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Metabolic Syndrome and Echocardiographic Left Ventricular Mass in Blacks

The Atherosclerosis Risk in Communities (ARIC) Study

Cecil M. Burchfiel, PhD, MPH; Thomas N. Skelton, MD; Michael E. Andrew, PhD; Robert J. Garrison, PhD; Donna K. Arnett, PhD; Daniel W. Jones, MD; Herman A. Taylor, Jr, MD

Background—The metabolic syndrome has been associated with cardiovascular disease, but few studies have examined its relationship with subclinical measures such as echocardiographic left ventricular (LV) mass. This relationship is likely to be of particular importance in blacks, in whom both the metabolic syndrome and LV hypertrophy are common.

Methods and Results—Echocardiography, performed at 1 of 4 sites in the Atherosclerosis Risk in Communities (ARIC) Study, was used to assess LV dimensions in 1572 black women and men aged 49 to 75 years in 1993–1996. Participants were categorized by number of metabolic syndrome characteristics (hypertension, dyslipidemia [low HDL cholesterol or high triglycerides], and glucose intolerance). Age-adjusted mean LV mass indexed by height (g/m) increased in a stepwise gradient with increasing number of metabolic syndrome disorders (none, any 1, any 2, all 3) in both women and men (125.1, 143.9, 153.7, 169.3 and 130.5, 148.7, 160.8, 170.2, respectively; $P < 0.001$, tests for trend). Associations were diminished slightly by adjustment for smoking, alcohol intake, and education; additional adjustment for waist circumference resulted in some attenuation, but associations remained statistically significant. Analyses focusing on components of LV mass revealed that posterior wall and interventricular septal thickness, but not LV chamber size, were significantly and independently associated in general with the number of metabolic syndrome disorders. Consistent with these findings, relative wall thickness was also associated with number of disorders. Associations were similar across age and central adiposity. Hypertension had a strong influence on LV mass with additional contributions from dyslipidemia and glucose intolerance; strong synergistic effects of the syndrome beyond its individual components were not observed.

Conclusions—In this cross-sectional population-based study of black women and men, the degree of metabolic syndrome clustering was strongly related to LV mass and its wall thickness components. These associations are consistent with a possible influence of underlying factors such as insulin resistance or other vascular processes on myocardial thickening and not on chamber size. (*Circulation*. 2005;112:819-827.)

Key Words: diabetes mellitus ■ echocardiography ■ hypertension ■ hypertrophy ■ lipids

Opportunities to understand pathological alterations in cardiac structure and function have been greatly enhanced by the widespread application of echocardiography in clinical practice, clinical research, and epidemiology. Glucose intolerance, hypertension, and abnormal lipid profiles are several silent disorders that often occur together. Parallel development of methodology used to define and understand the natural history of these risk factors has important implications not only for prevention but also for interventions that might protect against the numerous and often debilitating cardiovascular consequences of these disorders. These consequences include diabetic retinopathy, renal disease, stroke,

and alterations in cardiac dysfunction and its associated congestive heart failure.^{1–6} Congestive heart failure, although not as well documented and less understood than other consequences, occurs frequently in the black population,⁷ in which the risks of type 2 diabetes⁸ and hypertension⁹ are elevated and lipid abnormalities commonly coexist.

The evaluation of the Atherosclerosis Risk in Communities (ARIC) Jackson, Miss, field center participants with echocardiography permits the first large-scale assessment of cardiac structure and function in a middle-aged to elderly black sample. These participants were also examined for the presence of glucose intolerance, hypertension, and lipid abnor-

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malities, an adverse combination of risk factors referred to initially as the insulin resistance syndrome¹⁰ and subsequently as the metabolic syndrome.¹¹ The purpose of this report is to identify and quantify relationships between the metabolic syndrome and specific echocardiographic measurements of cardiac dimension (wall thickness and chamber size) involved in determination of left ventricular (LV) mass.

Methods

Study Population

The ARIC Study is a prospective population-based investigation of risk factors for atherosclerosis, coronary heart disease, and stroke in 4 US communities. In 3 of these communities (Forsyth County, North Carolina; Washington County, Maryland; and the suburbs of Minneapolis, Minn), probability sampling of residents was used. In the fourth community, Jackson, Miss, a representative sample was selected from black residents of the city through the use of driver's license and state identification card lists. Details of the selection process have been published previously.¹² A total of 15 792 participants aged 45 to 64 years from these communities were recruited and examined at baseline between 1987 and 1989. Approximately 12% of participants from Forsyth County were black, and residents of the other 2 sites were predominantly white. Baseline response rates were approximately 65% for 3 of the communities and 46% for Jackson, a rate that was identical for the black population of Forsyth County. Follow-up examinations were conducted every 3 years on average, and 93%, 86%, and 80% of survivors completed the second (1990–1992), third (1993–1995), and fourth (1996–1998) examinations, respectively.

Echocardiographic studies were performed at the Jackson site between 1993 and 1996. Because this procedure became available just after the third examination began, 323 participants who missed the opportunity during the third examination had the procedure performed in 1996 as part of their fourth examination. For these 323 individuals, values of all variables collected at the time of their fourth examination were used. Measurement protocols for the third and fourth visits for key variables were the same. Of 2445 participants who had an echocardiographic examination, 1730 had adequate measurements enabling a valid estimate of LV mass. A total of 79 nondiabetic subjects who fasted <8 hours, 12 participants who lacked necessary information used to define the metabolic syndrome, and 67 who had prevalent coronary heart disease (defined as myocardial infarction, coronary bypass surgery, or angioplasty) were also excluded, leaving 1572 participants available for analysis.

Echocardiographic Measurements

Details of the echocardiographic examination and interpretation are described elsewhere.¹³ Briefly, image acquisition was performed with the Acuson XP128/10c echo machine. Steerable 2-dimensional directed M-mode was used, and the Freeland Systems CineView digital imaging computer provided control of the resolution and timing of image acquisition and storage. Serial frames showing cardiac motion throughout the cardiac cycle were available, and full-screen acquisition of M-mode or spectral Doppler data was used for quantitative measurements. The reader was able to select the best available single frame from several full screens that were stored by 2 trained nurses. Quantitative measurements were obtained from the parasternal short-axis view with the M-mode cursor positioned through the center of the ventricle. A cardiologist (T.N.S.) performed all echocardiographic readings. Variability within and between sonographers and within the reader was assessed during the examination period with the use of a 2% random sample. The intrasonographer and intersonographer correlation for LV mass between the first and second scan was 0.94 and 0.82, respectively. The intrareader intraclass correlation coefficient for LV mass was 0.98.

Components of LV mass, LV internal dimension (LVID), interventricular septal thickness (IVST), and posterior wall thickness (PWT) were all measured at end-diastole (d) with the use of a

leading-edge technique. Relative wall thickness was calculated as the ratio of the sum of IVST and PWT to LVID. Estimates of LV mass were calculated according to American Society of Echocardiography criteria applied to the formula of Troy et al¹⁴: LV mass (g) = 1.05[(LVID_d + IVST_d + PWT_d)³ - (LVID_d)³].

Further adjustment for the tendency to overestimate LV mass based on anatomic measurements at autopsy as proposed by Devereux et al¹⁵ was not used to enable comparisons with initial findings from the Framingham Heart Study.¹⁶ Thus, calculated LV mass estimates in this study may be approximately 20% higher than studies in which this anatomic adjustment was applied. To take into account differences in body size that might influence cardiac size, LV mass estimates were divided by height to create an LV mass index.

Other Measurements

Trained technicians conducted comprehensive interviews and performed clinic assessments using standardized protocols. Details of these procedures have been reported previously.^{12,17} Smoking habits and alcohol use were ascertained by interview. Participants were categorized as current, former, and never smokers. Participants were also classified by alcohol drinking status, and drinkers were asked the usual number of drinks consumed per week, taking into account beverage type. Six categories were created, including nondrinkers, former drinkers, <1 drink per week, 1 to 6 drinks per week, 7 to 21 drinks per week, and ≥22 drinks per week. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Waist circumference was determined by horizontal measurement of maximum girth at the umbilicus. Blood pressure (BP) was measured with a random zero sphygmomanometer following a standardized protocol, and the mean of the second and third measurements was used in this report.

Blood was drawn after the patient had fasted overnight. HDL cholesterol,¹⁸ triglyceride,^{18,19} and glucose levels¹⁸ were measured enzymatically with a Cobas-Fara II centrifuge autoanalyzer (Hoffmann-La Roche). HDL cholesterol was measured after precipitation of non-HDL lipoproteins by dextran sulfate and magnesium chloride, and glucose was determined by a hexokinase method. Estimates of intraindividual variability in plasma measurements have been reported previously.^{20,21}

Metabolic Syndrome

Hypertension was defined as systolic BP ≥130 mm Hg, diastolic BP ≥85 mm Hg, or self-reported antihypertensive medication use during the 2-week period before the clinic examination. Dyslipidemia was defined as a low HDL cholesterol level (<40 mg/dL in men and <50 mg/dL in women) or as an elevated triglyceride level (≥150 mg/dL). Glucose intolerance was defined by the presence of diabetes (self-reported physician diagnosis of diabetes, use of insulin or oral hypoglycemic medication, or fasting glucose level ≥126 mg/dL) or impaired fasting glucose (fasting glucose level ≥110 mg/dL) according to American Diabetes Association criteria.²² The metabolic syndrome was defined as the presence of hypertension, dyslipidemia, or glucose intolerance with cut points consistent with the National Cholesterol Education Program's Adult Treatment Panel III report.²³ Waist circumference was not included in the definition to allow assessment of its role in potentially accounting for and modifying associations of other metabolic syndrome components with LV dimensions and mass. Participants were categorized according to the number of metabolic syndrome disorders that they had (none, any 1 of the disorders, any 2, or all 3 disorders).

Statistical Analysis

Differences in the percentage of women and men who had no metabolic syndrome disorders or any 1, any 2, or all 3 disorders were evaluated with a χ^2 test. Age- and risk factor-adjusted estimates of mean LV mass/height and its components (wall thicknesses and chamber size) were calculated and compared according to the number of disorders by a general linear models approach with ANCOVA and a contrast specifying a test for linear trend across the

TABLE 1. Characteristics of Women and Men From the Jackson Site of the ARIC Study, 1993–1996

	Women (n=1044)	Men (n=528)
Age, y	59 (6)	59 (6)
Education, %		
Less than high school	36	36
High school or vocational	28	27
College or professional	35	37
Systolic BP, mm Hg	131 (21)	131 (21)
Diastolic BP, mm Hg	76 (10)	79 (11)
Hypertension treatment, %	54	42
Hypertension, %	72	67
HDL cholesterol, mg/dL	60 (18)	50 (17)
Triglycerides, mg/dL	113 (61)	121 (96)
Dyslipidemia, %	38	39
Glucose, mg/dL	121 (56)	122 (58)
Diabetes, %	24	21
Glucose intolerance, %*	36	35
BMI, kg/m ²	31.5 (6.4)	28.2 (4.6)
Waist, cm	104 (16)	99 (12)

Values are means (SD) or percentages.

*Glucose intolerance is defined as diabetes or impaired fasting glucose (see text).

4 metabolic syndrome categories.²⁴ A series of models was used for women and men separately: (1) with adjustment for age; (2) with adjustment for age, smoking status, alcohol intake, and education; and (3) with adjustment for age, smoking status, alcohol intake, education, and waist circumference. BMI was also evaluated in place of waist circumference. Additional models were used to assess potential interactions by examining these associations in younger (<60 years) and older (≥60 years) participants and in those who were less centrally obese and more centrally obese with the use of Adult Treatment Panel III cut points for waist circumference of 88 cm in women and 102 cm in men.²³

In addition to analyses that focused on the number of metabolic disorders, ANCOVA models were also used to compare the influence of individual components of the syndrome (hypertension, dyslipidemia, and glucose intolerance) when summed together with that for having the syndrome itself (presence of all 3 components). For example, the influence of a single component such as hypertension was obtained by calculating the difference in adjusted mean LV mass index between those with a single component (eg, hypertension only) and those with no disorders, and similarly so for those with all 3 disorders versus those with no disorders. This approach allowed us to determine whether participants who had the metabolic syndrome had a much larger LV mass index (synergistic effect) compared with what would be expected if the influence of each component was only additive. It was also possible to determine which of the components had the greatest influence on LV mass index and its constituents. In this regard, we developed a 2-component model to further examine the influence of 2 syndrome components (dyslipidemia and glucose intolerance) after taking into account the third (hypertension). A probability value of <0.05 was considered statistically significant. Because no correction for multiple comparisons was made, the possibility of a type I error could be increased. All statistical analyses were performed with the use of the SAS²⁵ package.

Results

Descriptive characteristics of the women and men from the Jackson field site of the ARIC Study are presented in Table 1.

Participants examined between 1993 and 1996 ranged in age from 49 to 75 years, with a mean of 59 years. Mean BMI was relatively high, particularly for women (31.5 and 28.2 kg/m² for women and men, respectively), as was waist circumference. The prevalence of hypertension was also elevated, with 71.8% of the women and 66.5% of the men having the condition. Approximately 75% of women and 64% of men with hypertension were receiving antihypertensive treatment. Slightly more than one third of the sample had dyslipidemia, and just over one third had glucose intolerance. Diabetes was evident in 24% of women and 21% of men overall and in 68% of the women and 58% of men who had glucose intolerance.

When participants were categorized by the number of metabolic syndrome disorders (hypertension, dyslipidemia, and glucose intolerance), only 16% had none of these conditions. Nearly 38% had 1 of these conditions, another 32% had any 2, and 14% had all 3 conditions. Women had a slightly worse profile than men, although differences by gender were not statistically significant ($P=0.751$); proportions of participants with none, any 1, any 2, and all 3 metabolic syndrome disorders were 15.8%, 37.8%, 31.9%, and 14.5% in women and 17.6%, 37.9%, 31.4%, and 13.1% in men, respectively. For participants with 1 disorder, 27.3% had hypertension, 6.5% had dyslipidemia, and 4.0% had glucose intolerance. For those with 2 disorders, the combinations of hypertension with dyslipidemia and hypertension with glucose intolerance occurred with similar frequency (14.2% and 14.5%, respectively), whereas the combination of dyslipidemia and glucose intolerance was less common (3.0%). Prevalence of ≥2 disorders increased significantly with age among women but not among men (39.3%, 47.2%, 57.9%, 49.8% in women and 42.9%, 45.5%, 47.0%, and 43.4% in men for groups aged <55, 55 to 59, 60 to 64, and ≥65 years, respectively [tests for trend $P<0.021$ and $P=0.909$, respectively]).

Unadjusted mean LV mass (SD) was 235.7 g (71.8) in women and 282.0 g (87.1) in men. Age-adjusted mean LV mass indexed by height increased progressively with increasing number of metabolic syndrome disorders in both women and men (Tables 2 and 3). These trends were strong and statistically significant ($P<0.001$). Adjustment for age, smoking, alcohol use, and education (model 2) attenuated these trends slightly. Further adjustment for waist circumference (model 3) attenuated these associations further; however, LV mass/height remained significantly associated with the number of disorders in both women and men. Similar patterns were observed in general for 2 of the 3 components of LV mass, interventricular septal thickness and posterior wall thickness, in women and men. These associations were strong, graded, and remained statistically significant after adjustment in all 3 models. In contrast, trends in age-adjusted mean LV internal dimension according to the number of metabolic syndrome disorders were notably weaker, and these associations were attenuated with adjustment for smoking, alcohol intake, and education and disappeared completely with adjustment for waist circumference. Trends in mean relative wall thickness showed increases with increasing number of metabolic disorders that remained significant after adjustment in both women and men.

TABLE 2. Adjusted Mean Echocardiographic Indices According to Number of Metabolic Syndrome Disorders in Women, Jackson Site of the ARIC Study, 1993–1996

Model*	Metabolic Syndrome Disorders				P (Test for Trend)
	None	Any 1	Any 2	All 3	
LV mass/height, g/m					
1	125.1 (4.3)	143.9 (3.5)	153.7 (3.5)	169.3 (4.5)	<0.001
2	125.2 (4.9)	142.1 (4.2)	151.4 (4.2)	163.5 (5.2)	<0.001
3	126.4 (5.4)	138.3 (4.9)	141.8 (4.8)	150.4 (5.6)	<0.001
Interventricular septum, mm					
1	10.5 (0.2)	11.3 (0.2)	11.9 (0.2)	12.6 (0.3)	<0.001
2	10.4 (0.3)	11.1 (0.2)	11.6 (0.2)	12.4 (0.3)	<0.001
3	10.4 (0.3)	11.0 (0.3)	11.3 (0.3)	12.0 (0.3)	<0.001
Posterior wall thickness, mm					
1	10.6 (0.2)	11.3 (0.2)	11.8 (0.2)	12.6 (0.2)	<0.001
2	10.5 (0.2)	11.1 (0.2)	11.7 (0.2)	12.3 (0.2)	<0.001
3	10.5 (0.3)	11.0 (0.2)	11.3 (0.2)	11.8 (0.3)	<0.001
LV internal dimension, mm					
1	45.1 (0.6)	46.0 (0.5)	46.1 (0.5)	46.5 (0.6)	<0.001
2	45.5 (0.6)	46.3 (0.6)	46.3 (0.6)	46.3 (0.7)	0.20
3	45.6 (0.7)	46.0 (0.7)	45.5 (0.7)	45.2 (0.8)	0.44
Relative wall thickness					
1	0.47 (0.01)	0.50 (0.01)	0.52 (0.01)	0.55 (0.01)	<0.001
2	0.46 (0.01)	0.49 (0.01)	0.51 (0.01)	0.54 (0.01)	<0.001
3	0.46 (0.02)	0.48 (0.01)	0.50 (0.01)	0.53 (0.02)	<0.001

Values are adjusted means (SE).

*Model 1 adjusts for age and height (except for LV mass/height, for which height is not included in adjustment models); model 2 adjusts for model 1 variables plus smoking status, alcohol intake, and education; model 3 adjusts for model 2 variables plus waist circumference.

Patterns were similar when BMI was used in place of waist circumference. Associations were also similar in younger and older as well as in relatively less centrally obese and more centrally obese participants (data not shown). In addition, there was no evidence of statistical interaction involving waist circumference and the number of metabolic syndrome components on LV mass index (women, $P=0.660$; men, $P=0.396$).

Comparisons of LV mass index across categories of all possible combinations of metabolic syndrome components (8 categories instead of the 4 presented in Tables 2 and 3) were also examined to determine whether these components had a synergistic effect and which component had the greatest influence. Women having all 3 components of the syndrome demonstrated a similar yet slightly greater influence on the adjusted mean LV mass index ($151.5-127.4=24.1$ g/m, difference between all 3 versus zero disorders, respectively) compared with the sum of the individual influences of hypertension, dyslipidemia, and glucose intolerance considered separately [$(144.3-127.4)+(125.6-127.4)+(123.6-127.4)=11.3$ g/m], after adjustment for age, smoking status, alcohol intake, education, and waist circumference. Similarly, men with all 3 components showed a similar influence on adjusted LV mass index ($153.9-129.0=24.9$ g/m, all 3 versus zero disorders) compared with the sum of individual influences of the 3 disorders [$(150.3-129.0)+(121.4-129.0)+(136.8-129.0)=21.5$ g/m]. Differences in mean LV

mass index for women and men with hypertension alone compared with participants who had no disorders were statistically significant, whereas those involving dyslipidemia alone and glucose intolerance alone were not statistically significant. In addition, comparisons of LV mass index across categories of specific individual components of the metabolic syndrome indicated that those who had hypertension separately or in combination with dyslipidemia or glucose intolerance tended to have a larger LV mass/height than those who only had dyslipidemia or glucose intolerance alone (data not shown). To further assess whether dyslipidemia and glucose intolerance still had an influence on LV mass index once hypertension was taken into account, we created a 2-component metabolic syndrome variable representing occurrence of none, 1, or both of the nonhypertension metabolic syndrome components (dyslipidemia and glucose intolerance) without regard to hypertension. Hypertension status was included as a covariate in these models. Before adjusting for hypertension, we tested for statistical interaction between hypertension status and the 2-component variable with respect to LV mass index, and no interactions were present (women, $P=0.751$; men, $P=0.523$).

Without adjustment for hypertension, the 2-component definition of metabolic syndrome had statistically significant trends, with LV mass index, posterior wall thickness, and interventricular wall thickness similar to the 3-component definition. Adjustment for hypertension and age resulted in

TABLE 3. Adjusted Mean Echocardiographic Indices According to Number of Metabolic Syndrome Disorders in Men, Jackson Site of the ARIC Study, 1993–1996

Model*	Metabolic Syndrome Disorders				P (Test for Trend)
	None	Any 1	Any 2	All 3	
LV mass/height, g/m					
1	130.5 (6.7)	148.7 (5.8)	160.8 (5.8)	170.2 (7.1)	<0.001
2	115.9 (9.3)	133.1 (8.7)	145.9 (8.6)	153.1 (9.8)	<0.001
3	128.7 (9.8)	142.7 (9.1)	150.7 (8.9)	153.6 (10.1)	<0.001
Interventricular septum, mm					
1	10.5 (0.4)	11.3 (0.3)	11.7 (0.3)	12.1 (0.4)	<0.001
2	9.7 (0.5)	10.5 (0.5)	11.0 (0.5)	11.2 (0.6)	<0.001
3	10.2 (0.6)	10.9 (0.5)	11.2 (0.5)	11.3 (0.6)	0.009
Posterior wall thickness, mm					
1	10.6 (0.3)	11.5 (0.3)	11.9 (0.3)	12.4 (0.4)	<0.001
2	10.1 (0.5)	11.0 (0.4)	11.5 (0.4)	11.9 (0.5)	<0.001
3	10.7 (0.5)	11.4 (0.5)	11.7 (0.4)	11.9 (0.5)	0.001
LV internal dimension, mm					
1	46.5 (0.9)	46.9 (0.8)	47.7 (0.8)	47.7 (1.0)	<0.001
2	46.2 (1.2)	46.5 (1.1)	47.1 (1.1)	47.0 (1.2)	0.30
3	47.3 (1.3)	47.4 (1.2)	47.7 (1.2)	47.4 (1.3)	0.89
Relative wall thickness					
1	0.45 (0.02)	0.49 (0.02)	0.50 (0.02)	0.52 (0.02)	<0.001
2	0.43 (0.03)	0.46 (0.03)	0.48 (0.03)	0.49 (0.03)	0.002
3	0.44 (0.03)	0.47 (0.03)	0.48 (0.03)	0.49 (0.03)	0.029

Values are adjusted means (SE).

*Model 1 adjusts for age and height (except for LV mass/height, for which height is not included in adjustment models); model 2 adjusts for model 1 variables plus smoking status, alcohol intake, and education; model 3 adjusts for model 2 variables plus waist circumference.

some attenuation of the trend for LV mass index in women, yet the trend remained statistically significant ($P < 0.001$; mean \pm SE LV mass index (g/m) for 0, 1, and 2 disorders was 124.7 ± 3.8 , 131.5 ± 4.0 , and 144.7 ± 4.9 , respectively). In men, adjustment for hypertension and age led to a stronger attenuation of this association (test for trend $P = 0.078$; mean LV mass index [g/m] was 128.2 ± 6.2 , 135.4 ± 6.3 , and 138.6 ± 7.4 for 0, 1, and 2 disorders, respectively). Further adjustment for waist circumference and other covariates attenuated the trend across the number of disorders to nonsignificant levels (test for trend, $P = 0.084$ in women and $P = 0.961$ in men).

Discussion

The metabolic syndrome has been the focus of increased attention since Reaven¹⁰ suggested that it had an important etiologic role in type 2 diabetes, hypertension, and coronary artery disease. Our definition of the metabolic syndrome, which included hypertension, dyslipidemia, and glucose intolerance, corresponded with that used in his initial report,¹⁰ although cut points from the more recent Adult Treatment Panel III report were used for these metabolic risk factors.²³ The focus of the ensuing efforts included not only attempts to more precisely define metabolic syndrome but to enumerate its causes and, as in this report, its pathological correlates or consequences. Several reports^{11,26–28} have used definitions of

the metabolic syndrome that are comparable but not identical to the definition in this report.

In the ARIC Study, black and white participants were previously classified at the baseline visit by the presence of hypertension, diabetes, hypertriglyceridemia, low HDL cholesterol, and hyperuricemia.¹¹ Prevalence of ≥ 2 metabolic disorders in the present study, assessed ≈ 6 years later in those with adequate echocardiograms and with slightly different criteria, was somewhat higher in black women (46.4%) and men (44.5%) than in the entire ARIC cohort. In another investigation, a slightly different metabolic classification was applied to the ARIC participants, and the authors concluded that 3-year incidence of metabolic syndrome abnormalities was more likely to occur in participants who had elevated insulin levels, BMI, and central adiposity, regardless of gender or race.²⁸ Definitions of the metabolic syndrome, possible underlying mechanisms, and its consequences were recently summarized.²⁹

Contrary to the initial finding of an “intrinsic” abnormality of the myocardium in some diabetic subjects involving abnormal wall thinning and relaxation rather than hypertrophy,³⁰ echocardiographic studies of diabetic and control subjects have generally concluded that diabetic participants have elevated LV mass or increased prevalence of LV hypertrophy.^{31–33} Consistent with this report, the population-based Strong Heart Study⁶ and Hypertension Genetic Epide-

miology Network (HyperGEN) Study⁵ both reported significantly higher LV mass and wall thickness in diabetic compared with nondiabetic participants (13% and 3% higher LV mass in the 2 studies, respectively) after adjustment for age, BP, and BMI, yet nonsignificant differences were observed for LV internal dimension. In the large Cardiovascular Health Study of free-living elderly (aged ≥ 65 years), a small but significant elevation in LV mass ($\approx 3.1\%$ higher in women and 2.6% higher in men) was reported in the diabetic subgroup of their sample, after adjustment for body weight, BP, heart rate, and prevalent coronary and cerebrovascular disease.³⁴ In addition, the magnitude of associations between diabetes and LV mass appeared to be notably enhanced by obesity.³⁵

Results for studies of the association of glucose intolerance with LV mass have shown more disparate results. Whereas an elevated prevalence of hypertrophy was reported in hypertensive patients with glucose intolerance relative to those without glucose intolerance,³⁶ others found no such relationship in a series of nonobese hypertensive patients.³⁷ In addition, although neither insulin nor glucose levels were associated with LV mass index, HbA_{1c} and postload insulin were associated with relative wall thickness after adjustment for age, systolic BP, and BMI.³⁸ In the Framingham Heart Study, increasing LV mass and wall thickness were directly associated with glucose intolerance, particularly in women.³⁹

Although insulin or insulin resistance could play a role in LV hypertrophy, as indicated in some^{40–44} but not all^{45–48} studies, direct assessment of insulin resistance or of plasma insulin levels was not available in the present study. Another possible mechanism could involve elevations in systolic BP or pulse pressure, which in turn may result in increased arterial stiffness. Increases in systolic stress resulting from increased arterial stiffness have been shown to be a stimulus for LV wall thickening.^{5,49} Another common feature of most previous studies is their lack of black subjects. Because diabetes, hypertension, and presumably insulin resistance are highly prevalent in blacks,^{50,51} and there are suggestions that cardiac hypertrophy is relatively common,^{48,52,53} it is apparent that careful examination of associations involving measures of insulin resistance and indices of vascular function in relation to cardiac structure among blacks could provide important clues to potential underlying mechanisms.

Assessment of the independent effects of the metabolic syndrome components revealed that hypertension had a strong influence on LV mass index. Using a 2-component model with the presence of 0, 1, or 2 metabolic syndrome disorders, a trend of increasing LV mass index was more evident in women than in men. These results were consistent with a strong influence of hypertension on LV mass index, as recently documented in this sample⁵⁴ and in the Strong Heart Study.⁵⁵ In addition, the results also indicated that dyslipidemia and glucose intolerance contribute to the trend of increasing LV mass index even after hypertension was taken into account, particularly in women; however, some of this association appeared to be explained by central obesity. These results were consistent with findings from the HyperGEN Study that showed an association between progressively

increasing metabolic risk factors and LV mass indexed by height among normotensive and hypertensive participants.⁵⁶

We also did not find strong evidence of interaction or synergy among the individual syndrome components because the presence of all 3 components of the metabolic syndrome showed a similar yet slightly larger estimated excess in LV mass index, as was observed for the individual components when summed together. In contrast, a synergistic effect of the metabolic syndrome on carotid intima-media thickness was recently demonstrated beyond that expected from the additive influence of individual syndrome components.⁵⁷

The quantification of metabolic syndrome abnormalities may indicate the potential magnitude and, when related to target organ assessment, the potential pathological impact of underlying mechanisms. A recent study based on a national sample and utilizing a slightly different definition indicated that, among blacks, women had a 57% higher age-adjusted prevalence of the metabolic syndrome than did men.⁵⁸ The finding of the present report that black men were only slightly more likely than women to be free of metabolic syndrome abnormalities was somewhat unexpected, as was the finding that only $\approx 16\%$ of this middle-aged black sample was free of these abnormalities. Additionally, the fact that 46% of this sample had ≥ 2 metabolic syndrome abnormalities suggests a substantial potential impact of possible underlying factors such as insulin resistance, other hemodynamic changes, or perhaps obesity as a precursor of the metabolic syndrome in this sample.

Cardiac structural abnormalities were documented, specifically for LV wall thickening of both the posterior wall and interventricular septum. These 2 important cardiac dimension components of LV mass were consistently and strongly related to the number of metabolic syndrome abnormalities. These relationships were diminished slightly but not substantially through adjustment for (Tables 2 and 3), or stratification by, factors such as obesity that have been demonstrated by others^{59,60} to be related to LV wall thickening. Clearly, these wall thickness parameters were the dimension components that result in LV mass showing the same consistent and strong relationship across levels of metabolic syndrome abnormalities. The strong trends with relative wall thickness were also consistent with what would be expected if associations were observed with wall thickness but not chamber size. The association of the metabolic syndrome with relative wall thickness was consistent with results from the Strong Heart Study.⁵⁵ Moreover, echocardiographically determined LV mass, or LV mass index, has been implicated as a major contributor to cardiovascular disease outcomes including coronary heart disease,^{61,62} stroke,^{61,63} and congestive heart failure.^{64–66}

Findings of this report suggest that associations between the metabolic syndrome and cardiac structure are in general similar in strength among black women and men. As shown in Tables 2 and 3, women with all 3 metabolic syndrome disorders had an age-adjusted mean LV mass that was on average 35% greater than those with no abnormalities compared with a 30% differential for men. Mechanisms that might account for any gender differences are unknown. Multivariable adjustment for smoking, alcohol use, and edu-

cation had relatively little impact, and additional adjustment for obesity attenuated these associations only slightly. Because of the well-established and strong relationship between obesity, particularly central adiposity, and metabolic syndrome abnormalities, multivariable analyses that adjusted for these factors were included. The failure of measures of adiposity to fully attenuate the association between the metabolic syndrome abnormalities and LV wall dimensions may have important potential implications for prevention of cardiac hypertrophy in blacks. Findings based on 39 years of observation by the Framingham Heart Study appear to indicate that strategies such as hypertension control may be useful in blacks with LV wall thickening.⁶⁷

There was little evidence that metabolic syndrome abnormalities were related to LV internal dimension (Tables 2 and 3). These analyses clearly identified wall thickening, as opposed to chamber size, as the primary modality by which metabolic syndrome abnormalities may influence cardiac structure in general and LV mass in particular. Such a pattern of results is consistent with a previous report from the Framingham Heart Study demonstrating a differential influence of BP on wall thickness and not on chamber size.⁶⁸ This finding, which represents a potential explanation for hypertrophy in black subjects with metabolic syndrome, seems to be consistent with other attempts^{3,5,6,41,69} to identify underlying mechanisms of hypertrophy in other racial groups.

There were several strengths of this study. Assessments of associations were based on a large community-based sample of black women and men who have been understudied and appear to be at elevated risk for cardiovascular disease. Measurements of risk factors and echocardiographic indices were standardized and consistent with other epidemiological studies of cardiovascular disease.

There were also several potential limitations of this study. The cross-sectional design precluded assessment of the temporality of the observed associations and thus determination of causality. American Society of Echocardiography criteria applied to the Troy formula¹⁴ to estimate LV mass without adjustment for the tendency for overestimation at autopsy¹⁵ were used to enable comparisons with earlier studies. The LV mass estimates in the present study may be $\approx 20\%$ higher than studies using this additional adjustment; however, associations examined between the metabolic syndrome and LV mass are unlikely to have been influenced by this approach. Because we examined associations involving multiple LV dimensions, it is possible that some of the significant results may have been due to chance. Participants who had adequate echocardiographic measurements may have differed from the entire Jackson cohort. As recently reported, compared with participants who had inadequate echocardiograms, those with valid echocardiograms were slightly older and had slightly larger waist circumference, slightly higher cholesterol and glucose levels, and more diabetes and glucose intolerance and yet did not differ in levels of BMI, BP, HDL cholesterol, triglycerides, physical activity, and alcohol intake.¹³ Although prevalence of the metabolic syndrome was slightly underestimated by focusing on participants with valid echocardiograms in the present study, recent evidence suggested that risk for cardiovascular events or death did not differ for

those with adequate and inadequate echocardiograms.⁷⁰ It is possible that participants who survived from baseline (1987–1989) to the echocardiogram examination (1993–1996) may have been less likely to have the metabolic syndrome and to have LV abnormalities than those who did not survive; such a survivor bias, if present, would be likely to have reduced the associations observed.

It is also possible that associations observed in the present study may not be generalizable to nonblack populations, although similar underlying mechanisms would be expected. In addition, because the components of the metabolic syndrome tended to be highly correlated with each other, it would be difficult to detect completely separate effects of each component. It is possible that in assessments of the influence of dyslipidemia and glucose intolerance (2-component model) on the left ventricle after adjustment for hypertension, there could still be some residual confounding by BP. Similarly, assessment of potential influences of obesity on these associations may also be difficult to discern because of its strong relationship with the metabolic syndrome components. In addition, if a more direct measure of intra-abdominal obesity were available, perhaps a stronger impact of obesity would have been evident. Our results indicated that waist circumference and BMI attenuated relationships somewhat, yet associations of the metabolic syndrome with LV wall thickness and mass remained statistically significant.

In summary, this report identified a strong relationship between metabolic syndrome abnormalities and LV mass, as measured by the echocardiogram, in middle-aged to elderly black women and men. This relationship appeared to be equally strong in women and men and was consistently evident when the sample was stratified by age and waist circumference. In addition, multivariable adjustments for age, stature, cigarette smoking, alcohol consumption, and education had minimal influence on the results. The attenuation of trends with adjustment for waist circumference suggests a role for central obesity, yet significant associations between the metabolic syndrome and LV mass persisted. Although hypertension tended to have a strong influence on LV mass, dyslipidemia and glucose intolerance also contributed; there was no evidence of a strong synergistic effect of the syndrome beyond the influence of its individual components. When the components used to calculate LV mass were examined for their relationship with metabolic syndrome abnormalities, only wall thickness and not LV internal dimension was related to these metabolic syndrome abnormalities. These findings are consistent with a possible influence of underlying factors such as insulin resistance and a hemodynamic or vascular process on myocardial thickening.

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