns TL, Juonala M, Steinberger J, Sinaiko AR, et al. Cohort Profile: the international childhood cardiovascular cohort (i3C) consortium. *Int J Epidemiol*. 2013;42:86–96.
11. Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, Ben-Ami Shor D, Tzur D, Afek A, Shamiss A, et al. Body-mass index in 2.3 million adolescents and cardiovascular death in adulthood. *N Engl J Med*. 2016;374:2430–2440.
12. Urbina EM, Gidding SS, Bao W, Pickoff AS, Berdusis K, Berenson GS. Effect of body size, ponderosity, and blood pressure on left ventricular growth in children and young adults in the Bogalusa Heart Study. *Circulation*. 1995;91:2400–2406.
13. Li X, Li S, Ulusoy E, Chen W, Srinivasan SR, Berenson GS. Childhood adiposity as a predictor of cardiac mass in adulthood: the Bogalusa Heart Study. *Circulation*. 2004;110:3488–3492.
14. Toprak A, Wang H, Chen W, Paul T, Srinivasan S, Berenson G. Relation of childhood risk factors to left ventricular hypertrophy (eccentric or concentric) in relatively young adulthood (from the Bogalusa Heart Study). *Am J Cardiol*. 2008;101:1621–1625.
15. Zhang H, Zhang T, Li S, Guo Y, Shen W, Fernandez C, Harville E, Bazzano LA, Urbina EM, He J, et al. Long-term excessive body weight and adult left ventricular hypertrophy are linked through later-life body size and blood pressure: the Bogalusa Heart Study. *Circ Res*. 2017;120:1614–1621.
16. Berenson GS, McMahan CA, Voors AW, Webber LS, Srinivasan SR, Frank GC, Foster TA, Blonde CV. *Cardiovascular risk factors in children: The early natural history of atherosclerosis and essential hypertension*. New York, NY: Oxford University Press; 1980:47–123.
17. Sahn DJ, DeMaria AN, Kisslo JO, Weyman AF. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation*. 1978;58:1072–1083.
18. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol*. 1986;57:450–458.
19. Foppa M, Duncan BB, Rohde LE. Echocardiography-based left ventricular mass estimation. How should we define hypertrophy? *Cardiovasc Ultrasound*. 2005;3:17.
20. De Simone G, Kitzman DW, Chinali M, Oberman A, Hopkins PN, Rao DC, Arnett DK, Devereux RB. Left ventricular concentric geometry is associated with impaired relaxation in hypertension: the HyperGEN Study. *Eur Heart J*. 2005;26:1039–1045.
21. Ganau A, Devereux RB, Roman MJ, De Simone G, Pickering TG, Saba PS, Vargiu P, Simongini I, Laragh JH. Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J Am Coll Cardiol*. 1992;19:1550–1558.
22. Toprak A, Reddy J, Chen W, Srinivasan S, Berenson G. Relation of pulse pressure and arterial stiffness to concentric left ventricular hypertrophy in young men (from the Bogalusa Heart Study). *Am J Cardiol*. 2009;103:978–984.
23. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005;18:1440–1463.
24. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur J Echocardiogr*. 2016;17:1321–1360.
25. Chen W, Li S, Cook NR, Rosner BA, Srinivasan SR, Boerwinkle E, Berenson GS. An autosomal genome scan for loci influencing longitudinal burden of body mass index from childhood to young adulthood in white sibships: The Bogalusa Heart Study. *Int J Obes*. 2004;28:462–469.
26. Cook NR, Rosner BA, Chen W, Srinivasan SR, Berenson GS. Using the area under the curve to reduce measurement error in predicting young adult blood pressure from childhood measures. *Stat Med*. 2004;23:3421–3435.
27. Chen W, Li S, Srinivasan SR, Boerwinkle E, Berenson GS. Autosomal genome scan for loci linked to blood pressure levels and trends since childhood: the Bogalusa Heart Study. *Hypertension*. 2005;45:954–959.
28. Hanevold C, Waller J, Daniels S, Portman R, Sorof J. The effects of obesity, gender, and ethnic group on left ventricular hypertrophy and geometry in hypertensive children: a collaborative study of the International Pediatric Hypertension Association. *Pediatrics*. 2004;113:328–333.
29. Daniels SR, Loggie JM, Khoury P, Kimball TR. Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. *Circulation*. 1998;97:1907–1911.
30. Dhuper S, Abdullah RA, Weichbrod L, Mahdi E, Cohen HW. Association of obesity and hypertension with left ventricular geometry and function in children and adolescents. *Obesity*. 2011;19:128–133.
31. Ammar KA, Redfield MM, Mahoney DW, Johnson M, Jacobsen SJ, Rodeheffer RJ. Central obesity: association with left ventricular dysfunction and mortality in the community. *Am Heart J*. 2008;156:975–981.
32. Flack JM, Gardin JM, Yunis C, Liu K,CARDIA Research Group. Static and pulsatile blood pressure correlates of left ventricular structure and function in black and white young adults: the CARDIA study. *Am Heart J*. 1999;138:856–864.
33. Kaess BM, Rong J, Larson MG, Hamburg NM, Vita JA, Cheng S, Aragam J, Levy D, Benjamin EJ, Vasan RS, et al. Relations of central hemodynamics and aortic stiffness with left ventricular structure and function: the Framingham Heart Study. *J Am Heart Assoc*. 2016;5:e002693.
34. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. *J Am Coll Cardiol*. 1997;30:8–18.
35. Mottram PM, Marwick TH. Assessment of diastolic function: what the general cardiologist needs to know. *Heart*. 2005;91:681–695.
36. Fox ER, Taylor J, Taylor H, Han H, Samdarshi T, Arnett D, Myerson M. Left ventricular geometric patterns in the Jackson cohort of the Atherosclerotic Risk in Communities (ARIC) Study: clinical correlates and influences on systolic and diastolic dysfunction. *Am Heart J*. 2007;153:238–244.

SUPPLEMENTAL MATERIAL

Table S1. Standardized regression coefficients of BMI and SBP on LV structure and function measures by race (whites/blacks), adjusting for age, sex, heart rate, smoking and alcohol drinking.

Independent Variable	Dependent Variable							
	LVMI		LVEF		E/A ratio		E/e' ratio	
	White/Black	P*	White/Black	P*	White/Black	P*	White/Black	P*
Model 1								
Childhood BMI*	0.24/0.30,	0.088	-0.09/-0.07,	0.822	0.02/0.002,	0.805	0.11/0.11,	0.499
Childhood SBP*	0.06/0.09,	0.467	0.04/0.002,	0.627	-0.09/0.04,	0.026	0.11/0.15,	0.201
Model 2								
Adulthood BMI †	0.39/0.42,	0.234	-0.09/-0.09,	0.667	-0.09/0.01,	0.100	0.22/0.15,	0.526
Adulthood SBP †	0.16/0.28,	0.002	0.07/-0.07,	0.003	-0.13/-0.13,	0.928	0.21/0.31,	0.011
Model 3								
Total AUC of BMI ‡	0.36/0.39,	0.656	-0.08/-0.05,	0.694	-0.03/0.05,	0.219	0.19/0.15,	0.965
Total AUC of SBP ‡	0.15/0.26,	0.028	-0.002/-0.12,	0.015	-0.14/-0.11,	0.605	0.16/0.24,	0.056

* P-values for race difference

LVMI= left ventricular mass index; LVEF=left ventricular ejection fraction; E/A ratio=early to late peak diastolic mitral flow velocity ratio; E/e' ratio=ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity; BMI=body mass index; SBP=systolic blood pressure; AUC=area under the curve

*, adjusted for childhood age and then Z-transformed (mean=0, SD=1)

†, Z-transformed (mean=0, SD=1)

‡, adjusted for average age and then Z-transformed (mean=0, SD=1)

Table S2. Standardized regression coefficients of BMI and DBP on LV structure and function, adjusting for age, race, sex, smoking and alcohol drinking.

Independent Variable	Dependent Variable							
	LVMI		LVEF		E/A ratio		E/e' ratio	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
Model 1								
Childhood BMI*	0.27(0.03)	<0.001	-0.07(0.03)	0.017	0.02(0.03)	0.471	0.12(0.03)	<0.001
Childhood DBP*	0.03(0.03)	0.257	0.01(0.03)	0.636	-0.10(0.03)	<0.001	0.09(0.03)	0.003
Model 2								
Adulthood BMI†	0.38(0.03)	<0.001	-0.07(0.03)	0.022	-0.02(0.03)	0.399	0.19(0.03)	<0.001
Adulthood DBP†	0.16(0.03)	<0.001	0.02(0.03)	0.622	-0.19(0.03)	<0.001	0.19(0.03)	<0.001
Model 3								
Total AUC of BMI‡	0.38(0.03)	<0.001	-0.06(0.03)	0.069	0.02(0.03)	0.506	0.17(0.03)	<0.001
Total AUC of DBP‡	0.15(0.03)	<0.001	-0.08(0.03)	0.011	-0.19(0.03)	<0.001	0.17(0.03)	<0.001

LVMI= left ventricular mass index; LVEF=left ventricular ejection fraction; E/A ratio=early to late peak diastolic mitral flow velocity ratio; E/e' ratio=ratio of early peak diastolic mitral velocity/peak early diastolic mitral annular velocity; BMI=body mass index; DBP=diastolic blood pressure; AUC=area under the curve; β=standardized regression coefficient; SE=standard error

*, adjusted for childhood age and then Z-transformed (mean=0, SD=1)

†, Z-transformed (mean=0, SD=1)

‡, adjusted for average age and then Z-transformed (mean=0, SD=1)