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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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Abstract

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 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 4748 participants (mean age 61.9 years, 53.5% females, 61.7% non-whites). Logistic regression with stepwise selection was used to identify factors associated with false-positive (n=208) and false-negative (n=387), compared to true-positive (n=208) and true-negative (n=4041) ECG-LVH, respectively. A false-negative ECG-LVH status was associated with increased odds of Hispanic race/ethnicity, current smoking, hypertension, increased systolic blood

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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 ECG abnormalities (model generalized $R^2=0.29$). Both ECG-LVH and MRI-LVH were associated with increased risk of CVD events (HR (95% CI): 1.51(1.03,2.20) and 1.81(1.33,2.46), respectively). In conclusion, discrepancy in LVH detection by ECG and MRI can be relatively improved by considering certain participants characteristic. Discrepancy in diagnostic performance yet agreement on predictive ability suggests that LVH by ECG and imaging are likely to be two distinct, but somehow related phenotypes.

Keywords

Electrocardiogram; Cardiac MRI; Left ventricular hypertrophy; Left ventricular mass

Introduction

The current diagnosis of left ventricular hypertrophy by electrocardiogram (ECG-LVH) is based on finding ECG 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, 2, 3]. As a result, a significant proportion of cases with true anatomical LVH are misclassified by 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 ECG 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 non-fatal cardiovascular events

Methods

MESA is a prospective longitudinal study aimed to explore the prevalence, correlates and progression of subclinical cardiovascular disease (CVD) in a population-based multi-ethnic cohort. The description of the MESA study is provided elsewhere [9]. Briefly, between July 2000 and August 2002, 6,814 men and women aged 45–84 years old and free of clinically apparent CVD were recruited from six 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 ECG and cardiac MRI data were considered. Out of those, we excluded participants with major

ventricular conduction defect including those with complete bundle branch blocks or QRS duration ≥ 120 ms. After all exclusions, 4748 participants remained and were included in the analysis.

The MESA cardiac MRI protocol, image analysis, and inter-reader 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.

LV mass 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 LV mass (oLVM) was then determined from MRI in all MESA participants. Individual LV mass 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 LV mass (pLVM) = $8.17 * \text{height (in meters)}^{0.561} * \text{weight (in kilograms)}^{0.608}$ for men and $6.82 * \text{height (in meters)}^{0.561} * \text{weight (in kilograms)}^{0.608}$ for women* [11]

The 95th percentile cut-off value of (oLVM/ pLVM) was calculated as 1.31. This defines participants with observed LV mass more than 1.31 times of that predicted on the basis of height, weight and gender had LV mass greater than 95% of the reference population as constituting MRI-LVH for the purposes of this study.

Standard 12-lead ECGs were digitally acquired using a Marquette MAC 1200 electrocardiograph (Marquette Electronics, Milwaukee, Wisconsin) at 10mm/mV calibration and speed of 25 mm/sec. All ECGs were centrally read and coded at the Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Winston-Salem, NC. ECGs were visually inspected for technical errors and inadequate quality before being automatically processed with the GE Marquette 12-SL program 2001 version (GE Marquette, Milwaukee, WI). ECG abnormalities were classified as minor and major abnormalities using the Minnesota ECG Classification [12].

ECG- LVH was defined based on the following traditional ECG-LVH criteria which were calculated from the automatically measured ECG waveforms: Sokolow-Lyon voltage ($SV1 + RV5/V6 \geq 3.5$ mV and/or $RaVL \geq 1.1$ mV) [13] and/or gender-specific Cornell voltage [$SV3 + RaVL \geq 2.8$ mV (for men) and ≥ 2.0 mV (for women)] [14]. ECG-LVH was defined in this analysis as presence of positive ECG criteria by either the Cornell Voltage or Sokolow-Lyon criterion.

CVD events were adjudicated by an independent adjudication committee. A detailed description of the adjudication process has already been published [15]. In this analysis, we used composite outcome of fatal and nonfatal CVD events. These events included

myocardial infarction, resuscitated cardiac arrest, definite angina, probable angina (if followed by revascularization), stroke, transient ischemic attack, percutaneous transluminal coronary angioplasty, coronary stent, coronary atherectomy, coronary bypass graft, coronary or other revascularization, congestive heart failure, peripheral vascular disease, coronary heart disease death, stroke death, other atherosclerotic death or other CVD death.

Three seated blood pressure measurements were taken 5 min apart using an automated device (Dinamap Pro 100). The mean of the last two measurements was considered for analysis. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or history of intake of blood pressure lowering drugs. Trained technicians measured height, weight, and waist circumference following a standardized protocol. Diabetes was defined as current use of glucose-lowering medications, fasting glucose ≥ 126 mg/dl, or non-fasting glucose ≥ 200 mg/dl. Use of medication, current smoking, ethanol intake, income, and education were ascertained from standardized questionnaires.

Based on the baseline LVH status by MRI (gold standard) and ECG, participants were classified as having false positive, false negative, true positive or true negative ECG-LVH. Baseline characteristics of the study participants were then examined and compared across these categories of ECG-LVH using analysis of variance for the continuous variables and chi-square tests for the categorical variables.

Binary logistic regression models were used to identify baseline characteristics that are associated with false negative and false positive, compared to true negative and true positive ECG-LVH, respectively. These include age, sex, race/ethnicity, education, income, hypertension, systolic blood pressure, diastolic blood pressure, use of blood pressure lowering drugs, total cholesterol, HDL-cholesterol, family history of CVD, statin use, smoking status, LV ejection fraction, LV mass by MRI, QRS duration, QRS axis, ST/T abnormalities and minor/major ECG abnormalities. We first conducted bivariate analyses. Then, separate final models for predicting false negative and false positive were selected using a stepwise selection procedure.

CVD event rates and 95% confidence intervals (CI) were calculated by ECG LVH status. Cumulative incidence was estimated using Kaplan Meir method and compared using log-rank test across ECG LVH status. Cox proportional hazard (CPH) models were used to examine the association between baseline ECG-LVH status (false negative, false positive, true positive, true negative (reference group)) with incident CVD events. Three CPH models were created: Model 1 unadjusted; Model 2 adjusted for socio-demographic characteristics [age, sex, race/ethnicity and socioeconomic status], Model 3 adjusted for model 1 plus clinical and anthropometric variables [body mass index, systolic blood pressure, blood pressure lowering drugs, diabetes, total cholesterol, lipid-lowering drugs, smoking status]. Similar CPH models were used to examine the association of ECG-LVH (present vs. absent regardless of true or false) and MRI-LVH with incident CVD events. Statistical analyses were performed using SAS statistical software (Version 9.3, Cary, NC).

Results

These analyses included 4748 participants (age 61.9 ± 10.1 years, 53.5% females, 38.3% whites, 13.4% American Chinese, 25.8 % African American, 22.5 % Hispanic). MRI-LVH and ECG-LVH were present in 10.5% (n=499) and 6.7% (n= 320) of the participants, respectively. About 2.4% (n= 112) of the participants had LVH by both MRI and ECG (i.e. true positive ECG-LVH), and 85.1% (n=4041) did not have LVH by either method (i.e. true negative ECG-LVH). The remaining 12.5% (n=595) of the participants had either MRI-LVH but no ECG-LVH (n=387) (i.e. false negative ECG-LVH) or the opposite (n=208) (i.e. false positive ECG-LVH).

Table 1 outlines the characteristics of the study population by ECG-LVH status (true negative, false negative, false positive, true positive) using MRI-LVH as the gold standard.

In bivariate analyses, several factors were associated with false positive and false negative ECG-LVH compared to true ECG-LVH (negative and positive) status (Table 2). Using stepwise selection, Hispanic race/ethnicity, current smoking, hypertension, increased systolic blood pressure, prolongation of QRS duration, higher body mass index and presence of hypertension were associated with increased odds while increased ejection fraction was associated with lower odds of false negative ECG-LVH, compared to true negative ECG-LVH status (Model generalized $R^2 = 0.198$). On the other hand, Black race, Hispanic race/ethnicity, minor ECG ST/T abnormalities, increased systolic blood pressure and presence of any major ECG abnormalities were associated with lower odds of false positive ECG-LVH, compared to true positive ECG-LVH status (Model generalized $R^2 = 0.286$) (Table 3).

During a median follow-up of 8.5 years 341 CVD events occurred. As shown in Table 4, the incidence rates of CVD events were the highest in true positive ECG LVH, and the lowest in true negative ECG-LVH. Figure 1 shows cumulative incidence for CVD events by ECG-LVH Status.

Compared to true negative ECG-LVH, true positive ECG-LVH was associated with almost three-fold increased risk of CVD events. The increased risk remained significant after adjustment for socio-demographics, CVD risk factors and potential confounders (Table 4). False negative ECG-LVH was associated with increased risk in the socio-demographic model but the risk became not significant after further adjustment for CVD risk factor and potential confounders. The risk of CVD in the false positive ECG-LVH group was not significantly different from the risk associated with false negative ECG-LVH in any of the models (Table 4).

ECG-LVH (present vs. absent regardless of being true or false) was associated with increased risk of CVD events in the unadjusted model (Model 1 (HR (95%CI): 1.86 (1.32, 2.62), $p < 0.001$), the socio-demographic model (Model 2 (HR (95%CI): 1.49 (1.03, 2.15), $p = 0.036$) as well as the fully adjusted model (Model 3 (HR (95%CI): 1.51 (1.03, 2.20), $p = 0.035$). Similarly, MRI-LVH was associated with increased risk of CVD events in all models (HR (95%CI): 2.15 (1.63, 2.84) unadjusted model, 1.94 (1.45, 2.60) socio-demographic model, and 1.81 (1.33, 2.46) fully adjusted model; $p < 0.001$ in all models). No

significant interactions by sex or race/ethnicity were detected. Figure 2 shows the cumulative incidence for CVD events by ECG-LVH and MRI-LVH.

Discussion

In these analyses from the MESA study we sought to identify factors associated with false positive and false negative ECG-LVH, aiming to find an explanation for the discrepancies between LVH by ECG and MRI. We also examined the association between ECG-LVH (stratified by its diagnostic accuracy) and risk of CVD events. The key findings from our study are: 1) we have identified a number of factors associated with false positive and false negative ECG-LVH. However, these factors explained only about 20% ($R^2 = 0.198$) of the false negative ECG-LVH and 29% ($R^2 = 0.286$) of the false positive ECG-LVH; and 2) overall, ECG-LVH was predictive of CVD events regardless of its accuracy. Compared to true negative ECG-LVH, true positive ECG-LVH showed the strongest association with incident CVD events more than false negative and false positive ECG-LVH.

Identifying factors explaining the discrepancies between ECG-LVH and MRI-LVH, as we did in this study, has the potential to improve the diagnostic ability of the current ECG-LVH criteria. Whether incorporating these factors in the automated algorithms to diagnose LVH in the ECG machines would be feasible and useful needs further investigation. Nevertheless, the modest R^2 of the collective performance of these factors makes it unlikely that using these factors will dramatically enhance the diagnostic accuracy of ECG-LVH. With this in mind and given the established strong predictive value of ECG-LVH, it seems there is a disconnect between the diagnostic ability of ECG-LVH (which is at best modest) and its prognostic significance (which is very good and matches that of LVH by imaging). Hence, it is likely that LVH by ECG and imaging are two distinctive phenotypes although somehow related. In other words, the so called ECG-LVH is not totally a reflection of increase in LV mass but could also be secondary to increased myocardial tension, or neurohumoral and/or biochemical changes in the myocardium [16].

The idea that ECG-LVH could be a separate entity from imaging based-LVH is further supported by a genome-wide linkage analysis of ECG-LVH and echo-LVH in families with hypertension which showed stronger genetic signals for ECG-LVH than echo-LVH, and that the genetic determinants of each of these appear to be distinct [17].

The higher prevalence of MRI-LVH compared to ECG-LVH observed in our study accords with several previous reports in which anatomical LVH was determined by X-ray and echocardiography [18–20]. Differences in the prevalence estimates between ECG-based and imaging-based LVH and the inability to come up with perfect ECG-LVH criteria could probably be explained by the complex structural and functional remodeling of the myocardium that occur as a result of hypertrophy. In addition to changes in the size of left ventricle, structural changes at the tissue level including changes of cardiomyocytes, interstitial fibrosis, diminished coronary reserve and myocardial dysfunction [12–24] are common occurrences. These multi-dimension complex changes are not easily captured by a modality that depends on recording electric activity such as ECG.

As a result of the complex structural and functional remodeling of myocardium occurring as a result of hypertrophy, the conduction velocity is slowed, and consequently the sequence of ventricular activation is altered [25]. Using computer simulations, it has been shown that the mass and shape of the left ventricle in LVH are not the only determinant of QRS voltage, the key feature upon which almost all ECG-LVH criteria relies on [26, 27]. Diffuse or regional slowing in conduction velocity changes the sequence of ventricular activation in a way that is consistent with ECG-LVH patterns even in situations when the anatomy of left ventricle is not changed. These findings provide further support that the ECG criteria for LVH do not necessarily mirror changes in LV mass all the time, which explains the too many criteria, none of which provide a high level of diagnostic accuracy. Clearly, the usefulness of ECG-LVH as a tool for prediction of outcomes seems to surpass its value as a tool to diagnose anatomical LVH. Therefore, it may be the time to modify the current or create new ECG-LVH criteria with the main focus being prediction of outcomes rather than the anatomical correlates. It is expected, however, that ECG-LVH will be even more predictive if truly there is anatomical LVH. Notably, ECG-LVH criteria which combine repolarization abnormalities such as the Romhilt-Estes Score or the Framingham score have substantially higher risk for incident cardiovascular disease than criteria based solely on increased QRS amplitudes (3).

Our results should be read in the context of certain limitations. Although there are several ECG-LVH criteria, we only used Cornell Voltage and Sokolow-Lyon which may impact the generalizability of our results. Nevertheless, Cornell Voltage and Sokolow-Lyon are the most commonly used ECG-LVH criteria and both are considered among the best ECG LVH criteria in terms of diagnostic and prognostic ability [3]. Further, most of the large clinical trials addressing hypertension and LVH have used these criteria exactly the way we used in this analysis (i.e. LVH defined as presence of LVH by Cornell Voltage and/or Sokolow-Lyon) [28, 29]. Therefore, defining LVH in our study using Cornell Voltage and Sokolow-Lyon would be the most appropriate approach to address our study aims. Also, we decided to use only variables that could be easily obtained from ECG and participant characteristics. However, there could be other variables (e.g. p-wave indices), with potential value in explaining the discrepancy between ECG-LVH and MRI-LVH and we did not include. Despite these limitations, this report is the first to address the discrepancy between ECG-LVH and MRI-LVH (the current gold standard), in a large community-based ethnically diverse population.

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Figure 1.
Cumulative incidence for cardiovascular events by accuracy of the electrocardiographic left ventricular hypertrophy (ECG-LVH) using magnetic resonance imaging as a gold standard

Figure 2.
Cumulative incidence for cardiovascular events by left ventricular hypertrophy by electrocardiogram (ECG-LVH) and magnetic resonance imaging (MRI-LVH)

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

Mean $\pm$ SD or n (%)	True negative (n=4041)	False negative (n=387)	False positive (n=208)	True positive (n=112)	p value
Age (years)	61.6 $\pm$ 10.0	62.6 $\pm$ 10.3	63.7 $\pm$ 9.9	65.7 $\pm$ 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)	
Americans Chinese	549(13.6)	18(4.7)	57(27.4)	12(10.7)	<0.001
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 $\pm$ 4.89	29.5 $\pm$ 5.59	26.68 $\pm$ 4.66	28.22 $\pm$ 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 $\pm$ 19.62	138.07 $\pm$ 23.3	133.31, 23.98	151.49, 26.92	<0.001
Diastolic blood pressure (mmHg)	71.2 $\pm$ 9.9	75.42 $\pm$ 11.43	73.23 $\pm$ 10.91	79.52 $\pm$ 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 $\pm$ 35.12	194.04 $\pm$ 36.19	195.94 $\pm$ 36.54	195.12 $\pm$ 35.36	0.93
HDL-Cholesterol (mg/dL)	51.29 $\pm$ 15.05	51.53 $\pm$ 15.27	51.84 $\pm$ 12.46	51.99 $\pm$ 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)	

Mean $\pm$ SD or n (%) Variable	True negative (n=4041)	False negative (n=387)	False positive (n=208)	True positive (n=112)	p value
Current	479(11.9)	81(21.0)	20(9.6)	22(19.8)	
LV ejection fraction (%)	69.43 $\pm$ 6.9	66.94 $\pm$ 8.6	70.0 $\pm$ 7.4	66.7 $\pm$ 10.8	<0.001
LV mass (gm)	74.2 $\pm$ 12.7	101.8, 14.7	78.18, 12.2	108.1, 18.2	<0.001
QRS duration (ms)	90.7 $\pm$ 9.5	94.3 $\pm$ 9.7	95.1 $\pm$ 9.5	95.2 $\pm$ 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

HDL= High density lipoprotein; CVD= Cardiovascular disease; LV= Left ventricle; MRI= Magnetic resonance imaging

ECG-LVH status was defined using left ventricular hypertrophy by magnetic resonance imaging (MRI-LVH) as the gold standard

Table 2

Factors associated with false negative and false positive compared to true negative and true positive electrocardiographic left ventricular hypertrophy (ECG-LVH) in a bivariate logistic regression

Variable	False negative		False positive	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age (year)	1.01 (1.00, 1.02)	0.054	0.98 (0.96, 1.00)	0.080
Sex (men vs. women)	0.71 (0.58, 0.88)	0.002	1.03(0.65, 1.64)	0.896
Race/Ethnicity		<0.001		0.001
White	(Reference)		(Reference)	
Chinese-Americans	0.43 (0.26, 0.71)	0.001	1.22 (0.48, 3.10)	0.679
Hispanics	1.67 (1.28, 2.18)	<0.001	0.28 (0.12, 0.67)	0.004
Blacks	1.79 (1.39, 2.32)	<0.001	0.34 (0.16, 0.73)	0.006
Body mass index (kg/m ²)	1.07 (1.05, 1.09)	<0.001	0.93 (0.89, 0.98)	0.006
Income		<0.001		0.085
<\$20K	(Reference)		(Reference)	
>\$20k<\$50K	1.16 (0.88, 1.52)	0.284	0.98 (0.56, 1.69)	0.928
>\$50K	0.70 (0.53, 0.94)	0.017	1.87(0.99, 3.54)	0.055
Education		0.265		0.407
High School	(Reference)		(Reference)	
College	0.85 (0.65, 1.13)	0.263	1.40 (0.81, 2.43)	0.226
>College	0.75 (0.53, 1.06)	0.105	1.50 (0.75, 3.00)	0.257
Hypertension	3.47 (2.78, 4.33)	<0.001	0.33 (0.19, 0.58)	0.001
Systolic blood pressure (mmHg)	1.03 (1.03, 1.04)	<0.001	0.97 (0.96, 0.98)	<.001
Diastolic blood pressure (mmHg)	1.04 (1.03, 1.05)	<0.001	0.95 (0.93, 0.97)	<.001
Blood pressure lowering drugs	2.21 (1.79, 2.72)	<0.001	0.74 (0.46, 1.18)	0.207
Total cholesterol (mg/dL)	1.00 (1.00, 1.00)	0.841	1.00 (0.99, 1.01)	0.846
HDL-cholesterol (mg/dL)	1.00 (0.99, 1.01)	0.759	1.00 (0.98, 1.02)	0.925
Statin use	0.98 (0.73, 1.33)	0.911	0.93 (0.48, 1.81)	0.838
Diabetes Mellitus	1.85 (1.40, 2.45)	<0.001	0.41 (0.23, 0.76)	0.004
Family history of CVD	1.17 (0.94, 1.46)	0.147	0.91 (0.56, 1.47)	0.690
Smoking status		<0.001		0.041
Never	(Reference)		(Reference)	
Current	2.07 (1.56, 2.75)	<0.001	0.44 (0.22, 0.87)	0.018
Past	1.12 (0.88, 1.42)	0.356	1.07 (0.62, 1.83)	0.810
LV ejection fraction (%)	0.96 (0.94, 0.97)	<0.001	1.04 (1.01, 1.07)	0.002
MRI-LV mass (gm)	1.16 (1.15, 1.18)	<0.001	0.86 (0.83, 0.89)	<.001
QRS duration (ms)	1.04 (1.03, 1.05)	<0.001	1.00 (0.98, 1.02)	0.911
Abnormal QRS axis	1.16 (0.72, 1.86)	0.550	1.01 (0.41, 2.46)	0.982
Any ST/T abnormalities	2.70 (2.11, 3.47)	<0.001	0.34 (0.21, 0.55)	<.001
Minor ST/T abnormalities	2.99 (2.32, 3.85)	<0.001	0.37 (0.23, 0.61)	<.001
Major ST/T abnormalities	1.75 (1.06, 2.87)	0.028	0.27 (0.14, 0.49)	<.001

Variable	False negative		False positive	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Any major ECG abnormalities	1.79 (1.27, 2.52)	0.001	0.30 (0.18, 0.52)	<.001

ECG-LVH status was defined using left ventricular hypertrophy by magnetic resonance imaging (MRI-LVH) as the gold standard

HDL= High density lipoprotein; CVD= Cardiovascular disease; LV= Left ventricle; MRI= Magnetic resonance imaging

Table 3

Factors associated with false negative and false positive compared to true negative and true positive electrocardiographic left ventricular hypertrophy (ECG-LVH) using stepwise selection

Variable	False negative ECG-LVH			False positive ECG-LVH		
	Odds Ratio (95% CI)	p-value	Model R ²	Odds Ratio (95% CI)	p-value	Model R ²
Age (year)	0.99 (0.98, 1.00)	0.096		1.01 (0.98, 1.04)	0.594	
Sex (men vs. women)	0.39 (0.30, 0.51)	<0.001		0.87 (0.51, 1.50)	0.6214	
Race/ethnicity		0.003			0.0009	
Whites	Reference	--		Reference	--	
Chinese Americans	0.72 (0.42, 1.23)	0.230		1.18 (0.43, 3.27)	0.7458	
Blacks	1.32 (0.99, 1.75)	0.055		0.36 (0.15, 0.84)	0.0174	
Hispanics	1.56 (1.17, 2.08)	0.003		0.27 (0.10, 0.68)	0.0056	
Body mass index (Kg/m ²)	1.02 (1.00, 1.05)	0.038	0.198	-----	---	0.286
Smoking Status		<0.001		-----	---	
Never	Reference	--				
Current	2.03 (1.48, 2.79)	<0.001				
Past	1.10 (0.85, 1.43)	0.469				
Hypertension	1.86 (1.38, 2.50)	<0.001		-----	---	
Minor ST/T abnormalities	1.88 (1.41, 2.51)	<0.001		0.49 (0.27, 0.88)	0.017	
Left ventricular ejection fraction (%)	0.95 (0.93, 0.96)	<0.001				
QRS duration (ms)	1.05 (1.04, 1.06)	<0.001				
Systolic blood pressure (mmHg)	1.02 (1.02, 1.03)	<0.001		0.97 (0.96, 0.98)	<0.001	
Any major ECG abnormality	-----	---		0.39 (0.20, 0.75)	0.005	

Variables included in the backward selection analysis were those included in Table 1. Demographics were enforced into the model ECG-LVH status was defined using left ventricular hypertrophy by magnetic resonance imaging (MRI-LVH) as the gold standard

Table 4
Risk of cardiovascular events by electrocardiographic left ventricular hypertrophy (ECG-LVH) status

ECG-LVH status	Participants/ events (n)	Person-years	Event rate (95% CI) per 10000 person-years	Model 1		Model 2		Model 3	
				HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
True Negative	4026/267	30809	8.67 (7.69, 9.77)	Reference	--	Reference	Reference	Reference	--
True positive	111/18	749	24.04 (15.14, 38.15)	2.79 (1.73, 4.49)	<0.001	2.58 (1.54, 4.33)	<0.001	1.77 (1.03, 3.04)	0.038
False positive	207/14	1569	8.92(5.29, 15.07)	1.03 (0.60, 1.77)	0.909	1.28 (0.74, 2.20)	0.379	1.20 (0.69, 2.09)	0.517
False negative	386/42	2756	15.24 (11.26, 20.62)	1.76 (1.27, 2.43)	<0.001	1.83 (1.31, 2.56)	<0.001	1.38 (0.98, 1.96)	0.069

Left ventricular hypertrophy by magnetic resonance imaging (MRI-LVH) was used as the gold standard

Model 1: Unadjusted

Model 2 adjusted for socio-demographic characteristics [age, sex, race and socioeconomic status]

Model 3 adjusted for model 1 plus clinical and anthropometric variables [body mass index, systolic blood pressure, blood pressure lowering drugs, diabetes, total cholesterol, lipid lowering drugs and smoking status]