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Original Contribution

Association of Left Ventricular Hypertrophy With Incident Hypertension: The Multi-Ethnic Study of Atherosclerosis

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Increased left ventricular (LV) mass and changes in LV geometry may precede hypertension onset. The authors examined the associations of LV mass and geometry, assessed by cardiac magnetic resonance imaging, with hypertension incidence in 2,567 normotensive participants enrolled in 2000–2002 in the Multi-Ethnic Study of Atherosclerosis, an ethnically diverse, population-based, US study. Over a median follow-up of 4.8 years, 745 (29%) participants developed hypertension. In a fully adjusted model including baseline blood pressure, the relative risks of incident hypertension from the lowest to highest LV mass quartile were 1.00 (referent), 1.13 (95% confidence interval (CI): 0.89, 1.43), 1.28 (95% CI: 1.00, 1.63), and 1.78 (95% CI: 1.38, 2.30) ($P < 0.001$ for linear trend). Higher levels of LV concentric geometry, defined by higher LV mass to end-diastolic volume quartiles, were associated with higher risk of incident hypertension in a fully adjusted model ($P = 0.044$ for linear trend). In a final model containing both quartiles of LV mass and LV mass/volume along with all covariates including baseline blood pressure, higher LV mass quartiles were associated with incident hypertension ($P < 0.001$ for linear trend), whereas higher LV mass/volume quartiles were not ($P = 0.643$ for linear trend). In this multiethnic cohort, alterations in LV mass preceded hypertension onset among normotensive individuals.

hypertension; hypertrophy, left ventricular; magnetic resonance imaging; risk factors

Abbreviations: LV, left ventricular; MESA, Multi-Ethnic Study of Atherosclerosis; MRI, magnetic resonance imaging.

Hypertension is associated with markers of cardiovascular end-organ damage such as left ventricular (LV) hypertrophy. As such, LV hypertrophy is often thought to be a long-standing consequence of hypertension. However, some evidence suggests that increased LV mass precedes the onset of hypertension (1–6). Prospective studies have demonstrated a relation of higher levels of LV mass, assessed by echocardiography, with subsequent increases in blood pressure (1, 2) or a greater risk of incident hypertension (3–6) in individuals without hypertension. Thus, alterations in LV mass may contribute to a sustained increase in blood pressure. Although these data are intriguing, prior studies have been limited by a small sample size, adjustment for a limited number of possible confounders, a retrospective study design, and/or inclusion of a low number of African Americans and Hispanics, minority groups that have an increased risk of hypertension. Although 2 relatively large studies (4–6) have previously examined the relation between LV mass and incident hypertension, they were primarily restricted to a single ethnic group. One included white participants from the Framingham Heart and Offspring cohorts (4), and the other included American Indians from the Strong Heart Study (5, 6).

Hypertension is also associated with a spectrum of LV geometric changes (7, 8). LV concentric geometry—characterized by increased relative wall thickness (defined as the ratio of posterior wall thickness to LV radius) with and without increased LV mass on echocardiography—is one pattern observed in patients with hypertension (9). There is limited evidence that this geometric pattern may be associated with increases in blood pressure prior to the development of hypertension (1). Thus, in addition to the

degree of LV mass, an altered LV geometry, characterized by a concentric pattern, may contribute to hypertension onset.

Cardiac magnetic resonance imaging (MRI) is a well-validated methodology for assessment of 3-dimensional LV mass and geometry (10, 11), and it may allow for more in-depth investigation of the relation of LV mass and geometry with incident hypertension. We determined whether increased LV mass and, secondarily, concentric LV geometry, assessed by cardiac MRI, are associated with hypertension onset in the Multi-Ethnic Study of Atherosclerosis (MESA), an ethnically and geographically diverse, population-based cohort study of middle-aged and older men and women.

MATERIALS AND METHODS

Study population

Details of the MESA study design have been described elsewhere (12). Briefly, between July 2000 and August 2002, 6,814 community-dwelling adults aged 45–84 years and free of clinically evident cardiovascular disease were enrolled. Participants from 4 race/ethnic groups (white, African American, Hispanic, and Asian (primarily of Chinese descent)) were recruited from 6 US communities including Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; northern Manhattan, New York; and St. Paul, Minnesota. The study was approved by the institutional review boards of all sites, and written informed consent was obtained from all participants.

Of the 6,814 MESA participants, 5,004 (73%) completed the cardiac MRI testing at baseline (shortly after examination 1) and had technically adequate data for analysis. In addition to examination 1, blood pressure measurements were performed at subsequent examinations. Blood pressure data from examinations 1–4 were available for the analyses presented herein. Of the 5,004 participants with available cardiac MRI data at examination 1, we excluded those who had prevalent hypertension at examination 1 as defined below ($n = 2{,}315$), were missing examination 1 blood pressure values ($n = 1$), did not attend at least one follow-up visit ($n = 111$), and had no blood pressure measurements at follow-up despite attending the examination ($n = 10$). Thus, data for a total of 2,567 participants were available for analysis.

Baseline risk factor measures (examination 1)

Information on demographics, smoking, education, alcohol use, physical activity, and medical history were obtained using standardized questionnaires (12). Educational level was defined by the highest level achieved. Physical activity was defined as the total of all light, moderate, and vigorous activities multiplied by individual metabolic equivalent values for these activities. Anthropometric measurements of height and weight were determined with the use of calibrated scales. Body mass index was calculated as weight in kilograms divided by height in meters squared. Total cholesterol, high density lipoprotein cholesterol, triglycerides, and glucose were measured from blood samples obtained after a 12-hour overnight fast. The Friedwald equation was used to calculate low density lipoprotein cholesterol. Diabetes was defined as a fasting serum glucose $\geq$126 mg/dL or use of hypoglycemic drugs or insulin. Serum creatinine was measured, and estimated glomerular filtration rate was calculated by the Modification of Diet in Renal Disease equation. High-sensitivity C-reactive protein was measured using a particle enhanced immunonepholometric assay on a BNII nephelometer (Dade-Behring Inc., Newark, Delaware).

Baseline cardiac MRI

Cardiac MRI using 1.5-T magnets was performed a median of 16 days after examination 1; 95% of the MRI scans were completed by 11 weeks after examination 1 (13, 14). All MRI scans were acquired during short breath-holding at resting lung volume. A stack of short-axis images covering the entire left ventricle was acquired with time to repetition/time to echo as 8–10/3–5 milliseconds, flip angle 20°, 6-mm slice thickness, 4-mm gap, flow compensation, in-plane resolution 1.4–1.6 mm (frequency) $\times$ 2.2–2.5 mm. Images were transmitted using the DICOM transfer protocol to the MESA MRI reading center at Johns Hopkins University. Image data were analyzed using a semiautomated method (MASS software, version 4.2; Medis, Leiden, the Netherlands) by trained readers. The endocardial and epicardial myocardial borders were contoured, and the difference between the epicardial and endocardial areas for all slices was multiplied by the slice thickness and section gap and then multiplied by the specific gravity of myocardium (1.04 g/mL) to determine LV mass. Papillary muscle mass was included in the LV volume assessment and was excluded from LV mass assessment (13, 14). Repeat MRI measurements were performed on 79 randomly selected participants 3–6 months after the initial measurement. The technical error of measurement percentages of the mean were 6% and 4% for LV mass and LV end-diastolic volume, respectively, and the intraclass correlation coefficients were 0.98 and 0.98, respectively.

Blood pressure measurements and hypertension ascertainment (examinations 1–4)

Blood pressure was measured 3 times at 2-minute intervals using an automated oscillometric device (Dinamap Monitor Pro 100; GE Healthcare, Milwaukee, Wisconsin) after participants rested for 5 minutes in the seated position. Appropriate-sized cuffs were utilized for blood pressure assessment. Blood pressure was defined as the average of the second and third readings. Participants were asked about antihypertensive medication use.

Prevalent hypertension was defined by the presence of any of the following at examination 1: 1) self-reported history of hypertension, 2) systolic blood pressure $\geq$140 mm Hg or diastolic blood pressure $\geq$90 mm Hg, and/or 3) self-reported use of antihypertensive medication (15). As mentioned previously, these participants were excluded from the current analyses. For participants without hypertension at

baseline, the incidence of hypertension was defined as the first follow-up study examination with the presence of 1) systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, and/or 2) self-reported use of antihypertensive medication (15, 16).

Statistical analyses

The study population was divided into gender-specific quartiles of LV mass. Characteristics of the population and hypertension incidence were estimated for each quartile of LV mass. Unadjusted hypertension incidence rates were calculated as the number of events in each quartile of LV mass divided by the sum of person-years at risk. Time at risk was calculated as the number of days between examinations 1 and 4, unless a participant developed hypertension at an earlier visit (i.e., examinations 2 or 3) or did not attend examination 4. For those who developed hypertension, risk time was calculated as the time between examination 1 and the first examination at which hypertension was present. For those who did not attend examination 4, risk time was calculated as elapsed time from baseline to the last examination the participant attended (i.e., examination 2 for 74 participants and examination 3 for 84 participants).

Poisson regression was used to calculate the adjusted relative risks and 95% confidence intervals of hypertension associated with LV mass. Models with multivariable adjustment for covariates that might be related to LV mass and/or hypertension were fitted. Consistent with MESA guidelines, analyses were adjusted for body size by placing height and weight in the multivariable regression models. In the MESA study, LV mass indexed by height$^{2.7}$, which has not been validated for cardiac MRI, does not fully remove the correlation of this measure with weight or height (17). Models were also adjusted for additional potential confounders (all chosen a priori), including MESA site, age, gender, ethnicity, diabetes, cigarette smoking, alcohol use, educational level, physical activity, estimated glomerular filtration rate, C-reactive protein, and baseline blood pressure levels. Linear trends across quartiles were assessed by including quartile-specific median LV mass values as a continuous variable in the regression models. Deviation from linearity was assessed by including a quadratic term for each quartile. The association between LV hypertrophy and incident hypertension was also examined. LV hypertrophy was defined as levels greater than the gender-specific 95th percentile for LV mass (>203.5 g for men and >140.3 g for women), derived from a MESA reference sample, consisting of 822 participants who were of normal weight, did not have hypertension, and did not have diabetes or impaired fasting glucose levels (18).

Because angiotensin-converting enzyme inhibitors and angiotensin II antagonists may have been prescribed to participants with diabetes but without hypertension, we conducted sensitivity analyses for participants with and without diabetes. Additional analyses were conducted for subgroups defined by age (45–64 years and ≥65 years), gender, race/ethnicity, and prehypertension (systolic blood pressure 120–139 mm Hg or diastolic blood pressure 80–89 mm Hg).

We also examined the relation between LV concentric geometry, defined as the ratio of LV mass to end-diastolic volume (13), and incident hypertension. As recommended by MESA guidelines, parameters of body size were not used to index LV mass/volume ratio. There are only minor differences in the fit between models with LV mass/volume that adjust and do not adjust for body size (13). Otherwise, an analytical approach similar to the one used for LV mass was used. Abnormal LV mass/volume ratio was defined by levels greater than the gender-specific 95th percentile for LV mass/volume ratio (>1.47 g/mL for men and >1.29 g/mL for women), derived from the MESA reference sample (17).

To assess the independent association of LV mass and LV mass/volume ratio with incident hypertension, both variables were included in the same regression model. Variance inflation factors were calculated to examine the possible existence of multicollinearity among the measures. Statistical analyses were conducted with SAS 9.2 software (SAS Institute, Inc., Cary, North Carolina). P values of <0.05 were considered statistically significant.

RESULTS

Participant characteristics

Table 1 shows the baseline characteristics of the sample across quartiles of LV mass, before and after adjustment for height and weight. Linear trend for body mass index was not adjusted for height and weight because body mass index is estimated from both variables. After adjustment for height and weight, younger age, female gender, African-American ethnicity, cigarette smoking, alcohol use, higher levels of C-reactive protein, and higher levels of systolic blood pressure and pulse pressure were associated with higher levels of LV mass. Higher levels of body mass index were also associated with higher levels of LV mass. In contrast, Chinese ethnicity, reduced physical activity, and lower estimated glomerular filtration rate levels were associated with lower levels of LV mass after adjustment for height and weight.

Relation of LV mass with hypertension incidence

Over a median follow-up of 4.8 years (25th–75th percentiles: 4.5–5.0 years), 745 (29%) of the 2,567 participants developed hypertension. Higher LV mass quartiles were significantly associated with higher unadjusted incident hypertension rates (Table 2). This association remained significant in a fully adjusted model that included baseline blood pressure. Furthermore, there was no significant deviation from a linear trend across LV mass quartiles. The relation between LV mass and incident hypertension was similar across subgroups defined by age, gender, and race/ethnicity as well as among participants with and without diabetes and prehypertension (Figure 1).

The prevalence of LV hypertrophy was 13.1% in the study population and 52.2% among participants in the highest quartile of LV mass. In a fully adjusted model, LV hypertrophy was significantly associated with incident hypertension (relative risk = 1.41, 95% confidence interval: 1.15, 1.73; $P < 0.001$).

Table 1. Baseline Characteristics of MESA Participants Enrolled in 2000–2002 and Included in the Analysis of Incident Hypertension, by Quartile of Left Ventricular Mass

Characteristic	Quartile 1 (n = 641)	Quartile 2 (n = 642)	Quartile 3 (n = 642)	Quartile 4 (n = 642)	P-Trend[a]	P-Trend[b]
Left ventricular mass, g						
Women	<99.5	99.5–114.2	114.3–130.7	≥130.8		
Men	<139.2	139.3–160.7	160.8–183.5	≥183.6		
Mean age (SD), years	60.9 (9.9)	58.5 (9.7)	57.3 (9.1)	56.4 (8.9)	<0.001	<0.001
Female gender, %	51.8	51.9	51.9	51.7	0.978	<0.001
Ethnicity, %						
White	37.1	45.5	48.4	42.2	0.038	0.193
Chinese American	30.9	16.7	7.2	2.7	<0.001	<0.001
African American	12.2	14.3	19.8	30.8	<0.001	<0.001
Hispanic	19.8	23.5	24.6	24.3	0.051	0.421
Current smoker, %	9.2	12.6	13.9	22.0	<0.001	<0.001
Alcohol user, %	51.3	59.0	68.4	65.0	<0.001	<0.001
High school graduate, %	82.4	84.6	86.3	88.9	<0.001	0.116
Median physical activity (25–75th percentile), METs-minutes/week	6.7 (4.6–10.1)	7.5 (5.2–10.9)	7.6 (5.3–11.0)	8.2 (5.6–11.7)	<0.001	<0.001
Mean body mass index (SD), kg/m^2	24.1 (3.7)	26.2 (3.7)	27.5 (4.2)	29.9 (5.0)	<0.001	N/A
Median CRP (25–75th percentile), mg/L	1.2 (0.6–2.9)	1.4 (0.6–3.3)	1.5 (0.7–3.4)	1.9 (0.9–4.3)	<0.001	0.043
Mean eGFR (SD), mL/minute per 1.73 m^2	75.4 (13.7)	75.4 (13.9)	76.2 (14.2)	78.6 (14.7)	<0.001	0.009
Reduced eGFR[c], %	12.8	11.1	9.2	9.4	0.025	0.074
Microalbuminuria, %	4.2	4.7	5.8	6.9	0.024	0.427
Diabetes, %	4.5	5.3	6.5	6.1	0.147	0.444
Mean systolic blood pressure (SD), mm Hg	111.6 (13.2)	112.8 (12.8)	115.1 (12.7)	117.3 (12.3)	<0.001	<0.001
Mean diastolic blood pressure (SD), mm Hg	67.1 (8.6)	68.5 (8.6)	69.7 (8.6)	70.2 (8.5)	<0.001	0.790
Pulse pressure (SD), mm Hg	44.5 (10.6)	44.3 (10.4)	45.4 (9.9)	47.1 (10.2)	<0.001	<0.001

Abbreviations: CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent value; N/A, not applicable; SD, standard deviation.

[a] Unadjusted for body size.

[b] Adjusted for height and body weight, except for body mass index. Linear trend for body mass index was not adjusted for height and weight because body mass index is estimated from both variables.

[c] Defined by an eGFR of <60 mL/minute per 1.73 m^2.

Relation of LV geometry with hypertension incidence

Higher quartiles of LV mass to end-diastolic volume ratio were associated with significantly higher unadjusted rates of incident hypertension (Table 3). The linear trend across LV mass/volume quartiles was also significant in adjusted models. There was no significant deviation from a linear trend in unadjusted and adjusted models. In a fully adjusted model (Table 3, model 3), none of the individual upper 3 LV mass/volume quartiles was significantly associated with incident hypertension. The prevalence of abnormal LV mass/volume ratio was 9.2% in the study population. In a fully adjusted model, the relation between abnormal LV mass/volume ratio and incident hypertension was not significant (relative risk = 1.23, 95% confidence interval: 1.00, 1.51; $P = 0.051$).

After both LV mass quartiles and LV mass/volume quartiles were placed in the same model along with all covariates including baseline blood pressure, the relative risks of incident hypertension were 1.00 (referent), 1.13 (95% confidence interval: 0.89, 1.44), 1.37 (95% confidence interval: 0.99, 1.63), and 1.76 (95% confidence interval: 1.34, 2.30) for the lowest to highest quartile of LV mass ($P < 0.001$ for linear trend). In this model, the relative risks for incident hypertension associated with the lowest to highest quartile of LV mass/volume were 1.00 (referent), 1.01 (95% confidence interval: 0.80, 1.28), 0.97 (95% confidence interval: 0.76, 1.23), and 1.04 (95% confidence interval: 0.82, 1.31). The linear trend across LV mass/volume quartiles was not significant ($P = 0.643$). The correlation coefficient of LV mass with LV mass/volume was 0.44 ($P < 0.001$). Furthermore, the variance inflation factors for LV mass and LV mass/volume were 3.20 and 1.46, respectively, indicating no strong evidence of multicollinearity among the predictors (19).

DISCUSSION

Increased LV mass has been proposed to be a compensatory response to elevated blood pressure (20). However, evidence

Table 2. Incident Rates and Relative Risks of Incident Hypertension for MESA Participants Enrolled in 2000–2002, by Left Ventricular Mass Quartile

	No. of Cases	IR	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
			RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Quartile 1 ($n = 641$)	141	4.8	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Women (<99.5 g)										
Men (<139.2 g)										
Quartile 2 ($n = 642$)	154	5.3	1.08	0.86, 1.37	1.22	0.96, 1.54	1.22	0.96, 1.55	1.13	0.89, 1.43
Women (99.5–114.2 g)										
Men (139.2–160.7 g)										
Quartile 3 ($n = 642$)	182	6.2	1.28	1.01, 1.61	1.52	1.20, 1.94	1.57	1.23, 2.00	1.28	1.00, 1.63
Women (114.3–130.7 g)										
Men (160.8–183.5 g)										
Quartile 4 ($n = 642$)	268	9.2	1.82	1.43, 2.31	2.24	1.75, 2.88	2.32	1.80, 3.00	1.78	1.38, 2.30
Women (≥130.8 g)										
Men (≥183.6 g)										
P value[e]		<0.001	<0.001		<0.001		<0.001		<0.001	
P value[f]		0.345	0.420		0.762		0.887		0.415	

Abbreviations: CI, confidence interval; IR, incidence rate of hypertension (per 100 person-years); MESA, Multi-Ethnic Study of Atherosclerosis; Ref, referent category; RR, relative risk.

[a] Model 1 includes adjustment for height, weight, and MESA site.

[b] Model 2 includes adjustment for variables in model 1 + age, gender, and ethnicity.

[c] Model 3 includes adjustment for variables in model 2 + baseline information on diabetes, smoking, alcohol use, socioeconomic level (educational level), physical activity, estimated glomerular filtration rate, and C-reactive protein.

[d] Model 4 includes adjustment for variables in model 3 + baseline blood pressure levels (systolic and diastolic).

[e] Represents the linear trend across quartiles (with each quartile represented by the median value within the quartile).

[f] Represents the deviation from a linear trend across quartiles (with each quartile represented by the median value within the quartile).

is increasing that LV mass is associated with development of hypertension (1–6). A few population-based studies (4–6) have examined whether LV mass is associated with subsequent hypertension onset. Post et al. (4) found that, after adjustment for age, gender, body mass index, alcohol intake, and blood pressure levels, increased LV mass, assessed by M-mode echocardiography, predicted hypertension at 4 years of follow-up in 2,680 normotensive participants in the Framingham Heart Study and Framingham Offspring Study. De Simone et al. (5) showed that, after controlling for gender, body mass index, systolic blood pressure, homeostatic model assessment index, and diabetes, increased LV mass, assessed by M-mode or linear 2-dimensional echocardiography, was associated with incident hypertension over 4 years in 777 American Indians from the Strong Heart Study who had optimal blood pressure levels (<120/80 mm Hg). De Marco et al. (6) found a similar independent relation between LV mass and incident hypertension in 625 prehypertensive participants in the Strong Heart Study.

These studies enrolled a low number of African-American and Hispanic participants and controlled for a limited number of potential confounders. Our results extend the findings of these studies by demonstrating that increased LV mass, assessed by cardiac MRI, is associated with incident hypertension in a large, multiethnic, population-based cohort. This relation was present after adjustment for several important confounders. Findings were also consistent across age, gender, and race/ethnicity categories.

In the present study, although the linear trend for incident hypertension across LV mass/volume quartiles was statistically significant in a fully adjusted model, none of the upper 3 LV mass/volume quartiles was significantly associated with incident hypertension. Furthermore, abnormal LV mass/volume ratio was not significantly associated with incident hypertension in a fully adjusted model. Iso et al. (1) found, in normotensive men from a rural community in Japan, that increased LV mass was more strongly related to subsequent blood pressure increases in men with smaller LV chamber dimensions compared with men with larger LV dimensions, suggesting that LV concentric geometry may play a role in blood pressure increases. In contrast, other studies (3, 5, 6) found that LV concentric geometry, expressed as relative wall thickness, was not associated with incident hypertension. Reasons for these variable findings are unknown but may include differences in characteristics of the study population and in how LV concentric geometry on echocardiography was defined.

In the present study, in a model that contained both LV mass and LV mass/volume, the relation between LV mass quartiles and incident hypertension was unchanged. In contrast, the magnitude of the relative risks of incident hypertension associated with the upper 3 LV mass/volume quartiles became weaker, and the linear trend was no longer significant. These results suggest that LV concentric geometry does not contribute to hypertension onset in an LV-mass-independent manner.

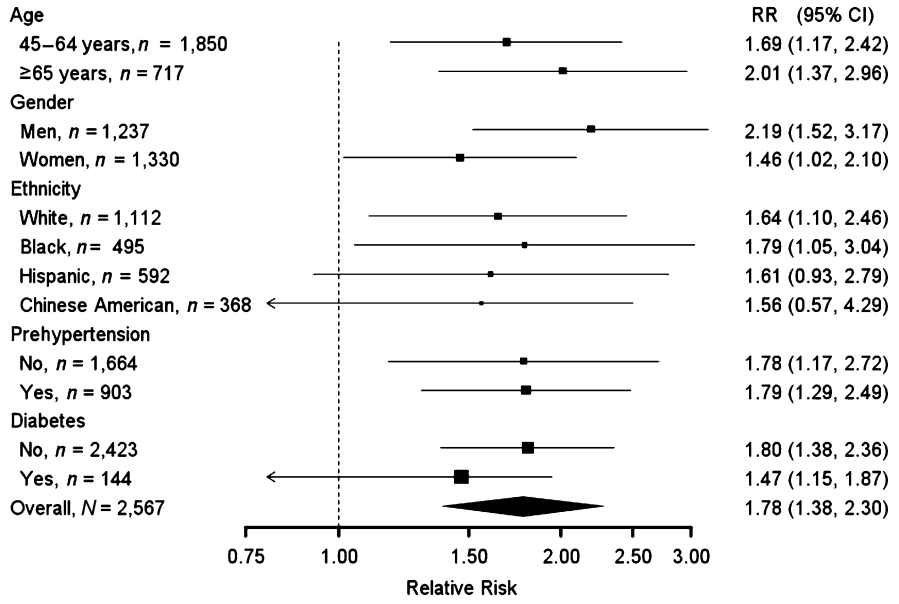

Figure 1. Subgroup analyses of the association between left ventricular mass and incident hypertension for Multi-Ethnic Study of Atherosclerosis participants enrolled in the study in 2000–2002. $P > 0.20$ for all interactions. Relative risks (RRs) for the highest quartile versus the lowest quartile (referent category) are adjusted for height, weight, study site, age, gender, ethnicity, diabetes, smoking, alcohol use, socioeconomic level (educational level), physical activity, estimated glomerular filtration rate, C-reactive protein, and baseline blood pressure levels (systolic and diastolic). Prehypertension was defined as a baseline systolic blood pressure of 120–139 mm Hg or a diastolic blood pressure of 80–89 mm Hg. Each box represents the relative risk, with its size being inversely proportional to its standard error. CI, confidence interval.

There are several possible explanations for our findings. The underlying mechanisms responsible for increased LV mass in the absence of hypertension, and for hypertension onset, are complex and probably multietiologic. Genetic factors could play a role in promoting myocardial hypertrophy and hypertension onset (21, 22). Extracardiac factors such as an exaggerated sympathetic drive and a dysregulated renin-angiotensin-aldosterone system (23), in addition to vascular structural changes such as arterial stiffness (8), may also have influenced both LV mass and later hypertension incidence.

Another explanation is that increased LV mass itself exacerbates the underlying mechanisms responsible for blood pressure elevation. Early in the course of hypertension, increased LV mass is associated with increased stroke volume, cardiac output, and central blood volume; later in the disease process, these parameters fall to normal levels, but systemic vascular resistance rises (24–26). Thus, in some individuals, increased LV mass may promote arterial hemodynamic changes in hypertension onset.

Finally, the relation between LV mass and incident hypertension could have been explained by elevated blood pressure levels at baseline, particularly in the prehypertension range. The risk of incident hypertension is higher for individuals with prehypertension than for those with optimal blood pressure levels (27). Additionally, prehypertension is also associated with markers of end-organ damage including increased LV mass (28) and cardiovascular events (29). However, the fully adjusted model included baseline blood pressure as a covariate, and the relation between LV mass and incident hypertension remained significant in this model. Results were also robust in analyses excluding participants with prehypertension, indicating that the independent relation between LV mass and incident hypertension is present even for individuals with optimal blood pressure levels. These findings are consistent with those reported by de Simone et al. (5).

Regardless of how LV mass and geometry are related to the development of hypertension, an argument could be made to perform imaging such as cardiac MRI or echocardiography to identify nonhypertensive individuals at risk of hypertension, because the risk for hypertension cannot be fully explained by demographics and clinical risk factors (30). However, it is premature to routinely recommend cardiovascular imaging of all hypertension-free individuals.

There are several limitations to our study. The follow-up period was relatively short, and blood pressure was measured at discrete time points during the follow-up period. Because the results of the cardiac MRI were available to the MESA participants, it is possible that initiation of antihypertensive medications was influenced by physician knowledge of the degree of LV mass, thereby affecting the outcome of incident hypertension. However, it is unlikely that a physician would start antihypertensive medications for a patient with increased LV mass without first confirming a diagnosis of hypertension. Furthermore, the relation between LV mass and incident hypertension was similar (data not shown) when the outcome was defined solely by blood pressure levels ($\geq$140/90 mm Hg). Additionally,

Table 3. Incident Rates and Relative Risks of Incident Hypertension for MESA Participants Enrolled in 2000–2002, by Left Ventricular Mass/Volume Quartile

	No. of Cases	IR	Model 1[a]		Model 2[b]		Model 3[c]	
			RR	95% CI	RR	95% CI	RR	95% CI
Quartile 1 ($n = 641$)	129	4.3	1.00	Ref	1.00	Ref	1.00	Ref
Women (<0.92 g/mL)								
Men (<1.03 g/mL)								
Quartile 2 ($n = 642$)	167	5.7	1.24	0.99, 1.57	1.23	0.97, 1.55	1.08	0.86, 1.37
Women (0.92–1.02 g/mL)								
Men (1.03–1.14 g/mL)								
Quartile 3 ($n = 643$)	180	6.1	1.29	1.03, 1.62	1.25	0.99, 1.57	1.07	0.85, 1.34
Women (1.03–1.14 g/mL)								
Men (1.15–1.28 g/mL)								
Quartile 4 ($n = 641$)	269	9.5	1.75	1.41, 2.17	1.66	1.34, 2.06	1.24	0.99, 1.55
Women (≥1.15 g/mL)								
Men (≥1.29 g/mL)								
P value[d]		<0.001	<0.001		<0.001		0.044	
P value[e]		0.634	0.861		0.831		0.710	

Abbreviations: CI, confidence interval; IR, incidence rate of hypertension (per 100 person-years); MESA, Multi-Ethnic Study of Atherosclerosis; Ref, referent category; RR, relative risk.

[a] Model 1 includes adjustment for age, gender, ethnicity, and MESA site.

[b] Model 2 includes adjustment for variables in model 1 + baseline information on diabetes, smoking, alcohol use, socioeconomic level (educational level), physical activity, estimated glomerular filtration rate, and C-reactive protein.

[c] Model 3 includes adjustment for variables in model 2 + baseline blood pressure levels (systolic and diastolic).

[d] Represents the linear trend across quartiles (with each quartile represented by the median value within the quartile).

[e] Represents the deviation from a linear trend across quartiles (with each quartile represented by the median value within the quartile).

blood pressure readings at baseline were obtained at a single visit, which may have resulted in inclusion of participants with prevalent hypertension. However, the results were not different when we excluded participants with blood pressures in the prehypertension range. Finally, because ambulatory blood pressure was not monitored, we cannot exclude the possibility that some participants with increased LV mass at baseline had masked hypertension (i.e., normal office blood pressure and elevated ambulatory blood pressure).

Strengths of the current study include the use of a large, multiethnic cohort drawn from several communities in the United States; the prospective study design; and the careful and standardized assessment of cardiovascular risk factors, including blood pressure readings across time. MESA is also the first large-scale epidemiologic study to use cardiac MRI to assess LV structure and function in enrolled participants (13, 14). Compared with other imaging modalities such as echocardiography, cardiac MRI has a higher degree of accuracy and reproducibility for assessing LV mass and geometry. Thus, MESA offered a unique opportunity to examine the independent relation of LV mass and LV concentric geometry with incident hypertension.

In summary, higher levels of LV mass and LV hypertrophy were significantly associated with a higher risk of incident hypertension for individuals who were initially normotensive, independent of baseline blood pressure levels and other explanatory factors. These findings suggest that the relation between hypertension and alterations in LV structure may involve more than one directional pathway. Future studies should confirm these findings and investigate the factors that increase LV mass in the absence of hypertension.

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