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Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy

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ABSTRACT

BACKGROUND Current electrocardiographic (ECG) criteria for the diagnosis of left ventricular hypertrophy (LVH) have low sensitivity.

OBJECTIVES The goal of this study was to test a new method to improve the diagnostic performance of the electrocardiogram.

METHODS The study was divided into 2 groups, a test and a validation cohort. In the test cohort, 94 patients were analyzed, including 47 with the diagnosis of hypertensive crisis and 47 with normal blood pressure at admission. Echocardiography was used to estimate the left ventricular mass index. Area under the curve (AUC) analysis was used for comparison of single and combined leads. The McNemar test was used to assess agreement among the ECG criteria against the left ventricular mass index. The proposed ECG criteria involved measuring the amplitude of the deepest S wave (S_D) in any single lead and adding it to the S wave amplitude of lead V_4 (SV_4). Currently accepted LVH ECG criteria such as Cornell voltage and Sokolow-Lyon were used for comparison. The validation cohort consisted of 122 consecutive patients referred for an echocardiogram regardless of the admitting diagnosis.

RESULTS The S_D was the most accurate single lead measurement for the diagnosis of LVH (AUC: 0.80; $p < 0.001$). When both cohorts were analyzed, the $S_D + SV_4$ criteria outperformed Cornell voltage with a significantly higher sensitivity (62% [95% confidence interval [CI]: 50% to 72%] vs. 35% [95% CI: 24% to 46%]). The specificities of all the criteria were ≥90%, with no significant difference among them.

CONCLUSIONS The proposed criteria for the ECG diagnosis of LVH improved the sensitivity and overall accuracy of the test. (J Am Coll Cardiol 2017;69:1694–703) © 2017 by the American College of Cardiology Foundation.

Several electrocardiographic (ECG) criteria have previously been proposed to diagnose left ventricular hyperthrophy (LVH), with modest differences in the degree of accuracy among them (1,2). At present, 37 different ECG criteria have been endorsed by the American Heart Association, a figure that suggests lack of consensus and often leads to confusion among clinicians (3,4). The specificity of the Cornell voltage criteria, the method considered to be the most accurate, is approximately 90%, with a sensitivity of only 20% to 40% (1,5).

In the present study, we tested the performance of novel criteria, taking into consideration the dynamic changes in voltage that occur within each electrocardiogram. We hypothesized that the summation of the amplitude of the deepest S wave in any lead (S_D) with the S wave in lead V_4 (SV_4) would improve upon the sensitivity of the other criteria, while maintaining an adequate specificity for the diagnosis of LVH.

METHODS

POPULATION. After obtaining approval from the institutional review board, 2 different cohorts of patients were selected (the test and the validation cohorts) based on the presumptive incidence of LVH. For the test cohort, all patients admitted to our

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institution from August to September 2013 with an available echocardiogram and electrocardiogram obtained during the same hospitalization were analyzed. The first 50 consecutive patients who were admitted under the diagnosis of hypertensive crisis and 50 additional patients with normal blood pressure and no major cardiovascular disease were selected. Ultimately, 6 individuals (3 from each group) were

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excluded from the analysis due to limited echocardiographic windows, leaving 94 patients for the study. Hypertensive emergency was defined as systolic blood pressure >180 mm Hg or diastolic blood pressure >120 mm Hg, with evidence of end-organ damage as defined by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Joint National Committee 7) (6). Hypertensive urgency was defined using the same cutoffs for blood pressure measurement but with no evidence of end-organ damage.

For the validation cohort, we selected the first 150 patients referred to our institution for an echocardiogram from January 2014 to February 2014 who had a concomitant electrocardiogram for review. The patients were selected regardless of the initial admitting diagnosis. Twenty-eight patients were not included in the analysis due to poor echocardiographic windows. In both cohorts, all patients with complete left or right bundle branch block or ventricular paced rhythm were excluded from the study.

Statistical analysis showed that with 100 patients in the test cohort (equal number of patients with hypertensive crisis and nonhypertensive crisis), there would be >90% power to detect a significant area under the curve (AUC) of 0.7 (vs. the null hypothesis of AUC of 0.5).

ECHOCARDIOGRAPHIC ANALYSIS. Transthoracic echocardiography was used as a method of reference to estimate left ventricular mass (3). Left ventricular

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

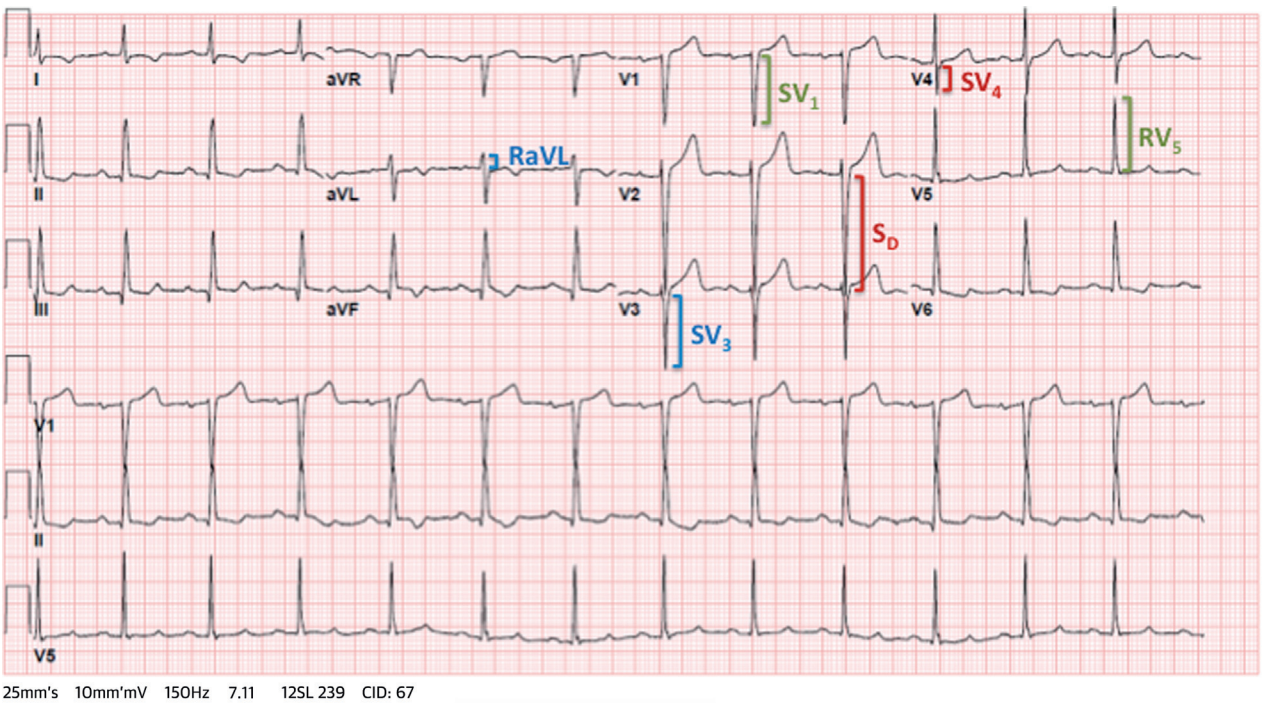
ECG = electrocardiographic

CI = confidence interval

LVH = left ventricular hypertrophy

S_D = deepest S wave in any lead

FIGURE 1 Sample Electrocardiogram



Electrocardiogram of a 71-year-old man that meets criteria for left ventricular hypertrophy based on the Peguero-Lo Presti criteria (deepest S wave in any lead and S wave in V_4 [$S_D + SV_4$]; 2.6 + 0.7 = 3.3 mV [male subjects ≥2.8 mV]). The diagnosis of moderate left ventricular hypertrophy was confirmed by echocardiogram (left ventricular mass index = 145 g/m^2). Note that most common classical electrocardiographic criteria are not met: Cornell voltage (RaVL+ SV_3; 0.4 + 1.6 = 2 mV [male subjects >2.8 mV]) and Sokolow-Lyon voltage (SV_1 + [RV_5 or RV_6]; 1.5 + 1.6 = 3.1 mV [male subjects ≥3.5 mV]).

TABLE 1 Echocardiographic Parameters of the Test and Validation Cohorts

	Test Cohort (n = 94)	Validation Cohort (n = 122)	p Value
Ejection fraction, %	59 ± 8	58 ± 13	0.35
Left ventricular mass, g	196 ± 79	201 ± 82	0.65
Left ventricular mass index, g/m^2	102 ± 40	107 ± 37	0.36
Left ventricular hypertrophy	30 (32)	51 (42)	0.18
Interventricular septum diameter, cm	1.23 ± 0.36	1.20 ± 0.29	0.43
Posterior wall diameter, cm	1.12 ± 0.29	1.14 ± 0.29	0.61
Largest wall diameter, cm	1.26 ± 0.35	1.25 ± 0.32	0.79
Left ventricular end-diastolic diameter, cm	4.46 ± 0.62	4.57 ± 0.84	0.27
Left ventricular end-systolic diameter, cm	2.93 ± 0.82	3.13 ± 1.07	0.12
Mitral inflow E-wave, m/s	0.94 ± 0.25	0.86 ± 0.31	0.04
Mitral inflow A-wave, m/s	0.76 ± 0.48	0.8 ± 0.31	0.54
Mitral inflow E-wave to A-wave ratio	0.91 ± 0.27	1.21 ± 0.73	<0.001
More than mild mitral regurgitation	4 (4)	9 (7)	0.50
More than mild aortic stenosis	1 (1)	4 (3)	0.53
Normal geometry	27 (29)	29 (24)	0.50
Concentric remodeling	36 (38)	42 (34)	0.65
Concentric hypertrophy	30 (32)	38 (31)	0.9
Eccentric hypertrophy	1 (1)	13 (11)	0.01

Values are mean ± standard deviation or n (%).

TABLE 2 Demographic Characteristics of the Test Cohort

	Normotensive (n = 47)	Hypertensive (n = 47)	p Value
Age, yrs	43 ± 7	66 ± 17	<0.001
Male	21 (45)	26 (55)	0.41
Body surface area	1.95 ± 0.28	1.94 ± 0.25	0.91
Hypertension	4 (9)	43 (92)	<0.001
Diabetes mellitus	0	15 (32)	<0.001
Chronic obstructive pulmonary disease	1 (2)	6 (13)	0.11
Heart failure	0	9 (19)	0.01
Dyslipidemia	11 (23)	18 (38)	0.18
Atrial fibrillation	1 (2)	5 (11)	0.21
Peripheral arterial disease	0	2 (4)	0.48
Myocardial infarction	0	10 (21)	0.003
History of percutaneous coronary intervention	0	8 (17)	0.01
History of coronary artery bypass graft	0	3 (6)	0.24
Systolic blood pressure, mm Hg	125 ± 13	175 ± 35	<0.001
Diastolic blood pressure, mm Hg	79 ± 11	93 ± 22	<0.001
Heart rate, beats/min	77 ± 14	79 ± 19	0.57
Use of beta-blockers	2 (4)	32 (68)	<0.001
Use of ACE inhibitors/ARBs	3 (6)	33 (70)	<0.001
Use of calcium-channel blockers	0	24 (51)	<0.001

Values are mean ± standard deviation or n (%).
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers.

end-diastolic and end-systolic measurements were obtained with the patient in a partial left lateral decubitus position according to recommendations by the American Society of Echocardiography (7,8). Frames with optimal visualization of interfaces and showing simultaneous visualization of the septum, left ventricular internal diameter, and posterior wall were used. A Level 3 echocardiographer performed the interpretations. Left ventricular mass was calculated by using the Devereux formula: left ventricular mass (g) = $0.80 \times \{1.04 \times [(\text{septal thickness} + \text{internal diameter} + \text{posterior wall thickness})^3 - (\text{internal diameter})^3]\} + 0.6$ g. The left ventricular mass was indexed according to body surface area. LVH was defined as a left ventricular mass index >115 g/m^2 in male subjects and >95 g/m^2 in female subjects (9).

ECG ANALYSIS. A single electrocardiogram for every patient was selected from the same day the echocardiogram was obtained. If this condition was not met, the next electrocardiogram available within the same hospitalization was used instead. All 12-lead ECG interpretations were independently reviewed by 2 cardiologists. Individual leads were analyzed by measuring the tallest R or R′ and the deepest S or QS complex in all the precordial and limb leads using the PR segment as baseline. In cases of voltage differences within the same lead, only the largest complex was selected. The proposed criteria was obtained by adding S_D to the S amplitude in V_4 ($S_D + SV_4$). Cutoff values with the best balance that allowed the highest sensitivity and specificity permissible, were identified by using sex specific coordinate AUC points. A $S_D + SV_4$ ≥2.3 mV for female subjects and ≥2.8 mV for male subjects were considered positive for LVH (**Figure 1**). In cases in which the S_D was found in lead V_4, the S wave amplitude was doubled to obtain the value $S_D + SV_4$.

The Cornell voltage criteria was used as the main comparison given its reputation as the most accurate of the reported measurements (1). The sex-specific Cornell voltage criteria was computed as the amplitude of R in aVL plus the amplitude of S or QS complex in V_3 ($RaVL + SV_3$) with a cutoff of >2.8 mV in men and >2.0 mV in women (5). Other LVH voltage criteria were also included in the analysis. The Sokolow-Lyon voltage was obtained by adding the amplitude of S in V_1 and the amplitude of R in V_5 or V_6 ≥3.5 mV ($SV_1 + RV_5$ or RV_6); the limb lead voltage criteria amplitude of R in aVL >1.1 mV (RaVL) and amplitude of R in L1 >1.4 mV (RL_1) (4,10).

STATISTICAL METHODS. The echocardiographic, ECG, and baseline clinical data were each obtained by two independent blinded reviewers. Continuous

variables that did not deviate substantially from the normal distribution were reported as mean ± standard deviation; otherwise, they were reported as median and interquartile range (25% to 75%). Categorical variables were reported as frequencies and percentages. A p value <0.05 was considered statistically significant.

AUC analysis was the statistical method used to estimate the predicted performance of all individual leads and the proposed criteria. The McNemar test was used to assess for lack of agreement comparing the ECG criteria against the gold standard (left ventricular mass index), and the results were reported as percentage with their respective 95% confidence interval (CI). All statistical analyses were performed by using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

TEST COHORT. The patients with hypertension in the test cohort (n = 47) comprised 33 cases of patients who had hypertensive urgency and 14 cases with hypertensive emergency. The incidence of LVH was similar between these 2 subgroups (61% vs. 57%, respectively; p = 0.90). There were no major ECG differences identified which were analyzed together as the "hypertensive group."

In the test cohort, 30 (32%) patients were diagnosed with LVH according to echocardiogram with mean ejection fraction of 59 ± 8%. The left ventricular mass and the left ventricular mass index were 196 ± 79 g and 102 ± 40 g/m^2, respectively (Table 1). When comparing the 2 groups, the hypertensive individuals were older, had a higher incidence of comorbidities, and were more likely to be prescribed antihypertensive medications (Table 2). Echocardiographic analysis showed a significant difference in ejection fraction, indexed LVH, and mitral inflow E-wave and A-wave ratio (Table 3). ECG analysis of the test cohort showed that the S waves in leads V_3 and V_4 were good predictors for the diagnosis of LVH. The S_D was the most accurate, continuous single linear measurement for the diagnosis of LVH (AUC: 0.80; p < 0.001) (Table 4). However, the diagnostic accuracy of the combined S_D plus SV_4 was better than any single lead when analyzed as continuous variables (AUC: 0.85 vs. 0.80 vs. 0.78) (Table 4, Figure 2).

The proposed $S_D + SV_4$ criteria (Peguero-Lo Presti) had nominally the best sensitivity (70%; 95% CI: 51% to 85%) followed by the Cornell voltage criteria with a sensitivity of 40% (95% CI: 23% to 59%). The specificity of these tests was 89% (95% CI: 79% to 95%) and 91% (95% CI: 89% to 96%), respectively. The only criteria that did not show lack of agreement with the gold standard was the proposed $S_D + SV_4$ criteria, with a p value of 0.62 according to the McNemar test. In addition, compared with Sokolow-Lyon voltage, RaVL and RL_1, the proposed criteria had a significantly higher sensitivity with nonsignificant differences in specificity based on the confidence intervals (Table 5).

TABLE 3 Echocardiographic Parameters of the Test Cohort

	Normotensive (n = 47)	Hypertensive (n = 47)	p Value
Ejection fraction, %	62 ± 3	57 ± 10	0.01
Left ventricular mass, g	151 ± 38	241 ± 83	<0.001
Left ventricular mass index, g/m^2	78 ± 18	126 ± 42	<0.001
Left ventricular hypertrophy	2 (4.3)	28 (60)	<0.001
Interventricular septal diameter, cm	1 ± 0.17	1.48 ± 0.35	<0.001
Posterior wall diameter, cm	0.94 ± 0.17	1.30 ± 0.28	<0.001
Largest wall diameter, cm	1 ± 0.15	1.50 ± 0.34	<0.001
Left ventricular end-diastolic diameter, cm	4.50 ± 0.38	4.40 ± 0.80	0.33
Left ventricular end-systolic diameter, cm	3 ± 0.43	2.90 ± 1.07	0.42
Mitral inflow E-wave, m/s	0.98 ± 0.15	0.89 ± 0.31	0.10
Mitral inflow A-wave, m/s	0.64 ± 0.48	0.89 ± 0.43	0.01
Mitral inflow E-wave to A-ratio	0.97 ± 0.18	0.87 ± 0.32	0.19
More than mild mitral regurgitation	0	4 (9)	0.13
More than mild aortic stenosis	0	1 (2)	0.9
Normal geometry	23 (49)	4 (9)	<0.001
Concentric remodeling	22 (47)	14 (30)	0.14
Concentric hypertrophy	2 (4)	28 (60)	<0.001
Eccentric hypertrophy	0	1 (2)	0.9

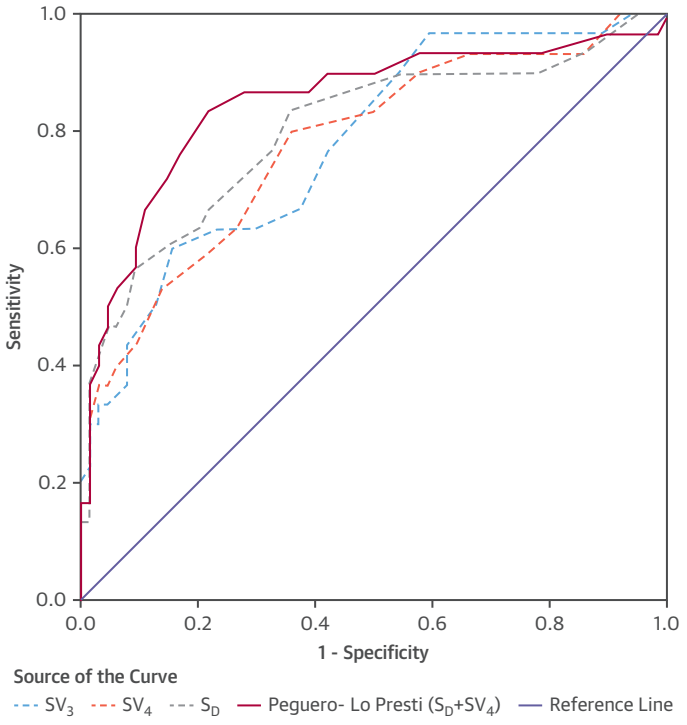
Values are mean ± standard deviation or n (%).

TABLE 4 AUC for Continuous Single Leads and the Proposed Criteria ($S_D + SV_4$) Predictive Performance of LVH in the Test Cohort

	AUC	p Value
RV_5	0.53	0.64
RV_6	0.57	0.29
SV_6	0.58	0.21
SV_1	0.60	0.14
SV_5	0.66	0.01
RL_1	0.68	0.01
RaVL	0.73	<0.001
SL_3	0.76	<0.001
SV_3	0.78	<0.001
SV_4	0.78	<0.001
S_D	0.80	<0.001
$S_D + SV_4$	0.85	<0.001

AUC = area under the curve; LVH = left ventricular hypertrophy; $S_D + SV_4$ = deepest S wave in any lead plus S wave in V_4.

FIGURE 2 AUC of the Test Cohort



Area under the curve of continuous single leads and the proposed criteria (deepest S wave in any lead and S wave in V_4 [$S_D + SV_4$]) representing the predictive performance of left ventricular hypertrophy in the test cohort.

TABLE 6 Demographic Characteristic of the Test and Validation Cohorts

	Test Cohort (n = 94)	Validation Cohort (n = 122)	p Value
Age, yrs	54 ± 17	68 ± 15	<0.001
Male	47 (50)	59 (48)	0.91
Body surface area, m^2	1.91 ± 0.27	1.87 ± 0.25	0.03
Hypertension	41 (44)	84 (69)	0.01
Diabetes mellitus	15 (16)	36 (30)	0.03
Chronic obstructive pulmonary disease	7 (7.4)	8 (7)	0.9
Congestive heart failure	9 (10)	17 (14)	0.41
Dyslipidemia	29 (31)	33 (27)	0.70
Atrial fibrillation	6 (6)	10 (8)	0.20
Peripheral vascular disease	2 (2)	9 (7)	0.14
History of myocardial infarction	10 (11)	11 (9)	0.89
History of percutaneous coronary intervention	8 (9)	10 (8)	0.9
History of coronary artery bypass graft	3 (3)	7 (6)	0.56
Baseline creatinine, mg/dl	0.97 ± 0.87	1.2 ± 1.1	0.11
Systolic blood pressure, mm Hg	150 ± 36	142 ± 29	0.10
Diastolic blood pressure, mm Hg	86 ± 18	79 ± 16	0.03
Heart rate, beats/min	78 ± 17	83 ± 20	0.04
Use of beta-blockers	34 (36)	49 (40)	0.58
Use of ACE inhibitors/ARBs	36 (38)	55 (45)	0.33
Use of calcium-channel blockers	24 (26)	26 (21)	0.61

Values are mean ± standard deviation or n (%).
Abbreviations as in Table 2.

VALIDATION COHORT. When comparing the test cohort versus the validation cohort, the latter group was an older population (age 68 ± 15 years vs. 54 ± 17 years) with a higher incidence of hypertension (69% vs. 44%) and diabetes mellitus (30% vs. 16%) (Table 6). Echocardiographic analysis revealed similar characteristics between them, with a 42% incidence of LVH (Table 1).

TABLE 5 McNemar Test Among the Electrocardiographic Criteria Against the Left Ventricular Mass Index in the Test Cohort

	Sensitivity (95% CI)	Specificity (95% CI)	McNemar Test*
RaVL	20 (8–39)	92 (83–97)	<0.001
RL_1	30 (15–49)	92 (83–97)	0.002
Sokolow-Lyon voltage	23 (10–42)	97 (89–100)	<0.001
Cornell voltage	40 (23–59)	91 (81–96)	0.014
$S_D + SV_4$ (Peguero-Lo Presti)	70 (51–85)	89 (79–95)	0.62

*A p value <0.05 indicates lack of agreement.
CI = confidence interval; $S_D + SV_4$ = deepest S wave in any lead S wave in V_4.

The ECG analysis of the validation cohort showed similar results as the test cohort, demonstrating the best continuous single lead performance of the S_D wave. Similarly, when combined and analyzed as a

TABLE 7 AUC for Continuous Single Leads and the Proposed Criteria ($S_D + SV_4$) Predictive Performance of LVH in the Validation Cohort

	AUC	p Value
RV_5	0.53	0.61
RV_6	0.62	0.02
SV_6	0.63	0.02
SV_1	0.72	<0.001
SV_5	0.68	0.001
RL_1	0.58	0.11
RaVL	0.59	0.09
SL_3	0.65	0.01
SV_4	0.71	<0.001
SV_3	0.75	<0.001
S_D	0.80	<0.001
$S_D + SV_4$	0.80	<0.001

Abbreviations as in Table 4.

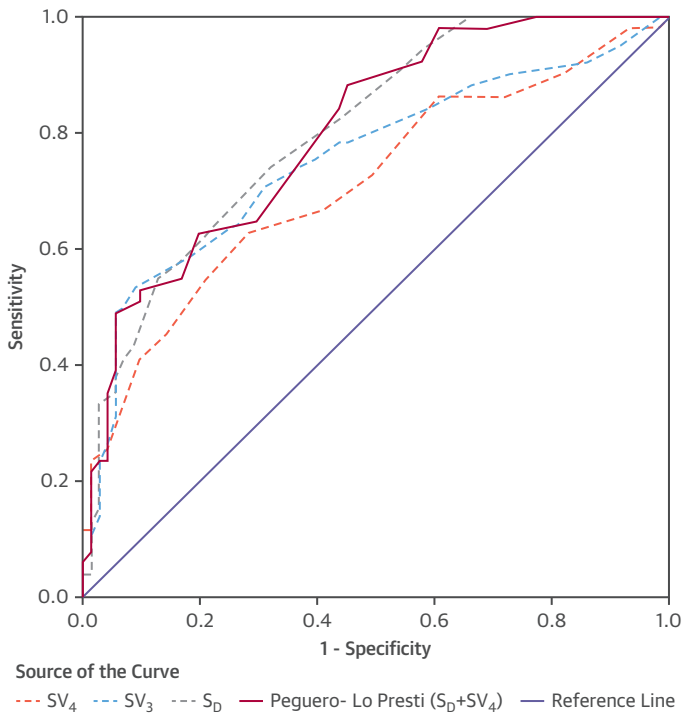
continuous variable, the diagnostic accuracy of $S_D + SV_4$ was similar to S_D (AUC: 0.80 vs. 0.80) (Table 7, Figure 3). However, when $S_D + SV_4$ was applied to both test and validation cohorts, the overall performance was better (AUC: 0.82 vs. 0.80), which reinforces the advantages of combining both measurements.

The proposed $S_D + SV_4$ criteria had nominally the best sensitivity (57%; 95% CI: 42% to 71%), followed by Cornell voltage (31%; 95% CI: 19% to 46%). The specificity of both tests was 90% (95% CI: 81% to 96%) and 93% (95% CI: 84% to 98%), respectively. In addition, compared with Sokolow-Lyon voltage, RaVL and RL_1, the proposed criteria demonstrated a significantly higher sensitivity with no significant differences in specificity (Table 8).

Combining both cohorts of patients, our measurement outperformed Cornell voltage with a significantly higher sensitivity (62% [95% CI: 50% to 72%] vs. 35% [95% CI: 24% to 46%]). The specificities of all the criteria were ≥90%, and there was no significant difference among them (Table 9). The comparison between the Cornel voltage and the Peguero-Lo Presti criteria showed lack of agreement with a p value <0.001.

According to Shourt and Fleiss analysis (with fixed effect), the intra-observer variability was 0.94 and the inter-observer variability was 0.80 (11).

FIGURE 3 AUC of the Validation Cohort



Area under the curve of continuous single leads and the proposed criteria deepest S wave in any lead and S wave in V_4 [$S_D + SV_4$]) representing the predictive performance of left ventricular hypertrophy in the validation cohort.

DISCUSSION

LVH is mainly determined by an increase in left ventricular mass, which can be estimated by the electrical voltage changes detected on the surface electrocardiogram. This principle makes the electrocardiogram an acceptable surrogate to detect changes in left ventricular mass. However, the cardiac electrical voltage does not exclusively depend on the amount of myocardium. Rather, it is dependent on active and passive electrical properties of the heart and torsum. These in turn are modified by influencing factors such as distance of left ventricular cavity-electrode, the location of the surface electrode, individual antrophometric differences, conduction abnormalities, fibrosis of the myocardium, and lung pathology (3,12). In addition, it has been described that the ECG voltage may vary significantly from day to day, between patients, or even within the same patient (4,13). All of these factors may attenuate the reproducibility of the test, leading to diagnostic errors.

Given the aforementioned pitfalls, measurement of the maximum voltage increase in any single lead would be more sensitive in identifying an increase in the ventricular mass, rather than using any fixed lead criteria. The S_D was the best single lead predictor of LVH in the studied cohorts (Tables 4 and 7, Figures 2 and 3). In fact, the sum of $S_D + SV_4$ in the studied population had a better diagnostic performance than the S_D individual lead (AUC: 0.82 vs. 0.80). The $S_D + SV_4$ criteria showed nominally an improved performance over the traditional LVH

TABLE 8 McNemar Test Among the Electrocardiographic Criteria Against the Left Ventricular Mass Index in the Validation Cohort

	Sensitivity (95% CI)	Specificity (95% CI)	McNemar Test*
RaVL	14 (6–26)	92 (83–97)	<0.0001
RL_1	14 (6–26)	93 (84–98)	<0.0001
Sokolow-Lyon voltage	14 (6–26)	99 (92–100)	<0.0001
Cornell voltage	31 (19–46)	93 (84–98)	<0.0001
$S_D + SV_4$ (Peguero-Lo Presti)	57 (42–71)	90 (81–96)	0.0053

*A p value < 0.05 indicates lack of agreement.
Abbreviations as in Table 5.

TABLE 9 McNemar Test Among the Electrocardiographic Criteria Against the Left Ventricular Mass Index in the Combined Population

	Sensitivity (95% CI)	Specificity (95% CI)	McNemar Test*
RaVL	16 (9–26)	92 (86–96)	<0.0001
RL_1	20 (12–30)	93 (87–96)	<0.0001
Sokolow-Lyon voltage	17 (10–27)	98 (94–100)	<0.0001
Cornell voltage	35 (24–46)	92 (86–96)	<0.0001
$S_D + SV_4$ (Peguero-Lo Presti)	62 (50–72)	90 (83–94)	0.0113

*A p value <0.05 indicates lack of agreement.
Abbreviations in Table 5.

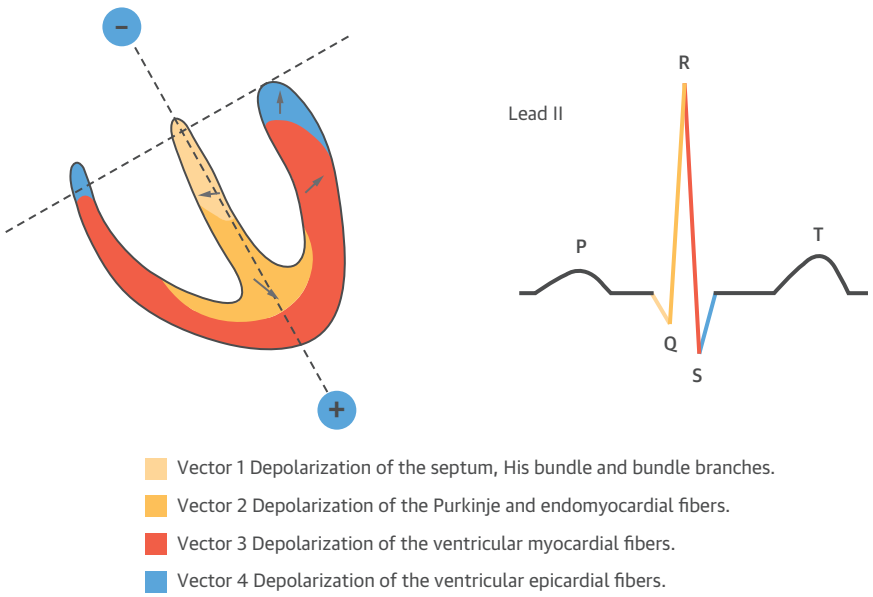
criteria when analyzed in the test and the validation cohort separately. However, when both cohorts were combined, there was a significant difference, noted mainly in the sensitivities, favoring the Peguero-Lo Presti criteria (Tables 5, 8, and 9).

Many of the traditional criteria had emphasized measuring the tallest amplitude of the R-wave in various leads. In contrast, the present study showed that the S waves of the precordial and limb leads had a better association with an increased left ventricular mass. Furthermore, this study showed that the R-wave or R′ complexes of many of the previously used criteria were, at best, fair predictors of LVH (Tables 4 and 7). One possible explanation for the improved performance shown in these 2 populations is that the vector generated by the depolarization of the ventricular free wall and myocardium may be better represented by the latter part of the QRS complex, the S wave.

The double layer of depolarization across the conduction system has multiple wave fronts moving in different directions. Simultaneous electrical wave fronts are summed, and a vector of depolarization with a specific direction and magnitude is defined. In the human heart, 4 vectors of depolarization have been described (Figure 2). The first 2 vectors represent depolarization of the septum, conduction system (His bundle, bundle branches, and Purkinje fibers), and endomyocardial fibers of the left ventricle (14). This is usually reflected in the first 30 ms of the ventricular depolarization. Late third and fourth vectors, which are believed to represent the depolarization of the myocardial and epicardial free wall of the left ventricle, occur no earlier than 50 ms (Figure 4) (15). Thus, it is plausible that changes in voltage that occur in patients with mild to moderate LVH are better represented by the latter part of the QRS complex, which corresponds to the S wave (Figure 5). Therefore, identifying these early changes may increase the sensitivity of the surface electrocardiogram (Central Illustration).

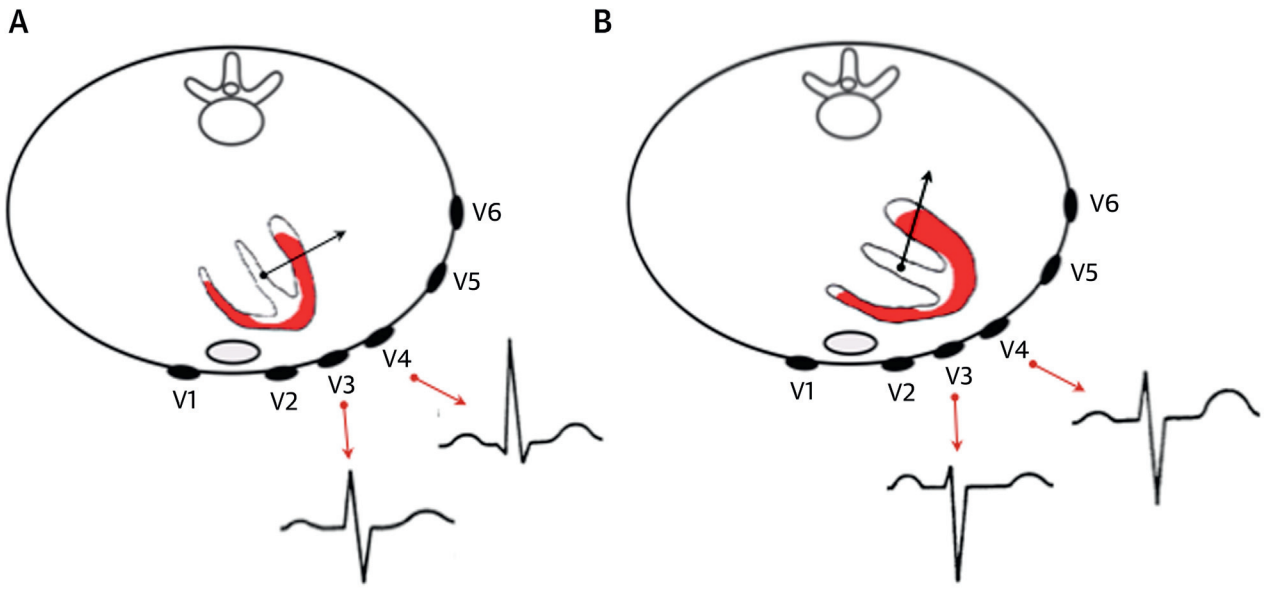
It has been suggested that the surface electrocardiogram mainly provides information about the electrical field generated by the heart and therefore

FIGURE 4 Mean Vectors of the Ventricular Depolarization



Sequence of vectors of ventricular depolarization based upon the anatomical distribution and resultant ECG tracing.

FIGURE 5 Ventricular Activation of the Precordial Leads Between a Normal Ventricle Versus LVH



In normal left ventricle **(A)**, the mean vector of myocardial fiber depolarization **(black arrow)**, is predominantly horizontal. The precordial lead V_3 will record an isoelectric QRS complex. In left ventricular hypertrophy **(B)**, the chamber grows leftward, inferiorly, and posteriorly changing the direction and magnitude of vector 3 **(black arrow)**. The precordial leads V_3 and V_4, will record a predominantly negative axis with increased amplitude of the S wave.

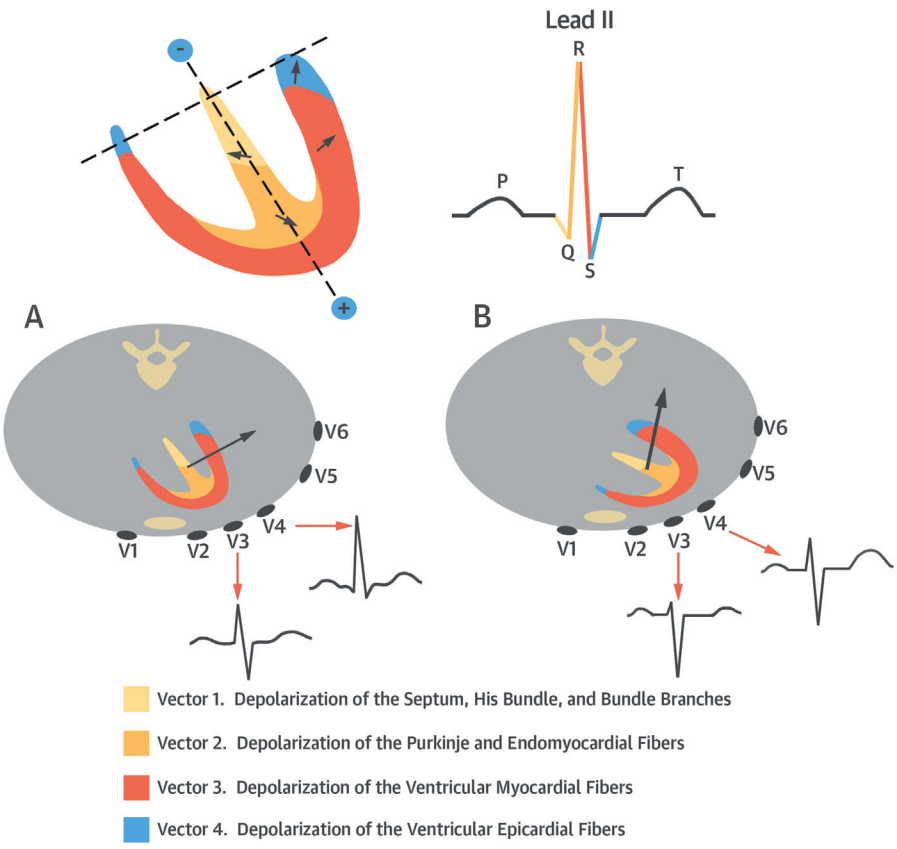
is not the best marker for left ventricular mass estimation. This discrepancy is best evidenced in amyloid cardiomyopathy, in which there is a severe increase in the left ventricular wall and left ventricular mass index according to echocardiogram, but up to 40% to 60% of the cases have low voltage on the surface electrocardiogram (16). In fact, LVH is not only the organ manifestation of hypertrophic growth of the cardiomyocytes but also of changes in the interstitium (17). Fibrosis and deposits of other material in the interstitium may dampen the voltage expression of the hypertrophic myocardium and limit the diagnostic capability of the surface electrocardiogram. This inherent limitation of the electrocardiogram is an important contributor to the high false-negative rate that all ECG criteria share. Nonetheless, the electrocardiogram continues to be an important low-cost tool for early screening and detection of LVH.

It is worth mentioning that the sensitivity of the proposed Peguero-Lo Presti criteria in the validation cohort decreased compared with the test cohort (70% vs. 57%). This finding may be related to the fact that the validation cohort was an older population with more comorbidities. Furthermore, this cohort had a higher incidence of eccentric hypertrophy, which is known to decrease the overall accuracy of the electrocardiogram (18). This observation has been demonstrated in other studies in which the sensitivity of the sex-specific Cornell voltage criteria, was lesser than was previously described (2,19).

STUDY LIMITATIONS. The limitations of this study include its single-center, retrospective design and relatively small sample size. In addition, there are known limitations to the AUC statistical method (20,21). Nonetheless, the methodology and overall populations were similar to those used in previous landmark ECG-LVH studies (22,23).

Another limitation is that the left ventricular mass and left ventricular mass index were estimated by using two-dimensional echocardiography, despite reports demonstrating superior accuracy of cardiac magnetic resonance imaging (3,12). In addition, the main determinant of LVH in this study was the left ventricular mass. This simplistic approach ignores the hypertrophic rebuilding of myocardial tissue that occurs in early stages and may contribute to the discrepancies seen among

CENTRAL ILLUSTRATION **Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy**



Peguero, J.G. et al. J Am Coll Cardiol. 2017;69(13):1694–703.

In normal left ventricle **(A)**, the mean vector of myocardial fiber depolarization **(black arrow)**, is predominantly horizontal. The precordial lead V_3 will record an isoelectric QRS complex. In left ventricular hypertrophy **(B)**, the chamber grows leftward, inferiorly, and posteriorly changing the direction and magnitude of vector 3 **(black arrow)**. The precordial leads V_3 and V_4, will record a predominantly negative axis with increased amplitude of the S wave.

electrocardiogram and echocardiogram measurements (17,24). Nonetheless, echocardiography is known to have good reproducibility for the diagnosis of LVH and remains the most frequently used method in clinical practice (25).

The proposed criteria did not improve upon the limitations of previous criteria in diagnosing LVH in patients with right or left bundle branch block, ventricular paced rhythm, concomitant right ventricular hypertrophy, and other cardiomyopathies, as these subgroups were excluded from the study. Racial differences in the diagnosis of LVH were not addressed in this study.

CONCLUSIONS

This $S_D + SV_4$ criteria provide a more sensitive measurement in the ECG diagnosis of LVH compared with the currently existing criteria and should be considered when applicable. However, further validation on a larger population is warranted before it becomes widely acceptable.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: When compared with Cornell voltage and other ECG criteria, the diagnosis of LVH can be enhanced by incorporating better representation of depolarization vectors in this disease.

TRANSLATIONAL OUTLOOK: Although a surrogate for more specific measurement of left ventricular mass, the electrocardiogram remains a widely available, relatively inexpensive diagnostic modality, and development of criteria that improve its diagnostic precision has implications for more efficient resource utilization.

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KEY WORDS electrocardiogram, left ventricular hypertrophy, novel criteria