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SD + SV4 diagnosis of left ventricular hypertrophy, a revaluation of ECG criterion by cardiac magnetic resonance imaging

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Abstract

Backgroud: Present electrocardiogram (ECG) criteria for diagnosing left ventricular hypertrophy (LVH) usually have low sensitivity, while the newly proposed SD + SV4 criterion, namely the deepest S-wave amplitude in any lead (SD) plus SV4 amplitude, has been reported to have higher sensitivity and accuracy compared with other existing criteria. We aimed to further evaluate the diagnostic value of the SD + SV4 criterion in reference to the gold standard cardiac magnetic resonance imaging (CMR) in LVH diagnosis.

Methods: This retrospective study enrolled 138 patients who received CMR examination—60 patients with reduced ejection fraction (EF) and 78 patients with preserved EF. The left ventricular mass index (LVMI) measured by CMR was used as the gold standard for diagnosing LVH.

Result: The diagnostic value of the SD + SV4 criterion was compared with other 4 commonly used criteria. By CMR, 29 out of 138 people (21%) were diagnosed with LVH in reference to CMR. The SD + SV4 criterion had markedly higher sensitivity in diagnosing LVH compared with other criteria, but no higher specificity. There was no significant difference in area under receiver operating characteristic (ROC) curve among these criteria. The SD + SV4 criterion was not markedly consistent with CMR in diagnosing LVH. Compared to the other criteria, the SD + SV4 criterion had the highest sensitivity in patients with reduced ejection fraction; however, the area under the curve (AUC) of the SD + SV4 criterion in patients with reduced EF was significantly lower than in patients with preserved EF.

Conclusion: The newly proposed SD + SV4 criterion did not have a better diagnostic value compared with other existing criteria, and the statistical power of the SD + SV4 criterion was influenced by EF.

KEYWORDS

CMR, electrocardiography, left ventricular hypertrophy, left ventricular mass index, SD + SV4 criterion

1 | INTRODUCTION

Left ventricular hypertrophy (LVH) is a common manifestation of preclinical cardiovascular disease that predicts cardiovascular morbidity and mortality in some conditions (Shah et al., 2011). A variety of risk factors including hypertension, obesity, and valvular heart disease may contribute to LVH, which is widely acknowledged to be a strong determinant of cardiovascular morbidity and mortality (Shao et al., 2019). In clinical practice, several methods have been used to assess LVH, including the electrocardiogram (ECG), echocardiography, and cardiac magnetic resonance (CMR). As a simple, economical, and convenient approach to obtain information on the electrical activity of the heart, the ECG is the most frequently used tools for screening of LVH. Up to now, over 30 electrocardiographic criteria have been proposed, but most of these have demonstrated high specificity but low sensitivity for diagnosing LVH (Bacharova & Ugander, 2014).

Recently, a novel criterion, termed the S_D + SV4 criterion, has been proposed by Peguero et al. (2017). The authors suggested that the sum of the amplitude of the deepest S wave in any lead (S_D) plus the S wave in lead V4 (SV4) improves the sensitivity for diagnosing LVH with ECG, while still maintain an adequate specificity. The authors purport the S_D + SV4 criterion has been reported to be superior to other ECG criteria in the diagnosis of LVH (Shao et al., 2019).

However, echocardiography was used as a diagnostic gold standard of LVH while assessing the SD + SV4 criterion in the study conducted by Peguero et al. Besides, most patients enrolled in their study had normal ejection fraction. Recently, CMR has been proposed to be a better diagnostic method for LVH (Grothues et al., 2002). In this study, we aimed to evaluate the consistency of the SD + SV4 criterion with CMR in patients with both normal EF and reduced EF, in order to revaluate the diagnostic value of the SD + SV4 criterion regarding LVH.

2 | METHODS

2.1 | Study population

This retrospective study is comprised of consecutively enrolled 138 patients who underwent CMR examination between September 2015 and January 2018 and had ECG recorded within 2 weeks of the CMR study. The patients were divided into two groups according to left ventricular ejection fraction (LVEF) by the CMR: those with reduced ejection fraction (LVEF <50%, $n = 60$) and those with preserved ejection fraction (LVEF ≥50%, $n = 78$). The exclusion criteria were as follows: (a) complete left or right bundle branch block; (b) unclear echocardiographic images; and (c) dextrocardia. All subjects signed written informed consent before enrollment in the study.

2.2 | Study protocol and evaluation criteria

Patient demographics including sex, age, and medical history were collected. The CMR, standard 12-lead ECG, and echocardiography examinations were conducted within each other 2 weeks. The left ventricular mass index (LVMI), which means left ventricular mass (LVM) divided by body surface area (BSA), calculated by CMR, was used as the diagnostic criterion for LVH. A cutoff of >83 g/m^2 in men and >67 g/m^2 in women was applied. The SD + SV4 criterion referred to the deepest S-wave amplitude (S_D) in any leads plus the S-wave amplitude in V4 (SV4). Based upon the study of Peguero et al, cutoff values of ≥2.8 mV in men and ≥2.3 mV in women were used to diagnose LVH by ECG (Peguero et al., 2017). Several other established ECG-used criteria for the diagnosis of LVH were also analyzed as reference, and these included (a) the S_D voltage criterion, defined as S_D ≥2.2 mV; (b) the sex-specific Cornell voltage criterion, computed as the amplitude of R in aVL plus the amplitude of S or QS complex in V3 (RaVL + SV3) with a cutoff of >2.8 mV in men and >2.0 mV in women (Casale et al., 1985); and (c) the Sokolow–Lyon voltage (Hancock et al., 2009) criterion, obtained by adding the amplitude of the S wave in V1 and the amplitude of R in V5 or V6, with cutoff in men and women of ≥3.5 mV. Figure 1 demonstrates the measurement of these criteria for LVH in a sample ECG.

2.3 | Statistical analysis

Statistical analyses were performed using SPSS 22.0 and MedCalc software. Categorical data were displayed as counts (percentage) and continuous data as means ± *SD* or median (interquartile range). The independent-samples *t* test was used for comparing continuous variables with normal distribution, while the chi-square test and the McNemar test were used to compare categorical variables. Receiver operating characteristic (ROC) curves were analyzed to assess the best cutoff values for ECG criteria. Consistency of different criteria was analyzed by the kappa test. *p* value less than .05 was considered statistically significant.

3 | RESULTS

A total of 138 patients (aged 28–60 years) including 94 males (68%) and 44 females (32%) were recruited in this study. The mean value of LVMI was 62.2 ± 29.2 g/m^2; 29 (21%) patients were diagnosed with LVH by CMR. The patients were divided into two groups: reduced EF (LVEF <50%) or preserved EF (LVEF ≥50%). There was no significant difference in gender, age, body weight, height, or relevant medical history between these two groups (Table 1).

As shown in Figure 2a and Table 2, area under the curve (AUC) values of the ROC curves of the 4 ECG criteria for LVH demonstrated no significant differences in the overall population. The Cornell criteria performed slightly better in patients with reduced LVEF (Figure 2b and Table 3), whereas the S_D and S_D + SV4 criteria performed slightly better in patients with LVEF >50% (Figure 2c and Table 3). As shown in Table 4, the S_D + SV4 criterion provided the highest sensitivity in patients with reduced LVEF and the second highest sensitivity in patients with normal LVEF (in whom the S_D criterion was most sensitive). However, the specificity of the S_D + SV4 criterion was lowest in all patients. The AUC

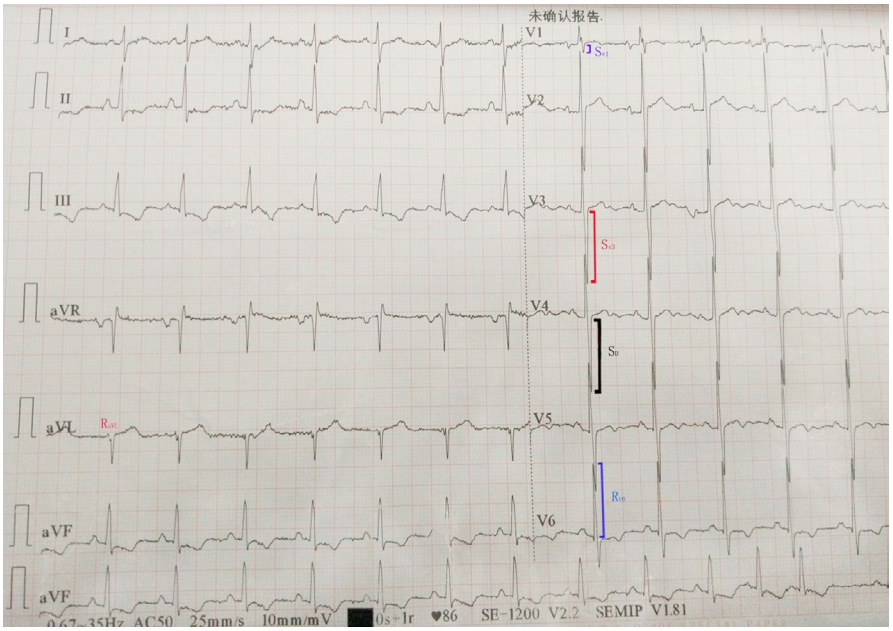


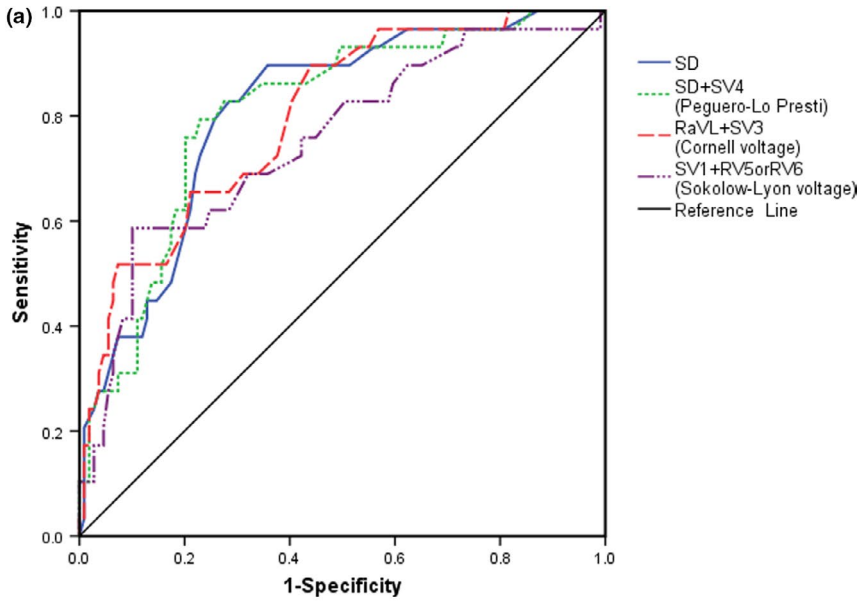
FIGURE 1 ECG example. Electrocardiogram of a 33-year-old woman that meets the criteria for left ventricular hypertrophy based on the Peguero–Lo Presti criterion (deepest S wave in any lead and S wave in V4[S_D + SV_4], 2.3 + 2.3 = 4.6 mV [female subjects ≥2.3 mV]) and based on the S_D voltage criterion (2.3 mV [female subjects ≥2.2 mV]). The diagnosis of left ventricular hypertrophy was confirmed by CMR (left ventricular mass index = 94 g/m^2). Note that 2 other established most common classical electrocardiographic criteria are not met: Cornell voltage criteria (RaVL + SV_3; 0.1 + 1.8 = 1.9 mV [female subjects >2.0 mV]) and Sokolow–Lyon voltage criteria (SV_1 + [RV_5 or RV_6]; 0.3 + 1.8 = 2.1 mV [female subjects ≥3.5 mV])

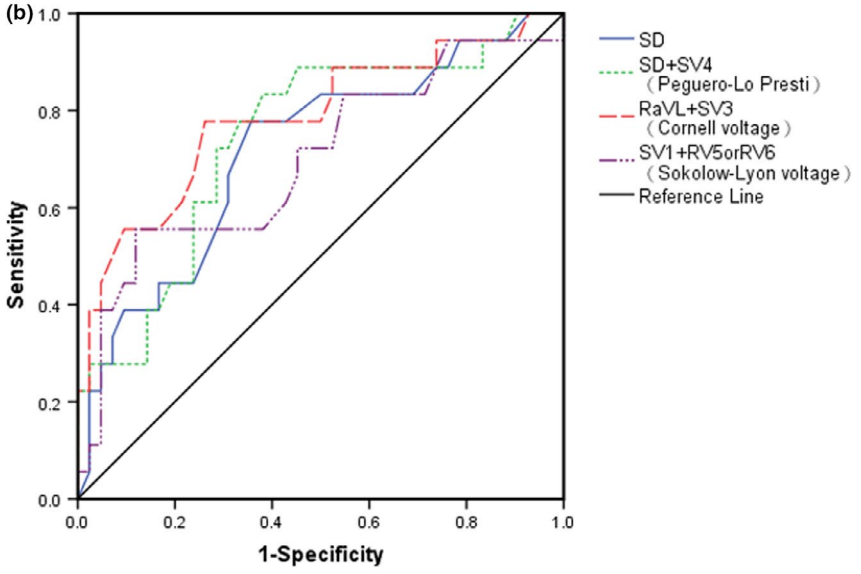
of the S_D + SV4 criterion was lower in patients with reduced LVEF than in patients with preserved LVEF (Figure 2, Table 3). These observations suggest that the diagnostic performance of the S_D and S_D + SV4 criteria (and likely other ECG-LVH criteria) is significantly influenced by LV function and geometry. As shown in Table 4, the agreement between ECG-LVH criteria and the presence of LVH by CMR varied greatly among the four ECG criteria as assessed by the McNemar and kappa tests. The McNemar test highlighted significant differences in diagnosing LVH between CMR and both the SD and the SD + SV4 criteria in all patients, whereas no marked difference was seen between the Cornell and Sokolow–Lyon criteria. The kappa test indicated poor agreement between CMR and all four ECG criteria for LVH (Table 4).

TABLE 1 Demographic characteristics of LVEF <50% group and LVEF ≥50% group

	Total population	LVEF <50% group *N* = 60	LVEF ≥50% group *N* = 78	*p* value
Male	94 (68)	45 (75)	49 (63)	.125
Age(y)	44 ± 16	44 ± 15	45 ± 17	.685
Height(cm)	171 ± 9	172 ± 8	171 ± 9	.577
Weight(kg)	72 ± 13	74 ± 13	70 ± 14	.100
Body surface area, m^2	1.84 ± 0.19	1.87 ± 0.18	1.81 ± 0.20	.137
BMI, kg/m^2	24.44 ± 3.62	25.03 ± 3.28	23.99 ± 3.83	.094
Hypertension grade 3, Hypertensive crisis, Hypertensive emergency	44 (32)	14 (23)	30 (38)	.055
Diabetes	9 (7)	5 (8)	4 (5)	.453
Heart failure	57 (41)	49 (82)	8 (10)	<.001
Dyslipidemia	36 (26)	14 (23)	22 (28)	.522
Atrial fibrillation	4 (3)	1 (2)	3 (4)	.453
Peripheral arterial disease	1 (1)	0 (0)	1 (1)	.382
Coronary heart disease	30 (22)	12 (20)	18 (23)	.667
Myocardial infarction	5 (4)	3 (5)	2 (3)	.451

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





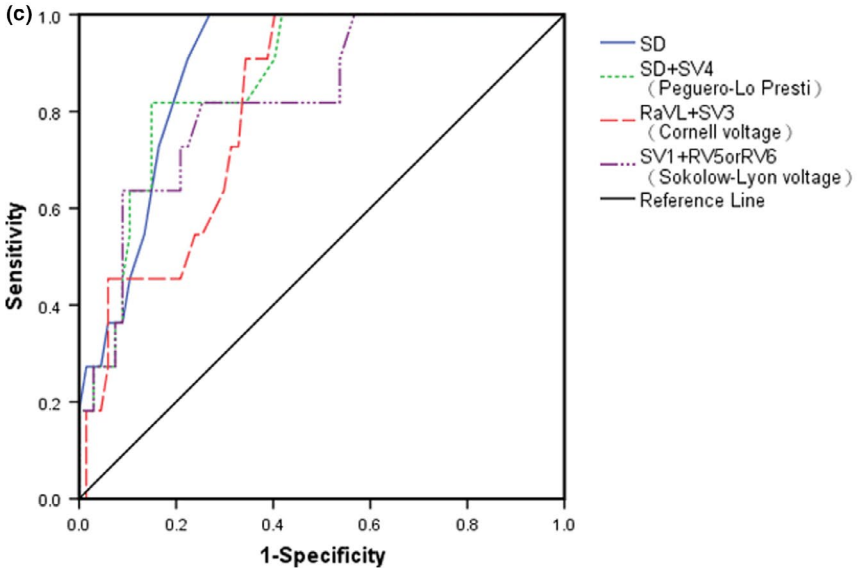


FIGURE 2 (a) ROC curves of 4 ECG-LVH criteria obtained in the entire study population. Area under the ROC curves of the four ECG-LVH criteria derived from all study subjects demonstrate slightly superior performance of the S_D and S_D + SV4 criteria compared with Cornell and Sokolow–Lyon criteria. (b) ROC curves of 4 ECG-LVH criteria obtained in patients with LVEF <50%. Area under the ROC curves of four ECG-LVH criteria demonstrates no significant differences between the four analyzed criteria. (c) ROC curves of 4 ECG-LVH criteria obtained in patients with LVEF >50%. Area under the ROC curves of four ECG-LVH criteria demonstrates S_D and S_D + SV4 criteria to be somewhat better than the Sokolow–Lyon and Cornell criteria

4 | DISCUSSION

Left ventricular hypertrophy has been shown to be an independent risk factor for high-risk cardiovascular outcomes (Agabiti-Rosei & Muiesan, 2002). Its detection is important. Currently, several methods are used in clinical practice to diagnose LVH, including the standard 12-lead ECG, echocardiography, and cardiac magnetic resonance (Brzozowska-Czarnek & Bryll, 2013). Echocardiography results are dependent upon the image acquisition skill of the operator and the patient's acoustic window (Armstrong et al., 2012). The estimation of LV mass by echocardiography is reasonable in normal ventricles, but the quantification of volumes and mass relies on geometric assumptions that do not apply to ventricles undergoing asymmetric cardiac remodeling such as cardiomyopathy (American College of Radiology et al., 2006; Lang et al., 2005). Cardiovascular magnetic resonance (CMR) overcomes the technical limitations of echocardiography, estimates LV mass independent of geometric assumptions, and has better accuracy and reproducibility. Bellenger et al have reported improved reproducibility of CMR compared with echocardiography in patients with heart failure (Bellenger et al., 2000). The ECG is the most convenient, economical, and user-friendly technique among above methods, and LVH assessed by electrocardiography has been shown to be a good marker of subclinical cardiac damage and a strong predictor of adverse cardiovascular events (Brinkley et al., 2018). The amplitude of the electrical signals depends not only on myocardial cell numbers, but also on the active and passive electrical characteristics of these cells. A number of electrocardiographic criteria for LVH have been proposed, among which the most commonly used are the Sokolow–Lyon criteria and the Cornell limb lead criteria. Like all ECG-LVH criteria listed in the 2009 multisociety guidelines for the interpretation of the ECG, these criteria have relatively low accuracy and low sensitivity. Therefore, there is clinical need, if possible, to derive new ECG-LVH criteria that demonstrate higher sensitivity without compromising specificity. The traditional ECG criteria emphasize the measurement of the R-wave amplitude in various leads (Dewey et al., 2008; Pewsner et al., 2007). Yet, the terminal component of the ECG signal (S wave) may better reflect the main depolarization vector of the ventricular free wall (Tse et al., 2016). Thus, it is conceivable 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. Given this, Peguero et al. (2017) proposed a novel criterion for diagnosing LVH, namely the S_D + SV4 criterion. They

TABLE 2 AUC of ROC curves of 4 ECG-LVH criteria in diagnosis of LVH in general

	AUC (95% confidence interval)	*p* value
S_D + SV4	0.808 (0.732–0.870)	<.001
Cornell	0.800 (0.723–0.863)	<.001
Sokolow–Lyon	0.752 (0.671–0.821)	<.001
S_D	0.810 (0.735–0.872)	<.001

Note: A *p* value < .05 indicates lack of agreement.

TABLE 3 AUC of ROC curves of 4 ECG-LVH criteria in diagnosis of LVH in patients with normal and reduced LV function

	LVEF <50%	LVEF ≥50%
ECG criterion	AUC	AUC
S_D + SV4	0.743 (0.613–0.847)	0.866 (0.770–0.932)
Cornell	0.787 (0.662–0.882)	0.811 (0.706–0.891)
Sokolow–Lyon	0.698 (0.566–0.810)	0.827 (0.725–0.903)
S_D	0.716 (0.585–0.825)	0.890 (0.799–0.950)

Notes: Numbers in parentheses indicate 95% confidence intervals. The AUC values of the 4 ECG-LVH criteria, in patients with normal and reduced LVEF, all demonstrated poor agreement between the presence of LVH by CMR and its prediction by ECG criteria (with *p* value < .001 for all measurements).

TABLE 4 Diagnostic performance of 4 ECG criteria for LVH

	LVEF <50%				LVEF ≥50%			
	Specificity	Sensitivity	McNemar value	Kappa value	Specificity	Sensitivity	McNemar value	Kappa value
S_D + SV4	57.1	83.3	0.001	0.105	74.6	81.8	<0.001	0.325
Cornell	88.2	55.6	0.581	0.458	88.1	45.5	0.791	0.311
Sokolow–Lyon	81.0	55.6	1.000	0.365	83.6	63.6	0.118	0.373
S_D	61.9	77.8	0.012	0.333	77.6	90.9	0.001	0.447

Notes: Sensitivity and specificity of each ECG-LVH criterion, as compared to gold standard of increased LV mass by CMR, are listed. The 2 parameters demonstrated a typical inverse relationship in most instances, except for the SD and SD + SV4 criteria, which demonstrated sensitivity and specificity >70% in patients with normal LV function (but not in those with LVEF <50%). A McNemar value <0.05 indicates poor agreement between the diagnosis of LVH by CMR and ECG criteria. The relationship between the diagnosis of LVH by CMR and ECG criteria by kappa values is as follows: K >0.75 = good agreement; K <0.4 = poor agreement; and K-values between 0.4 and 0.75 indicate moderate agreement. See text for further discussion.

suggested that the S_D + SV4 criterion showed improved performance over the existing LVH criteria. Recently, Cláudio Guerreiroa et al verified the S_D + SV4 criterion by CMR in European population (Guerreiro et al., 2020). However, their study has an important limitations. First, they diagnosed left ventricular mass using two-dimensional echocardiography. Second, they studied chiefly patients with normal LV function and were thus unable to observe the different diagnostic accuracy of ECG-LVH criteria in relation to LV function that we have observed. Third, their study population included no Asian subjects, so their findings cannot necessarily be extrapolated to such patients.

In our study, CMR imaging served as the gold standard for diagnosing LVH. Our results are less promising than those reported by Pergueo et al. We observed lower sensitivity and specificity values of the S_D + SV4 criterion than was reported by Pergueo and colleagues. One reason for our findings may be that the patients enrolled in our study included more patients with reduced LV function than in the Peguero study. The failing, dilating heart in patients may affect the overall electrocardial vector, reducing the ability. Too, our Asian patients may show different results than the European cohort studied by Pergueo et al. Like their study, our study has a relatively small sample size, and it is limited to an Asian population. We call for more studies on the diagnostic value of CMR on LVH in different populations.

Our findings suggest that the SD and SD + SV4 criteria do not improve the overall accuracy of LVH diagnosis, as their accuracy appears to be influenced by LVEF, a factor that has not been carefully examined in regard to existing ECG-LVH criteria. The quest for ECG criteria to diagnose LVH remains unfulfilled.

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CONFLICT OF INTEREST

The authors have declared that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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