Determinants of Discrepancies in Detection and Comparison of the Prognostic Significance of Left Ventricular Hypertrophy by Electrocardiogram and Cardiac Magnetic Resonance Imaging

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Despite the low sensitivity of the electrocardiogram (ECG) in detecting left ventricular hypertrophy (LVH), ECG-LVH is known to be a strong predictor of cardiovascular risk. Understanding reasons for the discrepancies in detection of LVH by ECG versus imaging could help improve the diagnostic ability of ECG. We examined factors associated with false-positive and false-negative ECG-LVH, using cardiac magnetic resonance imaging (MRI) as the gold standard. We also compared the prognostic significance of ECG-LVH and MRI-LVH as predictors of cardiovascular events. This analysis included 4,748 participants (mean age 61.9 years, 53.5% females, 61.7% nonwhites). Logistic regression with stepwise selection was used to identify factors associated with false-positive (n = 208) and false-negative (n = 387), compared with true-positive (n = 208) and true-negative (n = 4,041) ECG-LVH, respectively. A false-negative ECG-LVH status was associated with increased odds of Hispanic race/ethnicity, current smoking, hypertension, increased systolic blood pressure, prolongation of QRS duration, and higher body mass index and with lower odds of increased ejection fraction (model-generalized $R^2 = 0.20$). A false-positive ECG-LVH status was associated with lower odds of black race, Hispanic race/ethnicity, minor ST-T abnormalities, increased systolic blood pressure, and presence of any major electrocardiographic abnormalities (model-generalized $R^2 = 0.29$). Both ECG-LVH and MRI-LVH were associated with an increased risk of cardiovascular disease events (hazard ratio 1.51, 95% confidence interval 1.03 to 2.20 and hazard ratio 1.81, 95% confidence interval 1.33 to 2.46, respectively). In conclusion, discrepancy in LVH detection by ECG and MRI can be relatively improved by considering certain participant characteristics. Discrepancy in diagnostic performance, yet agreement on predictive ability, suggests that LVH by ECG and LVH by imaging are likely to be two distinct but somehow related phenotypes. **(Am J Cardiol 2015;115:515−522)**

The current diagnosis of left ventricular hypertrophy (LVH) by electrocardiogram (ECG) is based on finding electrocardiographic criteria that agree with increased left ventricular mass (LVM) as detected by imaging. However, it has been consistently reported that the magnitude of agreement is rather low.[1−3] As a result, a significant proportion of cases with true anatomic LVH are misclassified using ECG-LVH criteria. Despite this limitation, it has been repeatedly reported that ECG-LVH provides independent information on the cardiovascular risk even after adjusting for LVM by imaging.[3−8] Understanding possible reasons for the frequent discrepancy between common ECG-LVH criteria and increased LVM by imaging would help understanding the genesis of electrocardiographic changes that occur as a consequence of increased LVM. This information might possibly help in refining the current ECG-LVH criteria for the purpose of improved predictive ability and for detection of increased LVM. The primary aim of this study was to identify factors associated with false-positive and false-negative ECG-LVH, using cardiac magnetic resonance imaging (MRI) as the gold standard, in the Multi-Ethnic Study of Atherosclerosis (MESA). As secondary aim, we sought to examine the prognostic significance of false-positive and false-negative ECG-LVH as predictors of fatal and nonfatal cardiovascular events.

Methods

MESA is a prospective longitudinal study aimed to explore the prevalence, correlates, and progression of subclinical

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Table 1
Baseline participant characteristics stratified by electrocardiographic left ventricular hypertrophy (ECG-LVH) status

Mean ±SD or n (%) Variable	True negative (n=4041)	False negative (n=387)	False positive (n=208)	True positive (n=112)	p value
Age (years)	61.6± 10.0	62.6± 10.3	63.7± 9.9	65.7± 9.6	<0.001
Women	2118(52.4)	235(60.7)	121(58.2)	66(58.9)	0.004
White	1643(40.7)	125(32.3)	39(18.8)	10(8.9)	<0.001
Americans Chinese	549(13.6)	18(4.7)	57(27.4)	12(10.7)	
African American	953(23.6)	130(33.6)	80(38.5)	61(54.5)	
Hispanic	896(22.2)	114(29.5)	32(15.4)	29(25.9)	
Income					<0.001
<$20K	866(22.1)	88(23.7)	61(31.1)	38(36.2)	
$20-49K	1399(35.6)	165(44.4)	72(36.7)	46(43.8)	
>$50K	1662(42.3)	119(32.0)	63(32.1)	21(20)	
Education					0.002
<HS	646(16.0)	72(18.7)	46(22.12)	32(28.83)	
HS-College	2595(64.4)	247(64.16)	119(57.21)	59(53.15)	
>College	791(19.6)	66(17.14)	43(20.67)	20(18.02)	
Body mass index (kg/m^2)	27.6± 4.89	29.5± 5.59	26.68± 4.66	28.22± 4.5	<0.001
Hypertension	1511 (37.4)	261 (67.4)	128(61.5)	93 (83.0)	<0.001
Systolic blood pressure (mmHg)	122.93±19.62	138.07± 23.3	133.31, 23.98	151.49, 26.92	<0.001
Diastolic blood pressure (mmHg)	71.2± 9.9	75.42± 11.43	73.23± 10.91	79.52± 12.67	<0.001
Use of BP lowering drugs	1277(31.6)	195(50.5)	111(53.4)	68(60.7)	<0.001
Total Cholesterol (mg/dL)	194.42± 35.12	194.04± 36.19	195.94±36.54	195.12± 35.36	0.93
HDL-Cholesterol (mg/dL)	51.29± 15.05	51.53±15.27	51.84±12.46	51.99±15.65	0.91
Statin use	584 (14.5)	55(14.3)	28(13.5)	16(14.3)	0.98
Diabetes Mellitus	418(10.4)	68(17.6)	24(11.6)	27(24.1)	<0.001
Family history of CVD	1605(42.2)	166(46.1)	78(39.2)	42(41.6)	0.40
Smoking status					<0.001
Never	2095(52.0)	171(44.4)	124(59.6)	60(54.1)	
Former	1458(36.2)	133(34.6)	64(30.8)	29(26.1)	
Current	479(11.9)	81(21.0)	20(9.6)	22(19.8)	
LV ejection fraction (%)	69.43± 6.9	66.94± 8.6	70.0± 7.4	66.7± 10.8	<0.001
LV mass (gm)	74.2± 12.7	101.8, 14.7	78.18, 12.2	108.1, 18.2	<0.001
QRS duration (ms)	90.7±9.5	94.3± 9.7	95.1± 9.5	95.2±10.1	<0.001
Abnormal QRS axis	182(4.5)	20(5.17)	15(7.2)	8(7.1)	0.18
Any ST/T Abnormalities	445(11.0)	97(25.1)	56(26.9)	58(51.8)	<0.001
Major ST/T Abnormalities	116(2.9)	19(4.9)	20(9.6)	32(28.6)	<0.001
Minor ST/T Abnormalities	392(9.7)	94(24.3)	48(23.1)	50(44.6)	<0.001
Any major ECG abnormality	258(6.4)	42(10.9)	30(14.4)	40(35.7)	<0.001

ECG-LVH status was defined using left ventricular hypertrophy by magnetic resonance imaging (MRI-LVH) as the gold standard.
CVD = cardiovascular disease; HDL = high density lipoprotein; LV = left ventricle; MRI = magnetic resonance imaging.

cardiovascular disease (CVD) in a population-based multiethnic cohort. The description of the MESA study is provided elsewhere.[9] Briefly, from July 2000 to August 2002, a total of 6,814 men and women aged 45 to 84 years and free of clinically apparent CVD were recruited from 6 US communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan and the Bronx, New York; and St. Paul, Minnesota. For the purpose of these analyses, all MESA participants with good quality baseline electrocardiogram and cardiac MRI data were considered. Of those, we excluded participants with major ventricular conduction defect including those with complete bundle branch blocks or QRS duration $\geq$120 ms. After all exclusions, 4,748 participants remained and were included in the analysis.

The MESA cardiac MRI protocol, image analysis, and inter- and intra-reader reproducibility have been previously reported.[10] Briefly, base to apex short-axis fast gradient echo images (slice thickness 6 mm, slice gap 4 mm, field of view 360 to 400 mm, matrix 256 × 160, flip angle 20°, echo time 3 to 5 ms, repetition time 8 to 10 ms) were acquired using 1.5-T cardiac MRI scanners.[10] The reproducibility of this protocol was assessed on 79 participants with a technical measurement error of 6% and an intraclass correlation coefficient of 0.98.

LVM was measured as the sum of the myocardial area (the difference between endocardial and epicardial contours) times slice thickness plus image gap in the end-diastolic phase multiplied by the specific gravity of the myocardium (1.05 g/ml).[8] Observed LVM was then determined from MRI in all MESA participants. Individual LVM was predicted using the following allometric height and weight indexation equations previously derived from a separate reference MESA subpopulation of 822 men and women (47% Caucasians, 22% Chinese, 18% African-American, 13% Hispanics) without LVH risk factors: predicted LVM (pLVM) = 8.17 × height (in meters)$^{0.561}$ × weight (in kilograms)$^{0.608}$ for men and pLVM = 6.82 × height (in meters)$^{0.561}$ × weight (in kilograms)$^{0.608}$ for women.[11]