Prognostic Implications of Left Ventricular Mass Among Hispanics

The Northern Manhattan Study

Carlos J. Rodriguez, Fay Lin, Ralph L. Sacco, Zhezhen Jin, Bernadette Boden-Albala, Shunichi Homma, Marco R. Di Tullio

Abstract—Hispanics may carry a similar burden of increased left ventricular mass (LVM) as non-Hispanic blacks but whether LVM portends a worse outcome among Hispanics is largely unknown. We prospectively evaluated 1081 Hispanics enrolled in the Northern Manhattan Study during the period of 1993 to 2001. Subjects were aged ≥40 years and free of prior myocardial infarction or stroke. LVM was defined echocardiographically and indexed for height2.7. Cox proportional hazards models were used to assess the risk of vascular events with adjustments for age, gender, systolic blood pressure, diabetes, and smoking. LVM averaged 48.4 ± 15 gm/ht2.7 and on multivariate analysis was significantly associated with the combined end point of myocardial infarction, stroke, or vascular death (adjusted hazard ratio 1.34 per SD change in LVM [95% CI 1.10 to 1.63]). During a mean of 57 months of follow-up, 74 vascular events occurred. The annual rate of vascular events was 21.8 per 1000 patient-years in the highest quartile of LVM and 8.6 per 1000 patient-years in the lowest quartile (P = 0.007). These data demonstrate in a large population-based sample that increased LVM yields independent prognostic information among Hispanics, predicting a higher incidence of events attributable to vascular disease in this understudied population. Our findings identify the Hispanic population with increased LVM as a high-risk subgroup. (Hypertension. 2006;48:87-92.)

Key Words: hypertrophy ■ ethnic groups ■ epidemiology ■ prospective studies ■ hypertension ■ echocardiography

Epidemiologic data have shown that echocardiographic left ventricular hypertrophy (LVH) as defined by increased left ventricular mass (LVM) is an independent predictor of morbidity and mortality from vascular disease.1–4 Increased LVM has recently been shown to be an important independent modifiable risk factor for cardiovascular disease, with reduction of LVM during antihypertensive treatment being associated with lower rates of cardiovascular morbidity and mortality.5 Increased LVM has particular importance in minority populations. Non-Hispanic blacks are known to have a higher average LVM and have more prevalent and worse LVM-related outcomes than non-Hispanic whites,3,6–10 with generally less information available about Hispanics.

Hispanics appear to have an increased burden of increased LVM, comparable with non-Hispanic blacks.4,14 However, the prognostic value of increased LVM has not been demonstrated in Hispanics. The present study characterizes the prognostic value of left ventricular mass among Hispanics.

Methods

Subjects were participants in the NOrthern MAnhattan Study (NOMAS), a population-based prospective cohort study from Northern Manhattan, NY. The methods of subject recruitment and enrollment into NOMAS have been described elsewhere.4,15 Briefly, random digit dialing was performed, and community participants were enrolled. NOMAS entry criteria included (1) age ≥39 years, (2) no prior diagnosis of stroke, and (3) residing in Northern Manhattan for at least 3 months. Subjects with prior myocardial infarction at enrollment were excluded.

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from this analysis. The study was approved by the Institutional Review Board at Columbia University Medical Center (CUMC). Race-ethnicity was based on self-identification in response to a questionnaire modeled after the 2000 US census and conformed to the standard definitions outlined by Directive 15. As part of NOMAS, 1730 participants were self-identified as Hispanic and underwent extensive in-person evaluation. Of the participants, 1623 did not have a prior myocardial infarction. Transthoracic echocardiograms were performed on 1118 eligible subjects, of whom 1081 (97%) were technically adequate for analysis of LVM and are included in this study.

Baseline evaluation was performed at enrollment as previously reported. Assessments were conducted in English or Spanish, depending on the primary language of the participant. Cardiovascular risk factors were collected by direct interview using standardized questions adapted from the Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System or by medical record review. Hypertensive status was defined as a systolic blood pressure recording ≥140 mm Hg or a diastolic blood pressure recording ≥90 mm Hg based on the mean of the 2 readings of the blood pressure measurements, a patient’s self-report of a history of hypertension, or antihypertensive medication use. A history of diabetes mellitus was defined by a patient’s self-report of a history of diabetes, insulin use, oral hypoglycemic use, or a fasting glucose ≥126 mg/dL. Hypercholesterolemia was defined as total serum cholesterol ≥240 mg/dL or a patient’s self-report of hypercholesterolemia or the presence of lipid-lowering treatment. The presence of atrial fibrillation was documented based on the results of a current or past ECG. Body mass index was calculated as weight (kilograms) divided by height (meters) squared. Smoking was defined by a history of cigar or cigarette smoking.

Transthoracic echocardiography was performed and measurements taken according to standard two-dimensional protocols formulated by the American Society of Echocardiography (ASE). Two-dimensional–guided M-mode methods for determining LVM are widely used, have shown exceptional reliability, and have been well validated in autopsy studies. LV posterior wall thickness—(LV internal diameter)3

Since the ASE LVM overestimates autopsy LVM by 20%, the modified ASE formula proposed by Devereux et al was applied: LVM = 0.8 (ASE LVM) + 0.6

LVM was then indexed to body size by dividing raw LVM by height to the allometric power of 2.7 and analyzed as a continuous and categorical variable. LVH was defined as LVM to the allometric power of 2.7 and analyzed as a continuous and independent, and the NOMAS principal investigator (R.L.S.) adjudicated any disagreements. Myocardial infarction was defined by criteria adapted from the Cardiac Arrhythmia Suppression Trial and the Lipid Research Clinics Coronary Primary Prevention Trial requiring at least 2 of the 3 following criteria:

(1) ischemic cardiac pain determined to be typical angina; (2) cardiac enzyme abnormalities defined as abnormal creatine phosphokinase MB isoenzyme (CPK-MB) fraction or troponin I values; and/or (3) ischemic EKG abnormalities. The presence of a myocardial infarct was decided by consensus (C.J.R., M.R.D., S.H.). For subjects who died, deaths were classified as vascular or nonvascular based on information obtained from the family, medical records, and death certificate. Only vascular deaths were used for this analysis. The first cardiovascular event, whether stroke, myocardial infarct, or death, was counted as an end point for the purposes of this analysis. Because CUMC is the major hospital for entire catchment area of Northern Manhattan, the majority of events were hospitalized at CUMC, allowing access to information on admitting clinical syndrome, blood test, and imaging studies. For hospitalizations outside of CUMC, records were also obtained, however to avoid potential misclassification, the final adjudication of outcome event was made by a NOMAS investigator.

Statistical Methods
Means±SD were calculated for continuous variables, and proportions were used for categorical variables. The distribution of demographic and vascular disease risk factors was evaluated in the total cohort and among the groups with and without LVH using unified LVM criteria. Kaplan-Meier survival analysis was performed for vascular events with and without LVH, with the difference between groups evaluated by means of the log-rank test. Cox proportional hazards models were used to assess the risk of vascular events for LVH as a continuous variable with adjustments for significant covariates in univariate analysis. Statistical significance was determined at the α=0.05 level using 2-sided tests. Quartiles of LVM were derived, and the number of observed vascular events ascertainment in each quartile. Cutoffs for LVM quartiles are ≤38.2 gm/ht2.7, >38.2 gm/ht2.7 to ≤46.2 gm/ht2.7, >46.2 gm/ht2.7 to ≤55.4 gm/ht2.7, and >55.4 gm/ht2.7. Event rates, including multiple events in the same patient, are presented as the number per 1000 patient-years. Poisson regression model was used to compare person-year event rates between the highest and lowest quartiles. To determine whether the association between LVH and cardiovascular events differed by significant covariates, we tested for interactions in our multivariate model. Statistical analyses were conducted using SAS 8.2 computer software (SAS Institute, Cary, NC).

Results
Baseline cohort characteristics are summarized in Table 1. The distribution of our Hispanic population was 62% Domin-

**TABLE 1. Baseline Characteristics of the Study Population**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort (n=1081)</th>
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>65.3±8.5</td>
</tr>
<tr>
<td>Women, %</td>
<td>60.5</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>68.1</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>144.1±21.0</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>84.9±10.9</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>202.0±40.4</td>
</tr>
<tr>
<td>LDL, mg/dl</td>
<td>129.8±35.3</td>
</tr>
<tr>
<td>HDL, mg/dl</td>
<td>43.5±12.8</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>146.5±87.2</td>
</tr>
<tr>
<td>LVM, gm/ht2.7</td>
<td>48.4±15.0</td>
</tr>
<tr>
<td>Prevalence of LVH, %</td>
<td>35.7</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>22.7</td>
</tr>
<tr>
<td>Ever smoked, %</td>
<td>49.3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>28.2±4.9</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index.
ican Republic, 14% Puerto Rican, 12% Cuban, and 12% from Mexico, Central America, and South America. This was a predominantly elderly population, with a mean age of 65.3 years (age range 40 to 107 years). The majority were women. Hypertension was extremely common, with a mean systolic blood pressure of 144.1 mm Hg; approximately 68% of our community-based Hispanic cohort were hypertensive, 46.5% were hyperlipidemic, and 28.3% were obese (body mass index >30). Among the total cohort, mean LVM was 48.4±1.5 gm/ht2.7 with a prevalence of LVH of 35.7% using a unified gender-independent cutoff of 51 gm/ht2.7.

All 1081 subjects were followed for a mean of 57.4±23.3 months, during which 74 vascular events occurred (6.9% of the population). Overall, there were 29 subjects with a myocardial infarction (includes 2 subjects with stroke), 38 with stroke (including 5 subjects with myocardial infarction), and 27 with vascular deaths (includes 13 subjects with myocardial infarction and/or stroke). The median follow-up in those without events was 56 months with 90% having 36 months or more of follow-up. Variables found to be significantly associated with risk of vascular events on univariate analysis were age (P<0.0001), diabetes (P<0.0001), hypertensive status (P=0.003), prior tobacco history (P=0.02), and LVM (P<0.0001) (Table 2). Incidence of total vascular events by LVM quartiles is shown in Figure 1. The annual rate of vascular events was 21.8 per 1000 patient-years in the highest quartile of LVM and 8.6 per 1000 patient-years in the lowest quartile (P=0.007). Thus, being in the highest quartile of LVM carried an almost 3-fold risk of vascular events among our Hispanic cohort (unadjusted hazard ratio [HR] 2.6; 95% CI 1.4 to 5.2). Kaplan-Meier curves (Figure 2) show a 92% event-free survival for those without LVH and 88% for those with LVH at 84 months. The log rank test P value is 0.026.

With significant risk factors identified in univariate analysis, the possible departure of LVM from linearity was examined by including a term of squared LVM. The coefficients of squared LVM were not significantly different from zero (P=0.325 for combined vascular events, P=0.542 for myocardial infarction, P=0.724 for ischemic stroke and P=0.322 for vascular death). The results of multivariate analyses are shown in Tables 2 and 3. LVM was significantly associated with risk of stroke, myocardial infarction, or vascular death after adjustment for age, systolic blood pressure, diabetes, and smoking. The adjusted HR for combined vascular events was 1.34 per 15.0 gm/ht2.7 (1 SD) change in LVM (95% CI 1.10 to 1.63). Specifically, there was a 50% increase in risk of myocardial infarction, a 13% increase in risk of ischemic stroke (did not reach statistical significance), and a 70% increase in risk of vascular death per SD increase in LVM (Table 3). The relation between LVM and cardiovascular events did not differ by age, diabetic status, or systolic blood pressure (P>0.20 for each interaction).

### Discussion

LVM carries important and powerful prognostic information demonstrated mainly in non-Hispanic whites and non-Hispanic blacks. Hispanics currently represent the largest single minority ethnic group in the United States, however little prospective prognostic information has been available regarding LVM in Hispanics. We show for the first time that LVM has a significant prognostic value for cardiovascular events among Hispanics. In this population-based sample free of known stroke or myocardial infarction at baseline, we found that the HR for combined cardiovascular events increased by 34% for every 15.0 gm/ht2.7 increase in LVM.

**TABLE 2. Combined Vascular Events by Univariate and Multivariate Adjusted Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted Hazard Ratios (95% Confidence Intervals)</th>
<th>P Value</th>
<th>Adjusted Hazard Ratios (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM per SD, gm/ht2.7</td>
<td>1.46 (1.23–1.73)</td>
<td>&lt;0.0001</td>
<td>1.34 (1.10–1.63)</td>
<td>0.0033</td>
</tr>
<tr>
<td>Age</td>
<td>1.09 (1.06–1.12)</td>
<td>&lt;0.0001</td>
<td>1.09 (1.06–1.12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td>1.29 (0.82–2.04)</td>
<td>0.2767</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.46 (0.60–10.05)</td>
<td>0.2108</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.52 (1.59–4.00)</td>
<td>&lt;0.0001</td>
<td>2.57 (1.61–4.11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>1.02 (1.01–1.03)</td>
<td>0.0012</td>
<td>1.01 (0.99–1.02)</td>
<td>0.1600</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.92 (0.58–1.46)</td>
<td>0.7285</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of tobacco use</td>
<td>1.74 (1.09–2.78)</td>
<td>0.0208</td>
<td>1.79 (1.12–2.87)</td>
<td>0.0158</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.99 (0.95–1.04)</td>
<td>0.7395</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
independent of age, systolic blood pressure, diabetes, and smoking. The HRs for LVM and LVH in the Hispanic population are comparable in magnitude to the risk derived from previous community cohorts of other races. Furthermore, the prevalence of LVH in the Hispanic community has not been previously described. We document an LVH prevalence of 35.7% among Hispanics, which is substantially higher than that found in the predominantly white population of Framingham Heart Study\textsuperscript{2} and comparable with the LVH prevalence seen among non-Hispanic blacks.

No other cohort studying the prognosis of LVM has included a significant proportion of Hispanics. The Hypertension Optimal Treatment (HOT) echocardiographic substudy cohort, with a total of 527 participants, included 16% Hispanics, but did not study clinical outcomes among this particular subgroup.\textsuperscript{26} The HOT substudy investigators did demonstrate a higher LVM among Hispanics compared with Non-Hispanic whites and Non-Hispanic blacks.\textsuperscript{14} Because LVH is more common among Non-Hispanic black and female patients with coronary artery disease, it accounts for a greater population attributable risk in these groups than among Non-Hispanic white males\textsuperscript{6}; our results suggest that LVH has a significant public health impact among Hispanics as well.

In the National Health And Nutrition Examination Survey (NHANES) III, awareness, treatment, and control of hypertension were worse among Hispanics than among Non-Hispanic whites and Non-Hispanic blacks. Treatment of hypertension can decrease LVM, and recent data demonstrate that reduction of LVM during antihypertensive treatment, independent of therapy and blood pressure effect, is associated with decreased morbidity and mortality.\textsuperscript{5} With this background, our results demonstrate an increased risk of vascular events with increased LVM among Hispanics, suggesting that we may be underestimating and undertreating a major modifiable risk factor among this rapidly growing ethnic group.

Additionally, there is a remarkable dearth of information regarding the prevalence and correlates of hypertension in Hispanics in the United States. NHANES and the San Antonio Heart Study, where the Hispanics are of Mexican-American origin, report that the prevalence of hypertension is highest in non-Hispanic blacks and lowest in Mexican-Americans.\textsuperscript{27,28} However, in the Northeastern United States, the term "Hispanic" typically refers to people of Caribbean origin, who are presumably more closely related to non-Hispanic blacks than Mexicans.\textsuperscript{29} Very little has been published about the prevalence of hypertension in Caribbean-Hispanics, and NOMAS appears to be one of the few population-based studies to have recorded such data. Among Hispanic participants in NOMAS the prevalence of hypertension appears to be fairly high (68%). This contrasts with NHANES and the San Antonio Heart Study, where the prevalence of hypertension was highest among non-Hispanic blacks and lowest among Mexican-Americans.\textsuperscript{27,30} Hispanics in the United States are more likely to be living in poverty than non-Hispanic whites, according to the US census.\textsuperscript{31} There is suggestive evidence that the high prevalence of hypertension in non-Hispanic

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### TABLE 3. Risk of Outcome Events per SD Increment of Left Ventricular Mass Adjusted for Significant Covariates

<table>
<thead>
<tr>
<th>Outcome Event</th>
<th>Adjusted Hazard Ratios</th>
<th>95% CI</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction*</td>
<td>1.50</td>
<td>1.12–2.02</td>
<td>0.007</td>
</tr>
<tr>
<td>(n=1081, event=29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke†</td>
<td>1.13</td>
<td>0.84–1.51</td>
<td>0.434</td>
</tr>
<tr>
<td>(n=1081, event=38)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular death‡</td>
<td>1.70</td>
<td>1.33–2.18</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(n=1073, event=27)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for age, systolic blood pressure, diabetes, and smoking.
†Adjusted for age, systolic blood pressure, and diabetes.
‡Adjusted for age and systolic blood pressure.
blacks may be in part environmental and psychosocial, and thus possibly more related to low socioeconomic status than to genetic factors. Given that Hispanics in New York have similar socioeconomic status levels to non-Hispanic blacks, the NOMAS finding is not unexpected. However, if socioeconomic status was the predominant factor, then Mexican-Americans should also be similarly affected. Genes are obviously also important, as is their interaction with environmental and psychosocial factors. Further research is needed in this area.

Limitations
The cutoff values used in this study as reference were derived from predominantly Non-Hispanic white populations and thus may not necessarily apply to other races. Our population sample was predominantly Caribbean-Hispanic (88%), but other Hispanic subgroups were also represented with subjects reporting origins from Mexico and South America. Comparative studies of risk in Hispanics in comparison with other ethnic groups, or between Hispanic subgroups, will require larger data sources such as NHANES III.

Perspectives
Our data demonstrate in a large population-based sample that increased LVM yields independent prognostic information among Hispanics, predicting a higher incidence of adverse vascular events in this understudied population. Our findings identify the Hispanic population with increased LVM as a high-risk subgroup. Although no specific guidelines exist to address the issues of hypertension and LVH among the Hispanic population as has been done with non-Hispanic blacks, our study suggests that the Hispanic population is at high risk for hypertension and its adverse sequelae.

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Disclosures
None.

References


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