

Performance of Electrocardiographic Criteria for Echocardiographically Diagnosed Left Ventricular Hypertrophy in Chinese Hypertensive Patients

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BACKGROUND

Performance of electrocardiographic (ECG) criteria for echocardiographically diagnosed left ventricular hypertrophy (LVH) in Chinese hypertensive patients is not well known. We investigated the accuracy of various ECG criteria for the diagnosis of the echocardiographic LVH according to the new cutoff values of left ventricular mass (LVM) index (>115 g/m² for men and >95 g/m² for women) in Chinese hypertensive patients.

METHODS

Our study included 702 consecutive hypertensive inpatients including 92 (13.1%) concentric and 121 (17.2%) eccentric LVH on standard echocardiography. Diagnostic accuracy of 7 ECG criteria was evaluated by calculating sensitivity and specificity and by using the receiver operating characteristic curves.

RESULTS

The ECG criteria for the detection of the echocardiographically defined LVH had a sensitivity of 15%–31.9% and specificity of 91.6%–99.2%

overall, 20.7%–43.5% and 91.6%–99.2% concentric, and 7.4%–23.1% and 91.6%–99.2% eccentric. ECG diagnosis of LVH defined as the positive diagnosis of any of 4 ECG criteria including Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage had a sensitivity of 54% and specificity of 86.3% overall, 71.7% and 86.3% concentric, and 40.5% and 86.3% eccentric. After adjustment for confounding factors, various ECG criteria were significantly correlated with LVM, with standardized β coefficients from 0.20 to 0.39 ($P < 0.001$) and the highest coefficient for the Cornell product criterion.

CONCLUSIONS

All ECG LVH indexes had low sensitivity and high specificity in Chinese hypertensive patients. Combination of 4 or all ECG criteria might improve sensitivity without any loss of specificity.

Keywords: blood pressure; diagnosis; echocardiography; electrocardiography; hypertension; left ventricular hypertrophy

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Left ventricular hypertrophy (LVH) is common in patients with hypertension, and is associated with the risk of cardiovascular mortality and morbidity.^{1–3} Both electrocardiography (ECG) and echocardiography can be used for the diagnosis of LVH. Echocardiography has high sensitivity but limited availability and high technical requirement. In contrast, ECG is low cost and reproducible but has low sensitivity.^{4–7} ECG is a routine test for LVH detection in patients with hypertension in all major hypertension guidelines.^{8–11} It is recommended to every single hypertensive patient and especially suitable for LVH screening.

Several ECG criteria, such as the Sokolow–Lyon index, Cornell voltage or Cornell voltage duration product, and RavL, are available to assess LVH.⁹ Most of previous studies have been conducted in Caucasians,^{12–14} and the diagnostic performance of ECG criteria for Asians especially Chinese remains under investigation.¹⁵ A few previous studies of small sample size evaluated correlation between ECG criteria and LVH diagnosed with the old echocardiographic left ventricular mass index (LVMI) cutoff values (>125 g/m² for men and >120 g/m² for women) and showed inconsistent sensitivity and specificity in the Chinese population.^{16,17} Recent

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hypertension guidelines reduced the LVMI cutoff values of echocardiographic LVH diagnostic criteria to $>115 \text{ g/m}^2$ for men and $>95 \text{ g/m}^2$ for women.⁸⁻¹¹ In the present study, we aimed to assess the accuracy of these ECG criteria for the diagnosis of the newly defined echocardiographic LVH including both concentric and eccentric patterns in Chinese adult hypertensive patients.

METHODS

Study population

Our retrospective cross-sectional study included a total of 702 adult hypertensive patients, who admitted in the hypertension inpatient ward in Ruijin Hospital, Shanghai, China from December 2016 to November 2017. All these patients were at least 18 years old and had undergone a 12-lead standard ECG and 2-dimensionally guided M-mode echocardiography. The study protocol was approved by the ethics committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China. All patients gave informed written consent.

Exclusion criteria included valvular heart disease, previous myocardial infarction, left or right bundle branch block, pre-excitation syndrome, atrial fibrillation or flutter, hypertrophic cardiomyopathy, and pacemaker implantation. Patients with chronic kidney disease or diabetes mellitus were not excluded.

ECG recording and criteria for the diagnosis of LVH

A 12-lead standard ECG was performed by trained technicians at rest in the supine position with the MedEx apparatus (MedEx Technology Ltd, Beijing, China) with a speed and voltage regulation of 25 mm/s and 1 mV/10 mm, respectively. Seven ECG LVH criteria were evaluated, including the Sokolow–Lyon voltage, Cornell voltage index, Cornell product, Gubner index, RavL voltage, Rv_5 or Rv_6 voltage, and Lewis voltage, as recommended by the American Heart Association guidelines.¹⁸

Echocardiography

Standard 2-dimensional (2D) echocardiography was performed at rest by an experienced research sonographer blinded to clinical information and ECG findings using the Philips IE33 device (Philips, Eindhoven, The Netherlands). Left ventricular end-diastolic diameter (LVEDd), diastolic posterior wall thickness (PWTd), and diastolic interventricular septum thickness (IVSTd) were imaged from a parasternal long-axis window at the level of the mitral chords using 2D-targeted M-mode echocardiography. Left ventricular mass (LVM) was calculated according to the American Society of Echocardiography-cube formula: $LVM \text{ (g)} = 0.8 \times [1.04 \times \{(LVEDd + PWTd + IVSTd)^3 - (LVEDd)^3\}] + 0.6$. LVM was indexed for body surface area to obtain LVMI.^{19,20} LVH was defined as a LVMI $>115 \text{ g/m}^2$ in men and $>95 \text{ g/m}^2$ in women. The relative wall thickness (RWT) was calculated as the sum of anteroseptal and posterior wall thickness divided by LVEDd. LVH was classified

according to RWT as concentric (RWT ≥ 0.42) and eccentric patterns (RWT < 0.42).

Blood pressure measurement

Blood pressure was measured on the day of admission at the hypertension inpatient ward. An automated oscillometric electronic blood pressure monitor was used during the entire study period (Omron BP-1300, Omron Healthcare, Kyoto, Japan). Two consecutive readings were obtained with a 1-minute interval after at least 5 minutes rest in the seated position. These 2 blood pressure readings were averaged for statistical analysis.

Statistical analysis

Means (\pm SD) and proportions were compared by the Student *t* test and Fisher's exact test, respectively. We also performed analysis of variance for comparisons between the 3 groups according to the echocardiographic LVH status. Diagnostic accuracy for each ECG criteria was evaluated by calculating sensitivity and specificity and by the receiver operating characteristic curves. We also performed multiple linear regression analyses to analyze the relationship between the 7 ECG indexes and LVM after adjustment for age, sex, body mass index, systolic and diastolic blood pressure, diabetes mellitus, and chronic kidney disease. We reported the standardized β coefficients for the 7 ECG indexes. *P* values < 0.05 were considered to be statistically significant. Statistical analysis was performed using the SPSS software, version 17.0 (SPSS, Chicago, IL).

RESULTS

Clinical and echocardiographic characteristics of patients

The 702 study participants included 449 men (64%), and had a mean (\pm SD) age of 51.9 ± 15.2 years. The proportion of patients with echocardiographic LVH was 30.3% ($n = 213$), including 92 patients concentric and 121 patients eccentric. Table 1 shows the clinical characteristics of these patients with LVH and those with normal geometry ($n = 489$). The 3 groups significantly differed in most of the characteristics ($P < 0.05$), except for body mass index, body surface area, serum triglycerides, and fasting plasma glucose ($P > 0.05$). They also significantly differed in the use of all major classes of antihypertensive drugs ($P < 0.001$), except for angiotensin-converting enzyme inhibitors ($P = 0.58$).

Table 2 shows the echocardiographic measurements of left ventricular structure and function in the 3 groups of patients. Patients with concentric LVH had the greatest IVSTd, posterior wall thickness, RWT, LVM, and LVMI. Patients with eccentric LVH had the greatest left ventricular diastolic and systolic diameters and lowest left ventricular ejection fraction.

Sensitivity and specificity of various ECG criteria

The cutoff values for these 7 ECG criteria and sensitivity and specificity of various ECG criteria for echocardiographic

Table 1. Clinical characteristics of patients by echocardiographic left ventricular hypertrophy status

Characteristic	No LVH (n = 489)	Concentric LVH (n = 92)	Eccentric LVH (n = 121)	P (ANOVA)
Age (years)	50 ± 15	54 ± 14*	57 ± 14*	<0.001
Men (%)	67%	70%*	51%*,†	<0.001
Body mass index (kg/m ²)	25 ± 3	26 ± 4	26 ± 3	0.11
Body surface area (m ²)	1.82 ± 0.20	1.84 ± 0.20	1.78 ± 0.20	0.11
Systolic blood pressure (mm Hg)	154 ± 14	166 ± 13*	157 ± 16*	0.002
Diastolic blood pressure (mm Hg)	90 ± 12	92 ± 17	86 ± 16*,†	0.001
Heart rate (beats/minute)	81 ± 12	79 ± 11	77 ± 11*	0.002
Serum creatinine concentration (μmol/l)	76 ± 23	97 ± 50*	81 ± 28†	<0.001
Serum uric acid concentration (μmol/l)	341 ± 88	364 ± 99*	356 ± 99	0.04
Serum total cholesterol (mmol/l)	4.6 ± 0.9	4.7 ± 1.1	4.9 ± 1.4*	0.02
Serum triglycerides (mmol/l)	1.7 ± 1.0	1.9 ± 1.1	2.0 ± 1.5	0.14
Fasting plasma glucose (mmol/l)	5.8 ± 1.5	5.7 ± 1.0	5.4 ± 1.1	0.12
Use of antihypertensive drugs, n (%)				
Calcium-channel blockers	369 (75%)	88 (95%)	104 (85%)	<0.001
Angiotensin-converting enzyme inhibitors	135 (27%)	26 (28%)	28 (23%)	0.58
Angiotensin receptor blockers	146 (29%)	37 (40%)	80 (66%)	<0.001
β-Blockers	215 (43%)	60 (65%)	56 (46%)	<0.001
α-Blockers	117 (23%)	50 (54%)	42 (34%)	<0.001
Diuretics	132 (26%)	47 (51%)	57 (47%)	<0.001

Values are mean ± standard deviation. Abbreviations: ANOVA, analysis of variance; LVH, left ventricular hypertrophy.

*P < 0.05 vs. no LVH.

†P < 0.05 vs. concentric LVH.

Table 2. Left ventricular structure and function by echocardiographic left ventricular hypertrophy status

	No LVH (n = 489)	Concentric LVH (n = 92)	Eccentric LVH (n = 121)	P (ANOVA)
Left ventricular diastolic diameter (mm)	48.9 ± 3.7	51.8 ± 3.5*	53.5 ± 4.5*,†	<0.001
Left ventricular systolic diameter (mm)	31.2 ± 3.0	33.3 ± 3.5*	34.7 ± 4.8*,†	<0.001
Interventricular septal wall thickness (mm)	9.6 ± 1.0	12.3 ± 1.0*	10.5 ± 1.2*,†	<0.001
Posterior wall thickness (mm)	9.3 ± 0.8	11.9 ± 1.0*	10.0 ± 1.0*,†	<0.001
Relative wall thickness	0.38 ± 0.04	0.46 ± 0.03*	0.37 ± 0.03†	<0.001
Left ventricular mass (g)	163 ± 31	252 ± 48*	214 ± 54*,†	<0.001
Left ventricular mass index (g/m ²)	89 ± 12	137 ± 19*	120 ± 20*,†	<0.001
Left ventricular ejection fraction (%)	65.7 ± 3.7	64.6 ± 4.0*	63.7 ± 6.3*	<0.001

Values are mean ± standard deviation. Abbreviations: ANOVA, analysis of variance; LVH, left ventricular hypertrophy.

*P < 0.05 vs. no LVH.

†P < 0.05 vs. concentric LVH.

LVH are shown in Table 3. In general, all ECG criteria had low sensitivity (15%–31.9%) and high specificity (91.6%–99.2%), especially for eccentric LVH. Regardless of the LVH pattern, the Cornell product criterion had the highest sensitivity for the diagnosis of LVH (43.5% and 23.1% for concentric and eccentric LVH, respectively). ECG diagnosis of LVH according to any of the 4 ECG criteria including the Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage had similar sensitivity (54% vs. 56.8% for overall, 71.7% vs. 72.8% for concentric LVH, and 40.5% vs.

44.6% for eccentric LVH) and specificity (86.3% vs. 83.4%) as any of all 7 ECG criteria.

The receiver operating characteristic curve of various ECG criteria for LVH

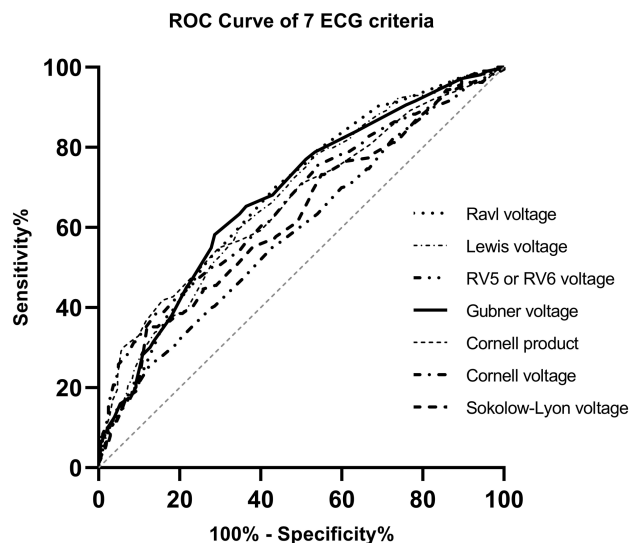
Figure 1 shows the receiver operating characteristic curve comparison for the performance of all 7 ECG criteria. All 7 ECG criteria showed poor performance in the entire range of the receiver operating characteristic curve with an area under the curve of <0.70 (Table 3).

Table 3. Sensitivity and specificity of various criteria for the diagnosis of echocardiographic left ventricular hypertrophy

Criterion	Sensitivity (%)	Specificity (%)	Area under curve
Sokolow–Lyon voltage (mV)			
Sv ₁ + Rv ₅ or Rv ₆ >3.5			
Total LVH	26.8	91.6	0.64
Concentric LVH	38.0	91.6	
Eccentric LVH	18.2	91.6	
Cornell voltage (mV)			
RavL + Sv ₃ >2.8 (men); RavL + Sv ₃ >2.0 (women)			
Total LVH	21.1	96.5	0.67
Concentric LVH	29.3	96.5	
Eccentric LVH	14.9	96.5	
Cornell product (mV ms)			
Cornell voltage × QRS duration >0.244			
Total LVH	31.9	96.3	0.68
Concentric LVH	43.5	96.3	
Eccentric LVH	23.1	96.3	
Gubner voltage (mV)			
R _I + S _{III} >2.5			
Total LVH	18.8	99.2	0.69
Concentric LVH	29.3	99.2	
Eccentric LVH	10.7	99.2	
RavL voltage (mV)			
RavL ≥1.1			
Total LVH	20.2	98.0	0.69
Concentric LVH	27.2	98.0	
Eccentric LVH	14.9	98.0	
Rv₅ or Rv₆ voltage (mV)			
Rv ₅ or Rv ₆ >2.7			
Total LVH	15.0	96.9	0.60
Concentric LVH	25.0	96.9	
Eccentric LVH	7.4	96.9	
Lewis voltage (mV)			
(R _I + S _{III}) – (R _{III} + S _I) >1.7			
Total LVH	19.2	98.4	0.68
Concentric LVH	20.6	98.4	
Eccentric LVH	18.2	98.4	
Four electrocardiographic criteria^a			
Total LVH	54.0	86.3	
Concentric LVH	71.7	86.3	
Eccentric LVH	40.5	86.3	
All 7 electrocardiographic criteria			
Total LVH	56.8	83.4	
Concentric LVH	72.8	83.4	
Eccentric LVH	44.6	83.4	

Abbreviation: LVH, left ventricular hypertrophy.

^aThe Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage criteria.

**Figure 1.** Receiver operating characteristic comparison of the area under the curves between various electrocardiographic criteria for the detection of left ventricular hypertrophy.**Table 4.** Multiple linear regression analysis between left ventricular mass and various electrocardiographic criteria

Electrocardiographic criteria	Left ventricular mass	
	Standardized β coefficient	<i>P</i>
Sokolow–Lyon voltage	0.31	<0.001
Cornell voltage	0.38	<0.001
Cornell product	0.39	<0.001
Gubner voltage	0.27	<0.001
RavL voltage	0.28	<0.001
Rv ₅ or Rv ₆ voltage	0.20	<0.001
Lewis voltage	0.23	<0.001

Adjusted for gender, age, body mass index, systolic and diastolic blood pressure, diabetes mellitus, and chronic kidney disease.

Relationship between various ECG criteria and LVM

After adjustment for age, sex, body mass index, systolic and diastolic blood pressure, diabetes mellitus, and chronic kidney disease, all 7 ECG criteria indexes were significantly associated with LVM ($P < 0.001$, Table 4). The Cornell product had the greatest standardized β coefficient among all 7 criteria indexes (β 0.39 vs. 0.20 to 0.38, $P < 0.001$).

DISCUSSION

Our key finding was that the ECG criteria had low sensitivity and high specificity in the diagnosis of the echocardiographic LVH, especially the eccentric pattern. Nonetheless, the use of any of the 4 ECG criteria including Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage or any of the 7 ECG criteria may improve the diagnostic sensitivity for LVH in Chinese hypertensive patients.

Although it is known that the ECG LVH criteria might be ethnic dependent, few studies explored this important issue, and no study has yet evaluated the performance of ECG criteria for the new echocardiographic LVH criteria in Asians. With the old echocardiographic LVH criteria for the diagnosis of LVH, several previous studies investigated the accuracy of ECG criteria in the detection of LVH in Asians.^{21–23} In 546 Chinese patients with hypertension, Xie *et al.* found that the Cornell voltage and product criteria had a higher sensitivity to detect echocardiographic LVH (28% and 36.6%, respectively).²¹ In 539 young army men in Taiwan, Su *et al.* found that the Cornell voltage and product criteria had better performance for the echocardiographic LVH than the Sokolow–Lyon criteria, with a sensitivity of 22.2%, 27.8%, and 8.3%, respectively.²² However, in 332 Korean patients seen in a cardiology department, Park *et al.* demonstrated that the Cornell product criterion was superior to the Sokolow–Lyon voltage criterion in women, but the opposite was true in men.²³

The low sensitivity of ECG criteria in the detection of LVH is probably typical for the Chinese and other eastern Asian populations. Other reasons may also play a part. A straightforward explanation could be the change of the echocardiographic criteria for the diagnosis of LVH.^{8–11} In our study participants, the prevalence of echocardiographic LVH increased from the old to the new criteria by 80.5%. If the old echocardiographic criteria would be used, the diagnostic sensitivity of the Cornell product criteria did increase to 41.5% with a specificity of 95.5%.

Peguero *et al.* recently reported a new criterion of the amplitude of the deepest S wave (S_D) in any single lead plus the S wave amplitude of lead V_4 , i.e., ($S_D + SV_4$).²⁴ In 94 hypertensive patients, the new ECG criterion had a higher sensitivity (62%) in the detection of LVH defined according to the new echocardiographic criteria than all the other ECG criteria (up to 35%).²⁴ In our present study, this new criteria, $S_D + SV_4$, also had a slightly higher sensitivity (44.6%) than the other criteria. However, it had much lower specificity (75.8%) and area under the curve (0.62).

Our findings on the slightly higher sensitivity of the Cornell product are in line with the results of several previous studies.^{21,22} The mechanisms for the difference remain unexplained. One possible explanation is that the Cornell voltage index includes a limb lead in addition to the precordial one, and hence is less dependent on the thickness of the chest wall.²⁵ In addition, combining QRS voltage with duration will further increase the area under the QRS complex in comparison with either QRS voltage or duration alone. Thus, the Cornell product may reflect the presence and severity of hypertrophy more accurately than ECG scores that involve only QRS voltage or duration.

Our observation on the even poorer sensitivity for the detection of eccentric hypertrophy remains under investigation. A possible explanation could be that the enlarged chamber and thinner wall thickness of the left ventricle influence both voltage and conductance and hence ECG evaluations of the heart. Left ventricular dilatation in eccentric LVH could

cause elongated distance of the intraventricular conductance pathways, which produces a stretching of the conduction system, and in turn reduces the power of conductivity.²⁶ Eccentric LVH may have even worse prognosis and hence even greater need for screening. It is imperative to further delineate the ECG characteristics of this pattern of LVH.

Previous studies often focused on the diagnostic sensitivity and specificity of single ECG criterion.^{27–29} Our current study found that any of the 4 ECG criteria including the Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage had a relatively higher sensitivity than each ECG criterion alone, without apparent compromise in specificity. These 4 ECG criteria are most commonly used with convenient acquisition by ECG devices and recommended by the European hypertension guideline.⁹ If applied properly and widely, this combined 4 ECG criteria approach might improve LVH screen in patients with hypertension.

Our study should be interpreted within the context of its limitations. First, our study examined only 7 of the numerous ECG criteria. Second, our study was a single center one. Most of our patients were from Shanghai or the nearby eastern China provinces. Our study therefore might be less representative than a multicenter study. Nonetheless, the current study built the ground for future studies on possible new ECG LVH diagnostic criteria in the Chinese or Asian population.

In conclusion, if the same cutoff values would be used in Chinese, the ECG criteria had high specificity but low sensitivity for the diagnosis of LVH, regardless of the pattern of LVH. Any of the 4 ECG criteria including the Sokolow–Lyon voltage, Cornell voltage, Cornell product, and RavL voltage, instead of a single ECG criterion, may have to be considered for the diagnosis of LVH in Chinese hypertensive patients.

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DISCLOSURE

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