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Newly proposed electrocardiographic criteria for the diagnosis of left ventricular hypertrophy in a Chinese population

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Abstract

Background: The electrocardiographic criteria currently available for the diagnosis of left ventricular hypertrophy (LVH) are low in sensitivity. Thus, we compared the diagnostic performance of newly proposed electrocardiographic criteria to the existing criteria in a Chinese population.

Methods: A total of 235 consecutive hypertensive patients, hospitalized in our department between May 2017 and April 2018, were included. They were divided into two groups based on the gold standard echocardiogram: those with (n = 116) and without LVH (n = 119). The newly proposed ECG criteria were calculated by summating the amplitude of the deepest S wave (S_D) in any single lead and the S-wave amplitude of lead V_4 (S_{V4}). The area under the curve was calculated and compared against the sex-specific Cornell limb lead and Sokolow–Lyon criteria.

Results: ECG analysis of the cohort showed that the newly proposed criteria had the highest sensitivity in diagnosing LVH (male: 65.5%; female: 81%), followed by the Cornell limb lead criteria (male: 55.2%; female: 56.9%). The specificities of both sets of criteria were higher than 70%, with no significant differences between them. Receiver operator curve analysis showed an optimal cutoff of \geq 2.1 mV for females (AUC: 0.832; 95% CI: 0.757–0.906) and \geq 2.6 mV for males (AUC: 0.772; 95% CI: 0.687–0.856).

Conclusion: The newly proposed $S_D + S_{V4}$ criteria provide an improved sensitivity for the ECG diagnosis of LVH compared to existing criteria, but its routine use will require further validation in larger populations.

KEYWORDS

cornell voltage criteria, ECG criteria, left ventricular hypertrophy, peguero-Lo presti criteria, sensitivity

1 | INTRODUCTION

Left ventricular hypertrophy (LVH) is a pathological adaptation to underlying cardiovascular disease and a strong determinant for cardiovascular morbidity and mortality (Bombelli et al., 2009; Gosse et al., 2012; Schillaci, Battista, & Pucci, 2012; Verdecchia et al., 2001). In recent years, studies have reported the reversible nature of LVH, which has led to a reduction in adverse clinical outcomes (Verdecchia et al., 2003). As such, the early and correct diagnosis of LVH is of paramount importance. The electrocardiogram (ECG), being simple, economic, and convenient, is one of the most common tools for the screening and diagnosis of LVH. However, 37 electrocardiographic

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FIGURE 1 An example

electrocardiogram of a 43-year-old man that meets criteria for left ventricular hypertrophy based on the newly proposed criteria (deepest S wave in any lead and S wave in V₄ [S_D + S_{V4}]; 1.7 + 1.2 = 2.9 mV [male subjects \ge 2.8 mV]). By contrast, LVH was not diagnosed using either the Cornell limb lead criteria (R_{aVL} + S_{V3}; 0.6 + 1.7 = 2.3 mV [male subjects \ge 2.8 mV]) or the Sokolow-Lyon criteria (S_{V1} + R_{V5}; 0.4 + 1.3 = 1.7 mV [male subjects \ge 3.5 mV])

criteria have been endorsed by the American Heart Association to date, the abundance of which leads to confusion among diagnosing clinicians (Bacharova & Ugander, 2014; Hancock et al., 2009). Moreover, most of these criteria have high specificities but low sensitivities overall, for instance, the Cornell voltage criteria, with 90% specificity but only 20%-40% sensitivity (Casale et al., 1985; Schillaci et al., 1994). Therefore, a new ECG standard with higher sensitivity and specificity must be explored with utmost urgency. Recently, Peguero et al. (2017) established novel ECG criteria that take the voltage amplitudes that occur within each lead into consideration. The authors found that the summation of the amplitude of the deepest S wave in any lead (S_{D}) with the S wave in lead V_{4} (S_{V4}) improves the sensitivity of the currently existing criteria, while maintaining an adequate specificity for the diagnosis of LVH. Our aim was to investigate the correlation of these novel ECG criteria in the diagnosis of LVH with hypertensive patients in a Chinese population.

2 | METHODS

2.1 | Study population

A total of 235 consecutive hypertensive patients who were hospitalized in our department between May 2017 and April 2018 were recruited sequentially for participation in the study. The patients were divided into two groups according to echocardiographic findings: those with LVH (n = 116) and those without LVH as controls (n = 119). Hypertension was defined as systolic blood pressure \geq 140 mmHg and/or diastolic blood pressure \geq 90 mmHg (Mancia et al., 2013), or if the patient was receiving any type of antihypertensive medication. Transthoracic echocardiography was used to diagnose LVH, defined as interventricular septum and left ventricular posterior wall thickness of over 11 mm each (Lang et al., 2016). Diabetes mellitus was defined as having a history of antidiabetic medication use or a fasting glucose level \geq 126 mg/dl (Nang et al., 2009). Hypercholesterolemia was defined as total cholesterol >220 mg/ dl, low-density lipoprotein cholesterol >140 mg/dl, high-density lipoprotein cholesterol <40 mg/dl, fasting triglycerides >150 mg/ dl, or if the patient was being medically treated for the condition. A smoking habit was defined as smoking >2 pack-years. The exclusion criteria were as follows: (a) atrial or ventricular arrhythmias, (b) complete left or right bundle branch block, (c) inability to obtain or unclear echocardiographic images, (d) a history of myocardial infarction, and (e) ventricular paced rhythm. All subjects provided written informed consent before enrollment in the study.

2.2 | Study protocol

Patient demographics (sex, age, and medical history) were collected, and the standard 12-lead ECG and echocardiography examinations were conducted during the same visit. Complete blood count (CBC) was taken on admission, using established clinical laboratory methods (Coulter BC-5380/6800 Hematology Analyzer; Mindray, Shenzhen, China) for white blood cell count (WBC), hemoglobin (Hb), and red blood cell distribution width (RDW). Uric acid (UA), serum creatinine (Cr), and fasting blood glucose (FBG) were measured after overnight fasting (12 hr) by a TBA-120 FR analyzer (Toshiba, Japan), using the turbidimetric method.

A transthoracic echocardiographic examination was performed in all patients using the Vivid-7 system equipped with a 2.4 MHz transducer (GE Medical Systems, Milwaukee, WI, USA). Left atrial diameter (LAD), interventricular septal thickness (IVST), left ventricular posterior wall thickness (LVPWT), and left ventricular end-diastolic diameter (LVEDD) were assessed. Left ventricular ejection fraction (LVEF) was determined from apical four-chamber and two-chamber views using Simpson's biplane formula. All echocardiographic data were analyzed by two investigators who were blinded to the clinical status of the study subjects.

2.3 | ECG analysis

A single 12-lead ECG (25 mm, s/10 mm, mV; Beijing Foton Electronic Medical Instrument Co. LTD FX-7402, China), taken on admission,

was selected for each patient. It was independently interpreted by two cardiologists (Q.S and L.M). 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. $S_D + S_{V4}$ criteria were defined as the summation of the amplitude of the deepest S wave in any lead (S_D) with the S wave in lead V_4 (S_{V4}). The sex-specific Cornell voltage criteria were computed as the amplitude of R in aVL plus the amplitude of S or QS complex in V_3 ($R_{aVL} + S_{V3}$) with a cutoff of >2.8 mV in men and >2.0 mV in women (Casale et al., 1985). The Sokolow–Lyon voltage criteria (Hancock et al., 2009) were obtained by adding the amplitude of the S wave in V_1 and the amplitude of R in V_5 or $V_6 \ge 3.5$ mV ($S_{V1} + R_{V5}$ or R_{V6} ; Figure 1).

2.4 | Statistical analysis

The normality of the distribution of each continuous variable was tested by the Kolmogorov-Smirnov test. Categorical variables were reported as counts (percentage) and continuous variables as means ± SD or median (interguartile range). Statistical analysis was performed using the independent sample t test for continuous variables with normal distribution and Mann-Whitney U for non-normally distributed data, while the chi-square test was used to compare categorical variables. Receiver operating curves (ROC) were analyzed to assess the best cutoff values for ECG criteria (S $_{\rm D}$ + S $_{\rm V4}$, R $_{\rm aVL}$ + S $_{\rm V3}$) to discriminate LVH from hypertensive patients. Multivariable regression analyses were performed in order to investigate the factors that influence ECG morphology for the newly proposed $S_D + S_{V4}$ criteria in the study population. Only p values < 0.05 were regarded as statistically significant. All tests were two-tailed, and analyses were performed using SPSS 17.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA).

3 | RESULTS

A total of 116 hypertensive patients with LVH (50% male; mean age 65.7 years), and 119 sex- and age-matched hypertensive patients without LVH (48.7% male; mean age 64.9 years) were included in our study. Both groups were comparable in terms of baseline characteristics, except for the higher incidences of stroke and renal insufficiency in the LVH group (p < 0.05; Table 1). Regarding the laboratory tests, the LVH group showed higher RDW, UA, and Cr levels, while WBC, Hb, and FBG levels did not differ significantly (Table 2). Echocardiographic analysis showed significantly higher LAD, LVEDD, LVPWT, and IVST, but similar LVEF (Table 2).

Electrocardiographic analysis revealed higher voltage values in the LVH group compared to the non-LVH group using both the newly proposed ($S_D + S_{V4}$; 2.35 ± 0.95 vs. 1.47 ± 0.61, *p* < 0.0001) and Cornell limb lead criteria ($R_{avL} + S_{V3}$; 1.68 ± 0.61 vs. 1.25 ± 0.51, *p* < 0.0001). By contrast, the Sokolow–Lyon criteria ($S_{V1} + R_{V5}$) found no significant difference between the groups (2.09 ± 0.86 vs.

TABLE 1	Baseline clinical and demographic properties of study
population	

	Non-LVH (n = 119)	LVH (n = 116)	p
Age, years	64.9 ± 9.8	65.7 ± 11.8	0.242
Sex, male (<i>n</i> , %)	58 (48.7)	58 (50.0)	0.847
Diabetes mellitus (n, %)	21 (17.6)	50 (43.1)	0.034
Hypercholesterolemia (n, %)	54 (45.4)	53 (45.7)	0.894
Coronary heart disease (n, %)	30 (25.2)	34 (29.3)	0.558
Stroke (n, %)	9 (7.6)	23 (19.8)	0.007
Renal insufficiency (n, %)	5 (4.2)	19 (16.4)	0.000
Smoking habit (n, %)	22 (18.5)	27 (23.3)	0.415
Previous medication (n, %	5)		
ACEI/ARB	67 (56.3)	79 (68.1)	0.181
Beta-blocker	24 (20.2)	31 (26.7)	0.151
ССВ	65 (54.6)	57 (49.1)	0.435
Diuretic	12 (10.1)	9 (7.8)	0.649

Note. ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocking agents; CCB, calcium channel blockers; LVH, left ventricle hypertrophy.

1.90 ± 0.71, p = 0.06). Subsequently, sensitivity and specificity values were compared between the different sets of criteria. The newly proposed criteria showed the best sensitivity (male: 65.5%; female: 81.0%), followed by the Cornell limb lead criteria (male: 55.2%; female: 56.9%), and finally the Sokolow-Lyon criteria (male: 63.8%; female: 51.7%). The specificity of the newly proposed criteria (male: 74.1%; female: 77%) and the specificity of the Cornell limb lead criteria (male: 75.9%; female: 94.0%) were both higher than that of the Sokolow-Lyon criteria (male: 56.9%; female: 59.0%).

Receiver operating characteristic curves were then constructed. This permitted optimal cutoff values to be determined according to the maximum Youden index (the sum of the sensitivity and specificity). With regards to the novel criteria, values of ≥ 2.6 mV for male (AUC: 0.772; 95% CI: 0.687–0.856) and ≥ 2.1 mV for female subjects (AUC: 0.832; 95% CI: 0.757–0.906) were considered positive for LVH (Figures 2 and 3). Our data suggest that the Cornell limb lead criteria predicted LVH at lower values (males: 2.04 mV; females: 1.71 mV) than in the guidelines (2.8, 2.0 mV, respectively). We also observed the same phenomenon in the standard of the Sokolow–Lyon criteria (males: 2.05 mV; females: 1.95 mV). This may suggest different cutoff values for Chinese ethnicity.

Multivariable regression analyses were performed in order to investigate the factors that influence ECG morphology for the newly proposed $S_D + S_{V4}$ criteria in the study population. A few of factors that were variably distributed in the population were selected for the regression analysis. We found that that age and LVEF were independently associated with ECG morphology for the newly proposed

TABLE 2	Laboratory, electrocardiographic, and
echocardiog	raphic parameters of the study populatior

	Non-LVH (n = 119)	LVH (n = 116)	р			
Laboratory parame	eters					
WBC Count (10*9/L)	6.99 ± 1.41	6.90 ± 1.59	0.663			
Hb (g/L)	138.46 ± 15.24	135.68 ± 19.40	0.227			
RDW (%)	12.72 ± 0.46	13.28 ± 0.90	0.000			
UA (μmol/L)	333.35 ± 79.00	365.44 ± 84.83	0.017			
Cr (μmol/L)	67.64 ± 14.12	88.83 ± 36.47	0.000			
FBG (mmol/L)	5.90 ± 1.60	5.88 ± 1.75	0.919			
Echocardiogram va	ariables					
LAD (mm)	37.30 ± 4.77	41.67 ± 6.67	0.000			
LVEDD (mm)	46.47 ± 4.10	48.04 ± 4.95	0.008			
LVPWT (mm)	9.00 ± 0.85	12.25 ± 1.10	0.000			
IVST (mm)	8.97 ± 0.93	12.45 ± 1.19	0.000			
LVEF (%)	62.05 ± 5.53	61.36 ± 7.14	0.415			
Electrocardiographic parameters						
Peguero-Lo criteria (S _D + S _{V4})	1.47 ± 0.61	2.35 ± 0.95	0.000			
Cornell limb lead criteria (R _{avL} + S _{V3})	1.25 ± 0.51	1.68 ± 0.61	0.000			
Sokolow-Lyon criteria (S _{V1} + R _{V5})	1.90 ± 0.71	2.09 ± 0.86	0.061			

Note. Cr: serum creatinine; FBG: fasting blood glucose; Hb: hemoglobin; IVST: interventricular septal thickness; LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVH: left ventricle hypertrophy; LVPWT: left ventricular posterior wall thickness; RDW: red blood cell distribution width; UA: uric acid; WBC: white blood cell.

 ${\rm S}_{\rm D}$ + ${\rm S}_{\rm V4}$: deepest S wave in any lead plus S wave in V₄. R_{avL} + S_{V3}: the amplitude of R in aVL plus the amplitude of S or QS complex in V₃. Sv₁ + Rv₅: the amplitude of S wave in V₁ plus the amplitude of R wave in V₅.



 $S_D + S_{V4}$ criteria in the study population for males (OR 1.041, 95% CI 1.004–1.077; OR 0.908, 95% CI 0.841–0.981; p < 0.05, respectively; Table 3), and only LVEF was independently associated with ECG morphology for the newly proposed $S_D + S_{V4}$ criteria in the study population for females (OR 0.901, 95% CI 0.813–0.998; p < 0.05; Table 4). In addition, chest lead voltage is, of course, heavily dependent on the location of the electrode. We showed a figure where we vary the position of V₄ electrode for a patient and record the consequent changes in S-wave voltage (Figure 4), so the accurate placement of electrode is the primary factor.

4 | DISCUSSION

LVH is an independent risk factor associated with a high risk of adverse outcomes (Agabiti-Rosei & Muiesan, 2002; Vakili, Okin, & Devereux, 2001). Currently, LVH can be diagnosed using the standard 12-lead ECG, as well as imaging methods such as echocardiography and cardiac magnetic resonance (CMR; Alfakih, Reid, Hall, & Sivananthan, 2006). Out of these three modalities, the ECG is most frequently used due to its convenient, economic, and user-friendly nature (Oseni et al., 2017; Vassiliou et al., 2014). 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 (Tse, Wong, Tse, & Yeo, 2016), but also on the active and passive electrical characteristics of these cells. These in turn are modified by influencing factors such as the difference between the surface electrodes and the myocardial tissue, electrodeposition, conduction abnormalities, myocardial fibrosis, emphysema, and other factors (Bacharova & Ugander, 2014; Casale, Devereux, Alonso, Campo, & Kligfield, 1987; Tse & Yeo, 2015).

A number of electrocardiographic criteria for LVH have been proposed, and the commonest used are the Sokolow-Lyon criteria (S-wave depth in V_1 + tallest R-wave height in V_5 - V_6 >35 mm for both genders) and the Cornell limb lead criteria (S-wave depth in V_3 + R-wave amplitude in aVL >28 mm in males and >20 mm in

FIGURE 2 Receiver operating curve of the three criteria for the diagnosis of left ventricular hypertrophy in the study population for males



FIGURE 3 Receiver operating curve of the three criteria for the diagnosis of left ventricular hypertrophy in the study population for females

TABLE 3 Multivariate logistic regression analysis on influencing ECG morphology for the newly proposed $S_D + S_{V4}$ criteria in the study population for males

	В	SE	Wald	p	OR	95% CI	
LAD	0.090	0.052	3.057	0.080	1.095	0.989	-1.211
LVEDD	0.023	0.067	0.124	0.725	1.024	0.898	-1.167
LVEF	-0.096	0.039	5.994	0.014	0.908	0.841	-0.981
age	0.042	0.019	4.607	0.032	1.041	1.004	-1.077
Hypercholesterolemia	-0.306	0.524	0.341	0.559	0.736	0.263	-2.058
Cr	0.001	0.007	0.018	0.892	1.001	0.987	-1.015
К	0.075	0.454	0.027	0.869	1.078	0.442	-2.626

Note. Cr: creatinine; LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction.

	В	SE	Wald	p	OR	95% CI	
LAD	0.062	0.052	1.451	0.228	1.064	0.962	-1.178
LVEDD	0.163	0.086	3.585	0.058	1.177	0.994	-1.394
LVEF	-0.105	0.052	4.013	0.045	0.901	0.813	-0.998
age	-0.013	0.029	0.198	0.656	0.987	0.934	-1.044
Hypercholesterolemia	-0.293	0.585	0.251	0.616	0.746	0.237	-2.347
Cr	0.020	0.016	1.563	0.211	1.020	0.989	-1.053
К	-1.233	0.655	3.545	0.060	0.291	0.081	-1.052

Note. Cr: creatinine; LAD: left atrial diameter; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction.

females; Okin, Hille, Kjeldsen, & Devereux, 2017). Although these criteria have high specificities, their sensitivities are low. A metaanalysis has shown that LVH diagnosed electrocardiographically is a poor predictor of echocardiographic diagnosis of LVH (sensitivity of 10.5%–21% and specificity of 89%–99%; Pewsner et al., 2007). Similar results were obtained in a study that compared the diagnostic yield of LVH to CMR (Jain et al., 2010). Therefore, there is a clinical need to devise new ECG criteria with higher sensitivity values.

The traditional ECG criteria emphasize measurement of the R-wave amplitude of the highest lead. Yet, the second part (S wave) can better

reflect the main depolarization vector of the ventricular free wall. In the human heart, four depolarization vectors have been described. The first 30 ms consists of depolarization of the interventricular septum and the left ventricular endocardium (Ramanathan, Jia, Ghanem, Ryu, & Rudy, 2006). The third and fourth vectors represent depolarization of the left ventricular myocardium and epicardial free wall, which occur no earlier than 50 ms within the start of ventricular depolarization (Durrer et al., 1970). 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.

TABLE 4 Multivariate logistic regression analysis on influencing ECG morphology for the newly proposed $S_D + S_{V4}$ criteria in the study population for females



FIGURE 4 An example picture of the consequent changes in S-wave voltage according to different position of V_4 electrode for a patient

The measurement of maximum voltage in any lead, rather than a fixed lead, would significantly increase the sensitivity. Therefore, identifying these early changes may increase the sensitivity of the ECG. Peguero et al. (2017) showed that the S_D is the best single lead with which to diagnose LVH, and furthermore, the diagnostic value of S_D + S_{V4} is higher than that of S_D alone. Our study also showed that S_D + S_{V4} criteria had nominally the best sensitivity (for male: 65.5%; for female: 81%), followed by the Cornell voltage criteria (for male: 55.2%; for female: 56.9%). Therefore, application of these novel criteria in the diagnosis of LVH in lieu of traditional indicators results in higher sensitivity and specificity.

4.1 | Limitations

Some limitations of this study should be considered. First, the study is from a single center with a relatively small sample size, for which the utility of the AUC statistical method may be limited (Cook, 2008, 2010). Secondly, interventricular septum and left ventricular posterior wall thickness were estimated by using twodimensional echocardiography, although better accuracy would be achieved using CMR (Bacharova & Ugander, 2014; Casale et al., 1987). Nonetheless, echocardiography is known to have good reproducibility for the diagnosis of LVH and remains the most frequently used method in clinical practice (Palmieri et al., 1999). Thirdly, subjects in this study were selected from a population that required echocardiography examinations. Therefore, our findings cannot be applied to the general and otherwise healthy population. Fourthly, we only compared the newly proposed criteria to the two commonest methods, the Cornell limb lead criteria, and Sokolow-Lyon criteria. We therefore cannot exclude the possibility that other criteria may perform with higher sensitivities than

the latter two criteria studied here. Finally, 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 that might influence the accuracy of the $S_D + S_{V4}$ criteria, as these subgroups were excluded from the study and axis shits also influence the amplitude of S wave in V₄. It needs large-scale studies to verify the accuracy of the $S_D + S_{V4}$ criteria on axis shits or intraventricular conduction delay. Moreover, we found that the cutoff values for LVH used in this study were lower than in the guidelines, which may be explained by ethnic differences in optimal cutoffs. The impact of ethnicity on the sensitivity and specificity of the newly proposed criteria in diagnosing LVH was not addressed in this study; further exploration is required in this area.

5 | CONCLUSIONS

The newly proposed $S_D + S_{V4}$ criteria provide an improved sensitivity for the ECG diagnosis of LVH compared to existing criteria, but its routine use will require further validation in larger populations. Early detection of LVH and interventions aimed at prevention and/or regression of LVH are to be encouraged. However, further validation on a larger population is warranted.

CONFLICTS OF INTEREST

None.

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