ORIGINAL RESEARCH

Clinical Correlates and Prognostic Significance of Change in Standardized Left Ventricular Mass in a Community-Based Cohort of African Americans

Ervin R. Fox, MD, MPH;* Solomon K. Musani, PhD;* Tandaw E. Samdarshi, MD, MPH; Jared K. Taylor, MD; Walter L. Beard, MD; Daniel F. Sarpong, PhD; Vanessa Xanthakis, PhD; Eric E. McClendon, MD, PhD; Philip R. Liebson, MD; Thomas N. Skelton, MD; Kenneth R. Butler, PhD; Thomas H. Mosley, PhD; Herman Taylor, MD, MPH; Ramachandran S. Vasan, MD, DM*

***Background*—**Though left ventricular mass (LVM) predicts cardiovascular events (CVD) and mortality in African Americans, limited data exists on factors contributing to change in LVM and its prognostic significance. We hypothesized that baseline blood pressure (BP) and body mass index (BMI) and change in these variables over time are associated with longitudinal increases in LVM and that such increase is associated with greater incidence of CVD.

***Methods and Results*—**We investigated the clinical correlates of change in standardized logarithmically transformed-LVM indexed to height2.7 (log-LVMI) and its association with incident CVD in 606 African Americans (mean age 58±6 years, 66% women) who attended serial examinations 8 years apart. Log-LVMI and clinical covariates were standardized within sex to obtain z scores for both visits. Standardized log-LVMI was modeled using linear regression (correlates of change in standardized log-LVMI) and Cox proportional hazards regression (incidence of CVD [defined as coronary heart disease, stroke, heart failure and intermittent claudication]). Baseline clinical correlates (standardized log-LVM, BMI, systolic BP) and change in systolic BP over time were significantly associated with 8-year change in standardized log-LVMI. In prospective analysis, change in standardized LVM was significantly (P=0.0011) associated with incident CVD (hazards ratio per unit standard deviation change log-LVMI 1.51, 95% CI 1.18 to 1.93).

***Conclusions*—**In our community-based sample of African Americans, baseline BMI and BP, and change in BP on follow-up were key determinants of increase in standardized log-LVMI, which in turn carried an adverse prognosis, underscoring the need for greater control of BP and weight in this group. **(*J Am Heart Assoc*. 2015;4:e001224 doi: 10.1161/JAHA.114.001224)**

Key Words: African Americans • blood pressure • cardiovascular disease • cardiovascular events • left ventricular mass risk factors

Cardiac structure as determined by echocardiography, is a powerful independent predictor for cardiovascular disease (CVD), morbidity, and mortality in African Americans, including in the high-risk Jackson cohort of the Atherosclerosis Risks in Communities (ARIC) Study.[1–4] This is of particular concern given the higher prevalence of cardiac hypertrophy (elevated left ventricular mass [LVM]) in African Americans compared with non-Hispanic white Americans.[5,6] It is unclear what factors contribute to the longitudinal progression of LVM in African Americans and if such progression of LV mass confers a greater risk of CVD events. Limited data suggest that change in body mass index (BMI) and blood pressure (BP) are key determinants of longitudinal changes in LVM over a 20-year period in the young biracial Coronary Artery Risk Development in Young Adults (CARDIA) Study.[7] It is unclear if the same factors are important in middle-aged adult African Americans or in the short-run (less than 20 years duration). On a parallel note, data from the Losartan Intervention for Endpoint Reduction in Hypertension randomized trial indicate that regression of LVM in treated hypertensive subjects is associated with improved CVD prognosis.[8,9] However, the prognostic significance of change

From the University of Mississippi Medical Center, Jackson, MS (E.R.F., S.K.M., T.E.S., J.K.T., W.L.B., T.N.S., K.R.B., T.H.M., H.T.); Jackson State University, Jackson, MS (D.F.S.); Boston University School of Medicine, Boston, MA (V.X.); Wake Forest University, Winston-Salem, NC (E.M.); Rush University Medical Center, Chicago, IL (P.R.L.); Boston University School of Medicine, Boston, MA (R.S.V.).

The editors had no role in the evaluation of this manuscript or in the decision about its acceptance. This manuscript was handled independently by Viola Vaccarino, MD, PhD, as a guest editor.

*Dr Fox, Dr Musani, and Dr Vasan contributed equally to this article.

Correspondence to: Ervin R. Fox, MD, MPH, FACC, Department of Medicine, Division of Cardiovascular Diseases, University of Mississippi Medical Center, 2500 North State Street, Jackson, MS 39216. E-mail: efox@umc.edu

Received July 18, 2014; accepted November 19, 2014.

in LVM in community-dwelling middle-aged African Americans remains unknown. The Jackson cohort of ARIC and the Jackson Heart Study provide a unique opportunity to study these questions. We hypothesized that greater BMI, BP, and increase in these variables over time are associated with longitudinal increase in LVM over time, and that this change in LVM portends an adverse prognosis in middle-aged African Americans.

Methods

The study population consisted of participants who were members of both the Jackson cohort of the Atherosclerosis Risk in Communities Study (ARIC) and the Jackson Heart Study. The ARIC Study is a prospective cohort study that was initiated in 1987 and focused on identifying the distribution and determinants of cardiovascular vascular disease (CVD) risk factors and events in 4 US communities (Forsyth County, North Carolina, Minneapolis, MN, Washington County, MD, and Jackson, MS).[10] Echocardiograms were performed in the Jackson (all African American) cohort at Exam 3 between 1993 and 1996. The Jackson Heart Study initiated in 2000 as an extension and expansion of the original Jackson cohort of the ARIC study. A total of 5301 participants were recruited, of which approximately 30% were surviving members of the Jackson cohort of ARIC.[11] Echocardiograms were performed at Examination one of the Jackson Heart Study between 2000 and 2004.

Participants were eligible for the current investigation if they received a transthoracic echocardiogram at both the examinations and had available data on key covariates (N=609). After excluding participants with previous myocardial infarction (MI) and missing covariates (n=3), 606 participants (67% women) were eligible for the present investigation. Informed consent was obtained and the research protocol was approved by the institutional review board of the Mississippi Medical Center for both the ARIC study and the Jackson Heart Study.

Covariates

For the current study, clinical covariates used in the analysis included age, sex, BMI, and systolic BP while lifestyle factors included education level, smoking status, heavy alcohol drinking, and physical activity. Covariate data was obtained both at the baseline and at the follow-up examinations. Changes in continuous covariates between baseline and follow-up were included in the analysis assessing change in LVM.

BMI was defined as the weight divided by the height in meters squared (kg/m^2). Daily alcohol consumption were assessed by the validated food frequency questionnaires[12] and participants were defined as alcohol drinkers if they drank more than 14 drinks per week (men) or more than 7 drinks per week in women. Physical activity index was based on answers to questions related to exercise, sports, and recreational activities during interviews at annual follow-up.[13] Educational level was dichotomized for this study as either: (1) no high school degree or (2) high school/GED or higher. Smoking status was determined on interview and for this investigation classified as a dichotomous variable (current smoker—yes/no).

BP among treated hypertensive participants was imputed by adding 10 mm Hg to systolic BP and 5 mm Hg to diastolic BP to account for treatment.[14]

Echocardiographic Variables

In the ARIC study 2D, M-mode echocardiograms were performed by trained sonographers using the Acuson 128XP/10c equipped with 2.5, 3.5, and 5.0 MHz transducers. Reading of the echocardiogram was performed by one experienced cardiologist (T. N.S.). The intra- and inter-sonographer correlation of M-mode LVM was 0.94 and 0.82, respectively. The intra-reader correlation of M-mode LVM was 0.98.[15]

In the Jackson Heart Study echocardiograms were performed by 4 experienced sonographers using an HP 4500 (Hewlett Packard, Andover, MA) equipped with a 2.5 MHz transducer. Reading was performed by one experienced cardiologist with level III training in echocardiography (TES).[16] For quality control, comparisons of readings were performed with outside expert readers (PL). For the M-Mode measurements of LVM index, the correlation coefficient between readers was 0.70.

For the study, LVM was calculated using the American Society of Echocardiography corrected formula by Devereux[17] as follows:

$$\text{LVM (g)} = 0.8 \times 1.04[(\text{LV end diastolic diameter} + \text{IVST} + \text{PWT})^3 - (\text{LVIDD})^3] + 0.6$$

where IVST is interventricular septal wall thickness in diastole, PWT is posterior wall thickness in diastole, and LVIDD is left ventricular internal diameter in diastole. LVM was indexed to $\text{height}^{2.7}$ (LVMI) to adjust for body habitus.[18]

Cardiovascular Events

For this study, presence of a CVD event was defined as the first occurrence of any of these 4 major CVD outcomes (MI, fatal coronary heart disease [CHD], congestive heart failure, and stroke) or any of the 2 non-major outcomes (incident

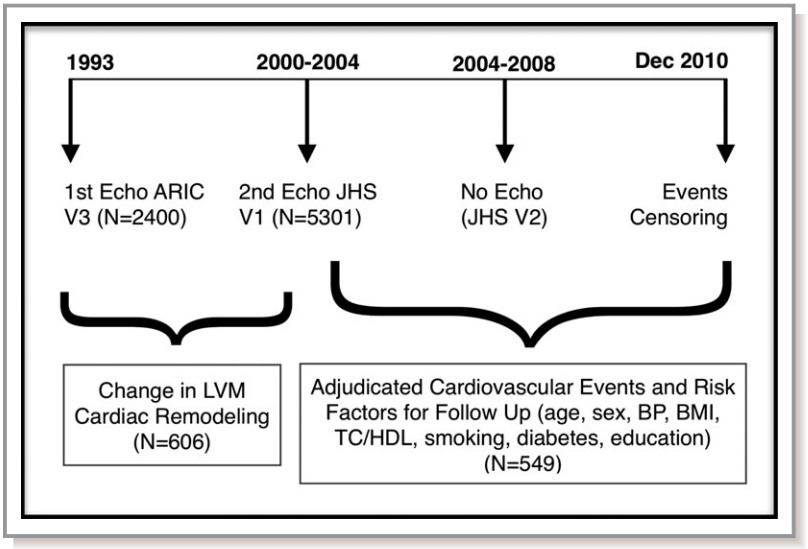

Figure. Time line for cardiac remodeling and cardiovascular events. ARIC indicates Atherorsclerosis Risk in Communities Study; BMI, body mass index; BP, blood pressure; JHS, Jackson Heart Study; LVM, left ventricular mass; TC/HDL, total cholesterol to high density lipid ratio; V1, visit one; V2, visit two; V3, visit three.

angina or intermittent claudication) between the date of the second echocardiogram and 2010. (See Figure) Individuals with history CVD between 1993 and the second echocardiogram (n=41) were excluded from this analysis.

Incident MI, fatal CHD, congestive heart failure, and stroke were determined through adjudication, while intermittent claudication and incident angina were determined from records on annual follow-up.

Annual follow-up records on Rose angina and intermittent claudication questionnaires were used to determine incidence of these events.

Cardiac remodeling was defined as change in standardized log indexed LVM between baseline and follow-up echocardiogram (see Figure).

Statistical Analysis

We constructed multivariable linear regression models to describe the relationship between baseline and follow-up LVM while adjusting for relevant baseline clinical correlates (age, gender systolic and diastolic BP, BMI) and lifestyle factors (ie, education, drinking, sports index, and smoking). Changes in continuous clinical correlates only between baseline and the follow-up cycle were also included in the model. Due to the skewed distribution, we log-transformed and standardized LVMI within sex to obtain z scores. All continuous clinical correlates were also converted into z scores before analysis. The standardization of LVMI (and other covariates) facilitates the assessment of change in LVMI without errors introduced by change in echocardiographic instrumentation and readers over time, and the logarithmic transformation renders similar standard deviations of LVMI for men versus women.[19] In additional analyses, we used log-LVMI and standardized within sex in a Cox proportional model to predict the first major cardiovascular events after confirming the assumption of proportionality of hazards. For these analyses (of incident

Table 1. Characteristics of the Study Sample Population

Covariates	Baseline Exam	Follow Up Exam*
Clinical correlates		
Age, y	58±6	66±5
Body mass index, kg/m^2	29.9±5.7	30.5±6.2
Systolic blood pressure, mm Hg	143±24	138±19
Diastolic blood pressure, mm Hg	85±13	80±10
z-log LVMI	0±1	0±1
Anti-hypertensive therapy, %	47.5	67.4
Hypertension status, %	46.9	77.2
Diabetes status, %	10.2	21.4
Lifestyle factors		
Education, %		
<High school	31	30
High school/GED or higher	69	70
Sports index	2.36±0.75	2.03±1.23
Heavy alcohol drinking, %	28.9	32.5
Current smoking, %	14	8

GED indicates general education degree; LVMI, left ventricular mass index.
*The mean follow up period was 9.3±1.9 years (median follow-up=10 years).

Table 2. Comparison of Clinical Correlates in those With LVM at Both Baseline and Follow-up Exams

	Participants With LVM at Baseline and Follow-up (N=606) Mean±SD or %	Participants Without LVM at Baseline and Follow-up (N=775) Mean±SD or %	*P* Value
Age, y			
Baseline exam	58.4 (57.9, 58.8)	59.3 (58.9, 59.7)	0.0015
Follow up exam	65.8 (65.3, 66.2)	66.6 (66.2, 67.0)	0.0040
Body mass index, kg/m^2			
Baseline exam	29.9 (29.4, 30.4)	30.8 (30.4, 31.3)	0.0031
Follow up exam	30.5 (30.0, 31.0)	31.8 (31.3, 32.2)	0.0005
Standardized LVM			
Baseline exam	3.49 (3.41, 3.57)	3.53 (3.43, 3.62)	0.58
Follow up exam	3.69 (3.61, 3.77)	3.80 (3.62, 3.98)	0.24
Systolic blood pressure, mm Hg			
Baseline exam	139 (137, 140)	138 (137, 140)	0.85
Follow up exam	131 (129, 1.32)	129 (127, 131)	0.28
Education, %			
Baseline exam			
<High school	31	36	
High school/GED or higher	69	64	0.16
Follow up exam			
<High school	30	33	
High school/GED or higher	70	67	0.36
Heavy alcohol intake			
Baseline exam	0.29 (0.25, 0.33)	0.28 (0.25, 0.32)	0.80
Follow up exam	2.21 (1.49, 2.93)	2.95 (2.08, 2.82)	0.21
Sport index			
Baseline exam	2.36 (2.30, 2.42)	2.31 (2.26, 2.36)	0.18
Follow up exam	2.02 (1.92, 2.13)	1.90 (1.82, 1.99)	0.07

Assoc. indicates associate; GED, general education degree; LVM, left ventricular mass.

CVD), covariates were defined at JHS examination 1 (with the exception of change in log-LVMI), and included age, sex, smoking, total cholesterol/HDL cholesterol ratio, and diabetes. We explored the structure of the relation between CVD events and log-LVMI by the use of regression cubic splines. For all statistical analyses we used SAS® software (SAS, 2005).

Results

The study sample consisted of 606 African-American participants (mean age at baseline 58±6 years, 66% women). Table 1 displays the characteristics of our study sample at baseline and at the follow-up examination, an average of 9.3±1.9 years apart (median follow-up=10 years). Participants without an echocardiogram at either or both examinations (and therefore excluded from our investigation) tended to be significantly older and had higher BMI. The other clinical correlates and lifestyle factors were not significantly different (Table 2).

Sex-specific characteristics of the study sample are displayed in Table 3. We observed significant bivariate age-adjusted Spearman's correlations of follow-up standardized log-LVMI with baseline standardized log-LVMI ($P<0.0001$), BMI ($P<0.0001$), systolic BP ($P=0.0003$), and education ($P=0.0001$) (Table 4). Education was inversely correlated to change in standardized log-LVMI whereas the other correlates were directly related. The highest correlation was with baseline standardized log-LVMI.

Correlates of 8-Year Change in LVMI

As presented in Table 5, 3 of the baseline clinical correlates (standardized log-LVMI, BMI, and systolic BP) and change in

Table 3. Sex Specific Summary Statistics of Sample Participants

	Women (N=401)		Men (N=205)	
	Mean	Std Dev	Mean	Std Dev
Age, y	58	5	58	6
Baseline body mass index, kg/m^2	30.8	6.2	28.1	4.3
Follow-up body mass index, kg/m^2	31.5	6.5	28.5	5.2
8 Year delta body mass index, kg/m^2	0.73	2.54	0.47	3.3
Baseline weight, kg	82.1	18.1	86.6	14.5
Follow-up weight, kg	84.3	18.1	88.5	16.8
8 Year delta weight, kg	2.35	7.80	1.59	10.48
Baseline systolic blood pressure, mm Hg	142	25.9	146	21
Follow-up systolic blood pressure, mm Hg	139	19	138	19
8 Year delta systolic blood pressure, mm Hg	−3.2	25.9	−8.1	20.3
Baseline diastolic blood pressure, mm Hg	83.5	13.4	86.6	11.0
Follow-up diastolic blood pressure, mm Hg	79.6	9.6	81.5	10.8
Baseline heavy alcohol use, %	22		43	
Follow-up alcohol use, %	26		47	
Baseline sport index	2.29	0.71	2.52	0.80
Follow-up sport index	2.03	1.23	2.01	1.24
Baseline cigarette smoking, %	11		21	
Follow-up cigarette smoking, %	6		13	
Education (baseline|follow-up)				
<High school, %	29.7|33.2		27.9|34.2	
High school/GED or higher	70.3|66.8		72.1|65.8	

GED indicates general education degree; Std Dev, standard deviation.

systolic BP were significantly associated with an 8-year change in standardized log-LVMI. Of the lifestyle factors, education only showed a significant (P=0.0267) association with LVM on follow-up. Overall, baseline standardized log-LVMI explained 16% of the inter-individual variation in LVM on follow-up.

Association of 8-Year Change in Standardized LVM With Incidence of CVD

During the 10-year study period, there were 81 CVD events (50 of which occurred in women). Among the CVD events, 21 were strokes, 20 were myocardial infarction, 17 were CHF, 10 were cardiac revascularization procedures, 5 were intermittent claudication, and 3 were incident angina. Distribution of correlates among those with and without CVD events stratified by sex in shown in Table 6.

Results of multivariable sex-pooled Cox proportional hazard regression analysis relating change in standardized log-LVMI to incidence of CVD on follow-up are presented in Table 7. A unit SD increase in delta log-LVMI was significantly associated with increased hazard ratio (HR) for CVD event [1.31 95%CI ([1.18, 1.93)], P=0.0011). Using penalized cubic

Table 4. Age-Adjusted and Sex Standardized Bivariate Correlations of 8 Year Change in Standardized Log LVMI

Clinical Correlates	Standardized Log LVMI at Baseline	Body Mass Index	Delta Body Mass Index	Systolic Blood Pressure	Delta Systolic Blood Pressure	Heavy Alcohol	Smoking	Education
Pearson correlation	0.56*	0.37*	−0.05	0.15*	0.05	0.00	0.05	−0.16*
P value	<0.0001*	<0.0001*	0.25	0.0003*	0.31	0.96	0.21	0.0001*

Log-LVMI, logarithmically transformed left ventricular mass indexed to height$^{2.7}$. LVMI indicates left ventricular mass index.
*Significant correlation between age and sex adjusted variables and 8 year change in standardized log left ventricular mass index.

Table 5. Multivariable* Adjusted Correlates of 8-Year Change in Sex Standardized Log LVM Index

Variable	βeta±(SE)	*P* Value
Baseline standardized log LVMI	0.47±0.4	<0.0001†
Male sex	−0.19±0.13	0.14
Baseline age	0.03±0.04	0.42
Baseline body mass index	0.15±0.04	0.0002†
Delta body mass index	0.01±0.07	0.84
Baseline systolic blood pressure	0.11±0.04	0.0061†
Delta systolic blood pressure	0.19±0.04	<0.0001†
Baseline sports index	−0.03±0.04	0.45
Baseline education	−0.09±0.04	0.0267†
Baseline current smoking status	0.10±0.10	0.28
Baseline heavy alcohol drinking	0.06±0.08	0.45

All variables in this table were fitted in the multivariable model. LVMI indicates left ventricular mass index.
*The covariates adjusted for in the multivariable model are age, gender, systolic and diastolic blood pressure, body mass index, education, drinking alcohol, sport index and smoking.
†Significant relation between the variable and 8 year change in sex standardized log LVM index.

regression splines of risk of CVD event by change in standardized log-LVMI after multivariable adjustment (results not shown); we observed a non-linear relation between small changes in log LVMI and the risk of CVD events. Thus, we expressed log-LVMI into quartiles and collapsed the second and third quartiles into one group and made it the reference. As shown in Table 4, the risk of CVD events was significantly higher for greater changes in standardized log-LVMI. These findings suggest that cardiac remodeling represented by change in standardized log-LVMI affected CVD outcome in our study sample.

Discussion

Principal Findings

Over a follow-up period of 8 years between echocardiogram examinations, we observed that BMI and systolic BP at baseline and BP increase over time were associated with progression of standardized LVM. Further, over a 10-year follow-up after the second echocardiogram; increase in standardized LVM between visits was associated with incidence of CVD events including MI, stroke, heart failure, and death. These findings are disturbing given the high rates of hypertension and obesity in the African-American population predisposing them to cardiac hypertrophy. Evidence from the present investigation provides support that the risk factors (BMI and BP) may play a major role in the ethnic difference in incidence rates of LV hypertrophy and that the subsequent progression of cardiac mass independently predicts CVD outcomes. This investigation underscores the need for better BP and weight control in African Americans to prevent progressive cardiac remodeling and subsequent future CVD morbidity and mortality. Additionally, we confirm the findings from the 20-year longitudinal investigation led by Gidding et al. from the CARDIA Study by showing similar clinical determinants for progression in LVM in our middle-aged predominantly African-American study over a shorter-term follow-up (8-year versus 20-year).[20]

Blood Pressure and Body Mass Index Impact on Change in LVM

The etiology of cardiac damage with increased BP is complex and includes pressure overload, circulating and local factors such as angiotensin II, catecholamines, and endothelin, which promote vascular and myocyte growth, increased connective

Table 6. Distribution of Clinical Correlates Between Participants With and Without CVE Stratified by Sex

	Gender			
	Women (All CV Events)		Men (All CV Events)	
Clinical Correlates	No CVE (N=336)	CVE (N=50)	No CVE (N=153)	CVE (N=31)
ARIC age, y	57.7	60.4	57.7	59.2
Body mass index, kg/m^2	30.4	32.6	28.0	28.0
Systolic blood pressure, mm Hg	139.7	155.2	143.7	149.5
Diastolic blood pressure, mm Hg	82.8	87.6	85.9	87.6
Delta body mass index, kg/m^2	0.7	0.6	0.7	−0.2
Delta systolic blood pressure, mm Hg	−1.6	−14	−7.3	−6.5
Delta diastolic blood pressure, mm Hg	−3.1	−8.0	−4.5	−4.9
Delta body weight, lbs	6.5	2.7	5.1	−1.3
Delta indexed z-scored LVM	0.20	0.23	−0.10	0.30

CVE indicates cardiovascular events; LVM, left ventricular mass.

Table 7. Multivariable Adjusted Association of Change in Standardized Log LVMI to Incidence of Cardiovascular Disease on Follow-up

	Beta (SE)	Multivariable Adjusted Hazard Ratio (95% CI)	*P* Value
Quartiles of change in standardized log LVMI			
Q2 and Q3	Reference	—	—
Q1	0.30 (0.29)	1.36 (0.77, 2.40)	0.30
Q4	0.95 (0.26)	2.60 (1.55, 4.33)	0.0003
Delta standardized log LVMI	0.32 (0.12)	1.51 (1.18, 1.93)	0.0011

Baseline variables fitted in the model included: age, male sex, systolic BP, body mass index, triglycerides, total cholesterol, sport index, diabetes mellitus and current smoking. 95% CI indicates 95% confidence interval; BP, blood pressure; LVMI, left ventricular mass index; Qj, jth quartile.

tissue deposition and collagen cross-linking characterized by both perivascular and interstitial fibrosis.[21,22]

Hypertension and obesity both cause a state of overload (pressure and volume respectively) leading to increase in myocardial fibrils to compensate for increasing wall stress.[23] However, in addition to the biomechanical stress associated with hypertension and obesity, several of the biological pathways implicated in promoting these conditions directly influence cardiovascular structure over time and can induce an increase in LVM and vascular remodeling. Among these pathophysiologic pathways are: (1) increased activity of the sympathetic nervous system (SNS), (2) overproduction of sodium-retaining hormones and vasoconstrictors (endothelin and thromboxane), (3) long-term sodium intake, (4) increase or inappropriate activation of the renin-angiotensin-aldosterone system (RAAS), (5) deficiencies of vasodilators such as prostaglandins and nitric oxide, insulin resistance, and (6) increased activity of vascular growth factors.[24–28]

The SNS is activated in obesity and SNS activity contributes to an increase in BP and the development and maintenance of hypertension through stimulation of the heart, the peripheral vasculature, and kidneys causing increased cardiac output, increased vascular resistance, and fluid retention.[29] Chronic sympathetic stimulation induces vascular remodeling and LV hypertrophy by actions of norepinephrine on its receptors as well as the release of vascular trophic factors including transforming growth factor-β, connective tissue growth factor and fibroblast growth factor.[26,27]

Similarly, activation of RAAS is associated both with hypertension and obesity, and this biological pathway has direct effects that induce cardiac hypertrophy.[22,30] Both angiotensin II and aldosterone induce hypertrophy and hyperplasia of cardiac myocytes and vascular remodeling and both mediators stimulate the release of a number of growth factors and cytokines.[21,30,31] Thus local RAAS and alternative pathways of RAAS contribute significantly to the development of target-organ damage.

Mechanism Linking Change in LVM to CVD

In African Americans and other ethnic groups LV hypertrophy is associated with increased CVD after adjusting for traditional risk factors including hypertension.[3,4] One explanation is that as LVM progresses there is an increase in myocardial oxygen demand which in the presence of occlusive CHD and impaired coronary flow reserve make an individual more susceptible to myocardial ischemia and heart failure.[23,32] Subsequently, patients with LV hypertrophy are at increased risk of CVD due to a myocardial oxygen supply - demand mismatch. CVD events in these patients result more frequently because their hypertrophied hearts consume higher amounts of oxygen but receive lower coronary blood flow due to CHD and to a greater resistance to diastolic flow to the myocardium in the less compliant ventricle.[23]

Vascular remodeling of smaller vessels occurs along with cardiac remodeling in response to biomechanical stressors and activation of biological pathways and mediators.[27] Vascular remodeling may explain the relation of cardiac hypertrophy to claudication and stroke. With remodeling in small arteries there is an increase in large artery stiffness and accelerated atherogenesis resulting in an increased risk of vascular-related target organ damage.[27]

Limitations

In the current study, there were a large number of participants (N=775) who received echoes at only 1 of the 2 visits and were therefore excluded from the present analysis. Comparison of that group to the study sample show a significant difference in the prevalence of obesity at baseline and follow-up; however there were no statistically significant differences in the other covariates. This is not surprising as more obese participants are more likely to have uninterpretable echocardiograms due to poor acoustic windows. Therefore, there may be a selection bias introduced as a result of our study sample being less obese compared with the more general population. This limitation is counterbalanced by the advantage of being

able to assess change in standardized LVM and its independent impact on incident CVD events in a large prospectively followed community-based sample of African Americans.

Implications

ARIC investigators published a 20-year follow-up of participants from the first examination of the community and observed the prevalence of those meeting criteria of ideal cardiovascular health based on the American Heart Association's 2020 impact goals. They subsequently tracked the incidence of CVD outcomes in both African and European Americans in the cohort who met those goals. Investigators found that only 0.1% of participants, and fewer African Americans, had all 7 metrics at ideal levels, consistent with the national data.[33] These findings support the primary need to aggressively lower the risk factors burden in African Americans to change the growing racial disparity in CVD outcomes in the US. Our study findings suggest that change in cardiac mass may be an important intermediate phenotype that plays a role along the pathogenetic pathway from risk factors to CVD outcomes. BP and BMI are key modifiable risk factors that appear to play an important role in longitudinal cardiac remodeling in African Americans. These risk factors should be the major focus for preventive measures in this high-risk group based on the current investigation.

Conclusion

In our community-based sample of African Americans, we observed that baseline BMI and BP, and change in BP over time was positively associated with change in LVM over an 8-year period. Increase in standardized LVM was associated with greater risk of CVD events over a 10-year follow-up after the second echocardiogram. These findings underscore the need for greater control of BP and weight through diet and exercise to prevent development of cardiac hypertrophy and related risk of CVD events in this high-risk group.

Acknowledgments

The authors thank the Jackson Heart Study team (University of Mississippi Medical Center, Jackson State University, and Tougaloo College) and the ARIC study team and participants for their long-term commitment that continues to improve our understanding of the epidemiology of cardiovascular and other chronic diseases. Specifically, we acknowledge the efforts of cardiac sonographers (Melanie Omobude BA, RDMS, Shelia Morgan-Jones BA, RDCS, Cora Champion LPN, and Tara Harding RCS), surveillance abstractors (Debra Wilson, Jacqueline Mallet, Valerie Wallace, and Ethel Williams) and annual follow up interviewers (Belinda Johnson, Ida Berry, and LaShondra Upkins) for their diligence in collecting valuable information from the participants. The authors also thank the staff and participants of the ARIC study for their important contributions.

Sources of Funding

The Jackson Heart Study is supported by contracts HSN268201300046C, HHSN268201300047C, HHSN268201300048C, HHSN268201300049C, HHSN268201300050C from the National Heart, Lung, and Blood Institute on Minority Health and Health Disparities. This work was also supported by AHA Clinical Research Program award 13CRP14090010 (to Dr Xanthakis), by the Nation Heart, Lung and Blood Institute's Framingham Heart Study (N01-HC-25915), R01-HL-08675, RO1HL080124 (Vasan) and K99-HL-107642. The Atherosclerosis Risk in Communities Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).

Disclosures

None.

References

1. Fox ER, Taylor HA Jr, Benjamin EJ, Ding J, Liebson PR, Arnett D, Quin EM, Skelton TN. Left ventricular mass indexed to height and prevalent MRI cerebrovascular disease in an African American cohort: the Atherosclerotic Risk in Communities study. *Stroke*. 2005;36:546–550.
2. Taylor HA, Penman AD, Han H, Dele-Michael A, Skelton TN, Fox ER, Benjamin EJ, Arnett DK, Mosley TH Jr. Left ventricular architecture and survival in African-Americans free of coronary heart disease (from the Atherosclerosis Risk in Communities [ARIC] study). *Am J Cardiol*. 2007;99:1413–1420.
3. Benjamin EJ, Levy D. Why is left ventricular hypertrophy so predictive of morbidity and mortality? *Am J Med Sci*. 1999;317:168–175.
4. Nunez E, Arnett DK, Benjamin EJ, Liebson PR, Skelton TN, Taylor H, Andrew M. Optimal threshold value for left ventricular hypertrophy in blacks: the Atherosclerosis Risk in Communities study. *Hypertension*. 2005;45:58–63.
5. Kizer JR, Arnett DK, Bella JN, Paranicas M, Rao DC, Province MA, Oberman A, Kitzman DW, Hopkins PN, Liu JE, Devereux RB. Differences in left ventricular structure between black and white hypertensive adults: the Hypertension Genetic Epidemiology Network study. *Hypertension*. 2004;43:1182–1188.
6. Drazner MH, Dries DL, Peshock RM, Cooper RS, Klassen C, Kazi F, Willett D, Victor RG. Left ventricular hypertrophy is more prevalent in blacks than whites in the general population: the Dallas Heart Study. *Hypertension*. 2005;46:124–129.
7. Gidding SS, Liu K, Colangelo LA, Cook NL, Goff DC, Glasser SP, Gardin JM, Lima JA. Longitudinal determinants of left ventricular mass and geometry: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Circ Cardiovasc Imaging*. 2013;6:769–775.
8. Devereux RB, Dahlof B, Gerdts E, Boman K, Nieminen MS, Papademetriou V, Rokkedal J, Harris KE, Edelman JM, Wachtell K. Regression of hypertensive left ventricular hypertrophy by losartan compared with atenolol: the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) trial. *Circulation*. 2004;110:1456–1462.
9. Devereux RB, Wachtell K, Gerdts E, Boman K, Nieminen MS, Papademetriou V, Rokkedal J, Harris K, Aurup P, Dahlof B. Prognostic significance of left

ventricular mass change during treatment of hypertension. *JAMA*. 2004;292:2350–2356.

10. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. *Am J Epidemiol*. 1989;129:687–702.
11. Taylor HA Jr, Wilson JG, Jones DW, Sarpong DF, Srinivasan A, Garrison RJ, Nelson C, Wyatt SB. Toward resolution of cardiovascular health disparities in African Americans: design and methods of the Jackson Heart Study. *Ethn Dis*. 2005;15:S6–S17.
12. Carithers T, Dubbert PM, Crook E, Davy B, Wyatt SB, Bogle ML, Taylor HA Jr, Tucker KL. Dietary assessment in African Americans: methods used in the Jackson Heart Study. *Ethn Dis*. 2005;15:S6–S55.
13. Dubbert PM, Carithers T, Ainsworth BE, Taylor HA Jr, Wilson G, Wyatt SB. Physical activity assessment methods in the Jackson Heart Study. *Ethn Dis*. 2005;15:S6–S61.
14. Tobin MD, Sheehan NA, Scurrah KJ, Burton PR. Adjusting for treatment effects in studies of quantitative traits: antihypertensive therapy and systolic blood pressure. *Stat Med*. 2005;24:2911–2935.
15. Skelton TN, Andrew ME, Arnett DK, Burchfiel CM, Garrison RJ, Samdarshi TE, Taylor HA, Hutchinson RG. Echocardiographic left ventricular mass in African-Americans: the Jackson cohort of the Atherosclerosis Risk in Communities Study. *Echocardiography*. 2003;20:111–120.
16. Samdarshi TE, Taylor HA, Edwards DQ, Liebson PR, Sarpong DF, Shreenivas SS, Howard G, Garrison RJ, Fox ER. Distribution and determinants of Doppler-derived diastolic flow indices in African Americans: the Jackson Heart Study (JHS). *Am Heart J*. 2009;158:209–216.
17. 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.
18. de Simone G, Devereux RB, Daniels SR, Koren MJ, Meyer RA, Laragh JH. Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. *J Am Coll Cardiol*. 1995;25:1056–1062.
19. Lieb W, Xanthakis V, Sullivan LM, Aragam J, Pencina MJ, Larson MG, Benjamin EJ, Vasan RS. Longitudinal tracking of left ventricular mass over the adult life course: clinical correlates of short- and long-term change in the framingham offspring study. *Circulation*. 2009;119:3085–3092.
20. Gardin JM, Brunner D, Schreiner PJ, Xie X, Reid CL, Ruth K, Bild DE, Gidding SS. Demographics and correlates of five-year change in echocardiographic left ventricular mass in young black and white adult men and women: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *J Am Coll Cardiol*. 2002;40:529–535.
21. Robert V, Heymes C, Silvestre JS, Sabri A, Swynghedauw B, Delcayre C. Angiotensin AT1 receptor subtype as a cardiac target of aldosterone: role in aldosterone-salt-induced fibrosis. *Hypertension*. 1999;33:981–986.
22. Shahbaz AU, Sun Y, Bhattacharya SK, Ahokas RA, Gerling IC, McGee JE, Weber KT. Fibrosis in hypertensive heart disease: molecular pathways and cardio-protective strategies. *J Hypertens*. 2010;28(suppl 1):S25–S32.
23. Lorell BH, Carabello BA. Left ventricular hypertrophy: pathogenesis, detection, and prognosis. *Circulation*. 2000;102:470–479.
24. Miyauchi T, Masaki T. Pathophysiology of endothelin in the cardiovascular system. *Annu Rev Physiol*. 1999;61:391–415.
25. Malmqvist K, Ohman KP, Lind L, Nystrom F, Kahan T. Relationships between left ventricular mass and the renin-angiotensin system, catecholamines, insulin and leptin. *J Intern Med*. 2002;252:430–439.
26. Dang A, Zheng D, Wang B, Zhang Y, Zhang P, Xu M, Liu G, Liu L. The role of the renin-angiotensin and cardiac sympathetic nervous systems in the development of hypertension and left ventricular hypertrophy in spontaneously hypertensive rats. *Hypertens Res*. 1999;22:217–221.
27. Lan TH, Huang XQ, Tan HM. Vascular fibrosis in atherosclerosis. *Cardiovasc Pathol*. 2013;22:401–407.
28. Simko F, Simko J. The potential role of nitric oxide in the hypertrophic growth of the left ventricle. *Physiol Res*. 2000;49:37–46.
29. Mikhail N, Golub MS, Tuck ML. Obesity and hypertension. *Prog Cardiovasc Dis*. 1999;42:39–58.
30. Catena C, Colussi G, Marzano L, Sechi LA. Aldosterone and the heart: from basic research to clinical evidence. *Horm Metab Res*. 2012;44:181–187.
31. Sun Y, Ramires FJ, Zhou G, Ganjam VK, Weber KT. Fibrous tissue and angiotensin II. *J Mol Cell Cardiol*. 1997;29:2001–2012.
32. Nakano K, Corin WJ, Spann JF Jr, Biederman RW, Denslow S, Carabello BA. Abnormal subendocardial blood flow in pressure overload hypertrophy is associated with pacing-induced subendocardial dysfunction. *Circ Res*. 1989;65:1555–1564.
33. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J Am Coll Cardiol*. 2011;57:1690–1696.