Original Article

Electrocardiographic Criteria for Left Ventricular Hypertrophy in Asians Differs from Criteria Derived from Western Populations—Community-based Data from an Asian Population

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Abstract

Introduction: Electrocardiographic (ECG) criteria for left ventricular hypertrophy (LVH), such as the Cornell and Sokolow-Lyon voltage criteria were derived from Western populations. However, their utility and accuracy for diagnosing echocardiographic LVH in Asian populations is unclear. The objective of this study was to assess the accuracy of ECG criteria for LVH in Asians and to determine if alternative gender-specific ECG cut-offs may improve its diagnostic accuracy. Materials and Methods: ECG and echocardiographic assessments were performed on 668 community-dwelling Asian adults (50.9% women; 57 ± 10 years) in Singapore. The accuracy of ECG voltage criteria was compared to echocardiographic LVH criteria based on the American Society of Echocardiography guidelines, and Asian ethnicity and gender-specific partition values. Results: Echocardiographic LVH was present in 93 (13.6%) adults. Cornell criteria had low sensitivity (5.5%) and high specificity (98.9%) for diagnosing LVH. Modified gender specific cut-offs (18 mm in women, 22 mm in men) improved sensitivity (8.8% to 17.5%, 0% to 14.7%, respectively) whilst preserving specificity (98.2% to 94.2%, 100% to 95.8%). Similarly, Sokolow-Lyon criteria had poor sensitivity (7.7%) and high specificity (96.1%) for diagnosing LVH. Lowering the cut-off value from 35 mm to 31 mm improved the sensitivity in women from 3.5% to 14% while preserving specificity at 94.2%. A cut-off of 36 mm was optimal in men (sensitivity of 14.7%, specificity of 95.5%). Conclusion: Current ECG criteria for LVH derived in Western cohorts have limited sensitivity in Asian populations. Our data suggests that ethnicity- and gender- specific ECG criteria may be needed.

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Key words: Cornell, Ethnicity, Sokolow-Lyon, Voltage

Introduction

Traditionally, the diagnosis and assessment of left ventricular hypertrophy (LVH) was made with the use of electrocardiography (ECG) and echocardiography, and more recently, with cardiac magnetic resonance (CMR) imaging.[1] ECG remains widely used due to its convenience, low cost, widespread availability and high reproducibility. The importance of accurately detecting LVH has increased in recent years, with the recognition that LVH can be reversed with therapy, and that this can prevent or delay adverse clinical outcomes.[2,3] Since the development of ECG criteria for the diagnosis of LVH a hundred years ago,[4] numerous ECG voltage criteria for LVH have been proposed. Despite its high specificity, ECG voltage criteria for LVH has however, yielded poor sensitivity.[5]

Commonly used ECG voltage criteria for LVH include the gender-specific Cornell voltage criteria[6] and gender non-specific Sokolow-Lyon voltage criteria.[7] Many studies have been performed to evaluate these ECG voltage criteria[1,8] and some have suggested the use of ethnicity-[9,10] and gender-specific[6,8] ECG criteria can improve its sensitivity and maintain its high specificity in diagnosing LVH. These studies were however, based on Western populations, and there is a lack of similar studies in Asian populations.

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Taking into account the smaller body habitus of Asians, the applicability of such ECG criteria in Asian populations remains uncertain.

The purpose of this study was to assess the accuracy of these ECG voltage criteria for the diagnosis of echocardiographic LVH in a community-based cohort of Asian adults. We chose to evaluate the Cornell voltage criteria and Sokolow-Lyon voltage criteria due to their ubiquity and easy applicability. We further aimed to investigate if alternative gender-specific ECG cut-offs may improve the diagnostic accuracy of LVH in Asians.

Methods

Study Population

A total of 668 Asian adults (50.9% women; 57 ± 10 years) from the Singapore Longitudinal Ageing Study (SLAS) were included in this present study.[11] The SLAS involves whole population sampling of all residents (Singapore citizens and permanent residents) in contiguous precincts within 5 districts in the Southeast region of Singapore who were identified from a door-to-door census and invited to participate. Our study population therefore consisted of asymptomatic community-based adults who self-reported their ethnicity to be Chinese, Malay or Indian. All participants underwent standard 12-lead resting ECG and transthoracic echocardiography at a reference echocardiography laboratory as part of the control arm for a concurrent Singapore Heart Failure Outcomes and Phenotypes (SHOP) study.[12] Patients with a history of valvular heart disease, previous myocardial infarction, ventricular pre-excitation and left or right bundle branch block were excluded. The study was approved by the institutional ethics review committee. Written informed consent was obtained from all subjects.

Electrocardiography

Standard 12-lead ECGs were recorded at 25 mm/s and 10 mm/mV standardisation. All measurements were interpreted by experienced investigators blind to clinical information and echocardiographic measurements. ECG parameters of the 2 commonly used ECG voltage criteria for LVH, Cornell voltage criteria[6] (SV3+RaVL ≥28 mm for men; ≥20 mm for women) and Sokolow-Lyon voltage criteria[7] (SV1+RV5 or V6 ≥35 mm for both genders) were collected (Fig. 1).

Echocardiography

All subjects underwent standard M-mode and 2-dimensional (2D) and Doppler echocardiography at rest, performed by an experienced research sonographer using Vivid 7 Dimension and E9 ultrasound systems (General Electric Healthcare, Milwaukee, WI, USA) equipped with wideband transducers. In accordance with American Society for Echocardiography (ASE) recommendations,[13] left ventricular end-diastolic diameter (LVEDD), diastolic posterior wall thickness (PWTd) and diastolic septal wall thickness (SWTd) 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 based on the ASE-cube formula by Devereux et al.[13]

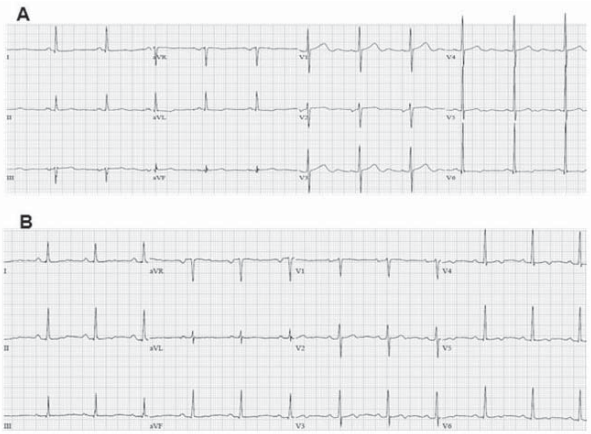

Fig. 1. Two ECG depictions about Cornell voltage and Sokolow-Lyon voltage. ECG in A is that of a 62-year-old woman with LVH: RaVL + SV3 = 24.5 mm (more than 22 mm); SV1 + RV5 or V6 = 44 mm (more than 35 mm). ECG in B is that of a 64-year-old man with no LVH: RaVL + SV3 = 7.5 mm (less than 28 mm); SV1 + RV5 or V6 = 24 mm (less than 35 mm).

$$LVM\ (g) = 0.8 \times [1.04 \times \{(LVEDD + PWTd + SWTd)^3 - (LVEDD)^3\}] + 0.6$$

LVM was indexed for body surface area (BSA) to obtain left ventricular mass index (LVMI). In accordance with ASE recommendations,[13] LVH was defined by LVMI >95 g/m^2 in women and >115 g/m^2 in men in our primary study.

Further recognising that the (ASE) criteria for LVH has not been validated in Asians, we also applied Asian-specific cut-offs derived in our own echocardiography laboratory[14] in secondary analyses, where LVH was defined by LVMI >96 g/m^2 in women and >106 g/m^2 in men.

Statistical Analysis

Data were presented as the mean ± SD for normally distributed parameters. Groups were compared using chi-square test for discrete variables and one-way analysis of variance (ANOVA) for continuous variables. Multiple linear regression models were used to analyse the relationship between LVMI, Sokolow-Lyon voltage, Cornell voltage by gender adjusted for age, body mass index (BMI) and hypertension status. Sensitivity and specificity for both Sokolow-Lyon voltage criteria and Cornell voltage criteria

were tested using different partition values for men and women both separately and as a combined cohort. Receiver operating characteristic (ROC) curves were used to compare the performances of both ECG voltage criteria for LVH. This was first tested using the ASE criteria for LVH as the gold standard, followed by the Asian-specific criteria for LVH[14] in secondary analyses. For all tests, a 2-tailed *P* value <0.05 was required for statistical significance. All analyses were performed using IBM SPSS Statistics software, version 21.0 (IBM Corporation, Armonk, NY, USA).

Results

Clinical, demographic, ECG and echocardiographic variables according to gender are presented in Table 1.

Except for BMI, LVEF, the prevalence of diabetes mellitus and Asian echo-defined LVH, all other variables were significantly different between women and men. Of note, men were slightly older and had a greater prevalence of hypertension. Using the Cornell ECG criteria, the prevalence of LVH was notably 0% in men and 2.9% in women, and using the Sokolow-Lyon criteria, the prevalence of LVH was 7.4% in men and 2.1% in women. Compared to women, men had higher LVM and LVMI. Women had greater prevalence of echocardiographic LVH than men.

Relationship of LVMI, Cornell Voltage and Sokolow-Lyon Voltage

Scatter plots of Cornell voltage (Figs. 2A and 2B) and Sokolow-Lyon voltage (Figs. 2C and 2D) showed a positive correlation with LVMI in men and women respectively (Cornell voltage: r = 0.320 and r = 0.315; Sokolow-Lyon: r = 0.227 and r = 0194, for men and women respectively and *P* <0.001 for all). These relationships remained statistically significant after adjusting for age, BMI, hypertension status, Cornell voltage (r = 0.312 and r = 0.209 for men and women respectively; *P* <0.001 for both) and Sokolow-Lyon voltage (r = 0.226 and r = 0.155 men and women respectively; *P* <0.001 for both).

Performance Comparison of Different Cut-off Values of ECG Criteria against ASE LVMI Cut-off for Echocardiographic LVH

Overall performance of Cornell and Sokolow-Lyon voltage cut-off values for LVH was assessed in terms of sensitivity and specificity (Table 2, Table 3 and Fig. 3).

To select the optimal cut-off criteria for our Asian population, we aimed for 95% specificity of the combined modified criteria[15] with preservation of overall accuracy in both sex-stratified and combined analyses.

Table 1. Clinical, Demographic, ECG and Echocardiographic Variables of Community-based Subjects by Gender

	Men (n = 328)	Women (n = 340)	*P* Value
Age (years)	58 ± 11	56 ± 9	0.015
Height (cm)	1.68 ± 0.06	1.55 ± 0.06	<0.001
Weight (kg)	69.89 ± 11.96	59.88 ± 10.78	<0.001
BMI (kg/m²)	25.10 ± 3.87	24.97 ± 4.37	0.665
BSA (m²)	1.79 ± 0.17	1.60 ± 0.15	<0.001
Smokers (%)	16.5	0.4	<0.001
Hypertension (%)	17.7	12.9	0.003
Diabetes mellitus (%)	4.5	3.6	0.322
LVM (g)	161.58 ± 38.74	123.69 ± 30.49	<0.001
LVMI (g/m²)	90.04 ± 20.01	77.20 ± 17.05	<0.001
LVEF (%)	63.46 ± 4.01	65.21 ± 4.01	0.432
Echocardiographic LVH (n, %)	34 (10.4)	57 (17)	0.013
Asian echocardiographic-defined LVH (n, %)	66 (20.2)	49 (14.6)	0.059
Sokolow-Lyon voltage (mm)	24.48 ± 6.96	22.16 ± 5.89	<0.001
ECG LVH by Sokolow-Lyon (%)	7.4	2.1	0.001
Cornell voltage (mm)	13.57 ± 5.31	10.91 ± 4.94	<0.001
ECG LVH by Cornell (%)	0	2.9	0.002

BMI: Body mass index; BSA: Body surface area; ECG: Electrocardiographic; LVEF: Left ventricular ejection fraction; LVH: Left ventricular hypertrophy; LVM: Left ventricular mass; LVMI: Left ventricular mass index

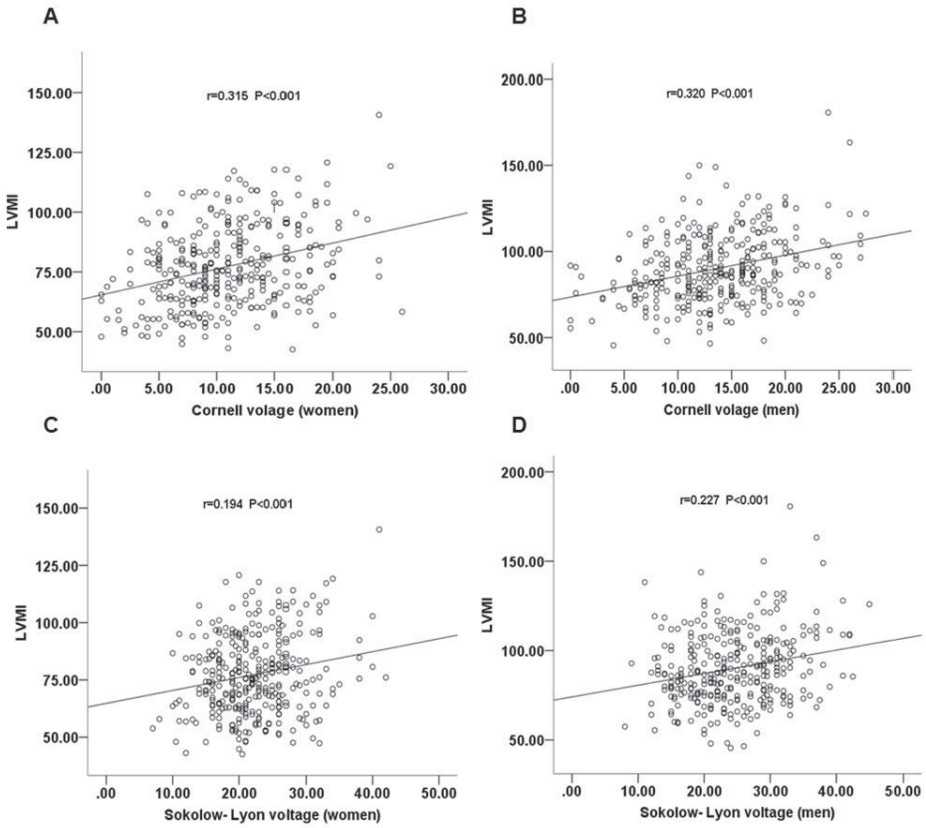

Fig. 2. Scatter diagrams showing the correlation between the left ventricular mass index (LVMI) and Cornell voltage or Sokolow-Lyon voltage in women (A and C) and men (B and D), respectively.

Table 2. Cornell Voltage Criteria Performance with Different Cut-off Values for Diagnosing ASE Echocardiographic LVH

	RaVL + SV3 Cut-off	Sensitivity %	Specificity %	Accuracy %	PPV %	NPV %
Women	14	40.4	79.1	72.5	28.4	86.6
	16	22.8	86.7	75.8	26	84.6
	18	17.5	94.2	81.2	38.5	84.8
	20	8.8	98.2	83	50	84
	22	5.3	98.9	83	50	83.6
	24	1.8	99.6	83	50	83.2
	26	0	100	83	0	83
	28	0	100	83	0	83
Men	14	70.6	60.1	61.2	17	94.6
	16	52.9	72.7	70	18.4	93
	18	35.3	85.0	79.8	21.4	93.9
	20	17.6	91.5	83.8	19.4	90.5
	22	14.7	95.8	87.5	29.4	90.6
	24	8.8	98.0	88.7	33.3	90.3
	26	2.9	99.0	89	25	89.9
	28	0	100	89.6	0	89.6
Cornell criteria		5.5	98.9	84.6	45.5	86.8
Modified Cornell criteria	Women >18 mm Men > 22 mm	16.5	95.0	84.3	34.9	87.7

ASE: American Society of Echocardiography; LVH: Left ventricular hypertrophy; NPV: Negative predictive value; PPV: Positive predictive value

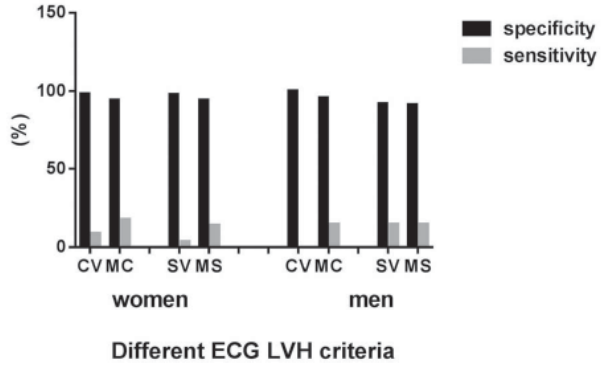

Fig. 3. A bar diagram comparing the sensitivity and specificity of the original Cornell voltage criteria (CV) and Sokolow-Lyon voltage criteria (SV) with that of the modified Cornell voltage criteria (MC) and Sokolow-Lyon voltage criteria (MS). The modified cut-off values preserved specificity while increasing sensitivity.

Overall, Cornell voltage criteria showed a low sensitivity (5.5%) and high specificity (98.9%) for the diagnosis of LVH among Asians, particularly in Asian men (Table 2). In Asian women, lowering the cut-off from 20 mm to 18 mm doubled the sensitivity (8.8% to 17.5%), but preserved specificity (98.2% to 94.2%). In Asian men, lowering the cut-off from 28 mm to 22 mm improved sensitivity (0% to 14.7%) and maintained specificity (100% to 95.8%). Hence, the modified Cornell criteria (SV3 + RaVL >22 mm in men and >18 mm in women) had 16.5% sensitivity, 95% specificity, 34.9% positive predictive value (PPV) and 87.7% negative predictive value (NPV) for the diagnosis of LVH.

Similarly, Sokolow-Lyon voltage criteria had poor sensitivity (7.7%) and high specificity (96.1%) for the diagnosis of LVH among Asians (Table 3). In Asian women, lowering the cut-off from 35 mm to 31 mm improved the sensitivity by 4 times from 3.5% to 14% while preserving a high specificity of 94.2%. In Asian men, increasing the cut-off to 36 mm maintained the sensitivity at 14.7% but improved the specificity from 92% to 95.2%. The modified Sokolow-Lyon criteria (S in V1+R in V5 or V6 >36 mm in men and >31 mm in women) doubled the sensitivity from its original 7.7% to 14.2%, yet retained a specificity of 95%, a PPV of 28.6% and a NPV of 87.1% for the diagnosis of LVH.

The PPV estimates provided in this study should be considered with caution: while PPV is often used to estimate the probability of true LVH among test-positive cases, such estimates can be misleading in non-hospitalised populations such as ours, where the true prevalence is low and the test (ECG in this case) has a high false positive rate.

The ROC area under curve (AUC) was 0.644 for the traditional Cornell voltage criteria and 0.586 for the

Table 3. Sokolow-Lyon Voltage Criteria Performance with Different Cut-off Values for Diagnosing ASE Echocardiographic LVH

	SV1 + RV5 or V6 Cut-off	Sensitivity %	Specificity %	Accuracy %	PPV %	NPV %
Women	25	45.6	75.2	70.1	27.7	86.9
	27	28.1	86.5	76.4	37.2	85.3
	29	19.3	90.9	78.5	30.6	84.4
	31	14.0	94.2	80.4	33.3	84
	33	5.3	97.1	81.3	27.3	83.1
	35	3.5	97.8	81.6	25	83
	37	3.5	98.2	81.9	28.6	83
Men	25	52.9	59.9	59.1	13.4	91.5
	27	44.4	67.1	65	14.4	91.5
	29	35.3	76.5	72.1	15	90.9
	31	23.5	84.8	78.3	15.4	90.4
	33	14.7	91.3	83.2	16.6	90.1
	35	14.7	92.0	83.9	17.9	90.2
	36	14.7	95.5	87	27.8	90.5
	37	8.8	96.9	87.6	25	90
Sokolow-Lyon criteria	35	7.7	96.1	83.8	24.1	86.6
Modified Sokolow-Lyon criteria	Women >31 mm Men >36 mm	14.2	95.0	83.3	28.6	87.1

ASE: American Society of Echocardiography; LVH: Left ventricular hypertrophy; NPV: Negative predictive value; PPV: Positive predictive value

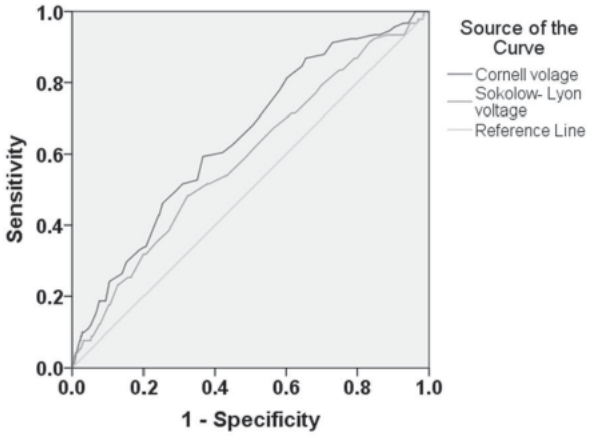

Fig. 4. Receiver operating characteristic (ROC) curve for 2 electrocardiography (ECG) criteria based on the American Society of Echocardiography (ASE) echocardiographic left ventricular hypertrophy (LVH). Cornell voltage criteria area under curve (AUC) = 0.644; Sokolow-Lyon voltage criteria AUC = 0.586.

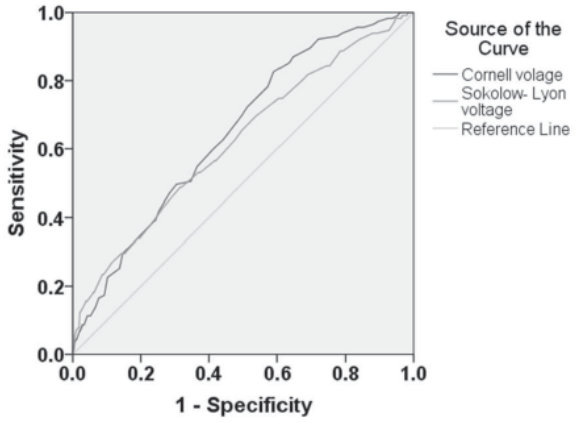

Fig. 5. Receiver operating characteristic (ROC) curve for 2 electrocardiography (ECG) criteria based on Asian-specific echocardiographic left ventricular hypertrophy (LVH). Cornell voltage criteria area under curve (AUC) = 0.649; Sokolow-Lyon voltage criteria AUC = 0.621.

traditional Sokolow-Lyon voltage criteria. However, pair-wise tests comparing the AUC for both criterion did not show any significant difference (P >0.05) (Fig. 4).

Secondary Analyses Using Asian-specific Echocardiographic Cut-offs for LVH

By applying the lower Asian echocardiographic LVMI cut-off for LVH as the gold standard, a further 32 men who did not meet the ASE LVMI cut-off were reclassified as having LVH, while 8 women were reclassified as not having LVH based on the higher Asian-specific echocardiographic LVMI cut-offs for women. With this new threshold, the standard Cornell criteria performed just as poorly for sensitivity (3.5% vs 5.5%) and had similar specificity (98.9% vs 98.9%) as when ASE defined cut-offs were used.

The standard Sokolow-Lyon criteria had higher sensitivity (13% vs 7.7%) and specificity (97.4% vs 96.1%) for LVH using Asian echocardiographic criteria as gold standard compared to using ASE criteria as gold standard.

We similarly derived modified cut-offs for both ECG criteria by maintaining specificity at 95% which were 18 mm for women and 22 mm for men for the Cornell criteria (which is identical to when the ASE LVH cut-off was used) and 30 mm for women and 35 mm for men with the Sokolow-Lyon criteria. Our modified criteria were associated with improved sensitivity with both criteria (Cornell criteria 13.1% vs 3.5%; Sokolow-Lyon criteria 19.1% vs 13%) (Table 4).

The ROC AUC was 0.649 for the traditional Cornell voltage criteria and 0.621 for the traditional Sokolow-Lyon voltage criteria. However, pair-wise tests comparing the area under the ROC curve for both criterion did not show any significant difference (P >0.05) (Fig. 5).

Table 4. Cornell and Sokolow-Lyon Criteria Performance for Diagnosing Asian-specific Echocardiographic LVH

ECG Criteria	Cut-off (mm)	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Cornell criteria	20 & 28	3.5	98.9	82.3	40.0	83.8
Modified Cornell criteria	18 & 22	13.1	95.0	80.7	34.9	83.8
Sokolow-Lyon criteria	35	13.0	97.4	82.6	51.7	84.0
Modified Sokolow-Lyon criteria	30 & 35	19.1	95.0	81.3	43.1	84.6

ECG: Electrocardiographic; LVH: Left ventricular hypertrophy; NPV: Negative predictive value; PPV: Positive predictive value

Discussion

The main finding in our study was that existing ECG criteria for LVH derived from Western cohorts had good specificity but unacceptably low sensitivity in a community-based Asian cohort. We also found that by modifying these criteria, it may be possible to improve their performance.

Traditional Cut-offs Perform Poorly in Non-Western Populations

The most commonly used ECG LVH criteria were originally derived from Western populations but are applied universally to all ethnic groups. In 1949, Sokolow and Lyon[7] compared the ECGs of 147 patients with cardiovascular disease and 151 healthy patients, to define the ECG changes associated with LVH. While many observations were reported, the ECG criterion that remains most commonly in clinical practice is the sum of the S wave in lead V1 plus the larger of the R wave in V5 or V6 greater than 35 mm. They found that the sensitivity of this criterion was 32% and specificity was 100. Notably, LVH was not confirmed with imaging techniques in this early seminal study. More recently, Casale et al[6] derived the Cornell voltage criteria from 414 "learning series" patients and 129 "test series" patients and the majority of whom had cardiovascular disease. They found that the R wave in lead aVL and the S wave in lead V3 correlated best with M-mode echocardiographic LVMI, and reported a sensitivity of 41% and specificity 90% in the learning series, and similar sensitivity of 41% but higher specificity of 98% in the test series. These 2 ECG criteria remain in general use largely due to their simplicity and accuracy as reported in the original series.

In contrast, the present study showed that the widely used Cornell and Sokolow-Lyon ECG voltage criteria for LVH had poor sensitivities in our Asian population. This is especially so for the Cornell voltage criteria in Asian men, where sensitivity in our cohort was 0%. The low sensitivities of Cornell voltage criteria and Sokolow-Lyon voltage criteria from our study (5.5% and 7.7%, respectively) is in sharp contrast to that found in the original reports of these criteria[6,7] (41% and 32%, respectively). A possible explanation for this is the higher LVMI cut-off of >132 g/m^2 for men and >109 g/m^2 for women was used to define LVH in the former study.[6] Other studies performed on largely Western populations that also found higher sensitivities and specificities for these criteria than in our cohort had used similar cut-off values.[5,8] The higher LVMI cut-off would have reduced the number of patients who would have been classified as having LVH and these patients would also have had higher LVM on average. Hence, they may also have higher voltages on their ECGs making it more likely that they would meet the ECG voltage criteria cut-off values and resulting in increased sensitivity of these criteria. In addition, the accuracy of ECG-LVH criteria have been reported to be substantially improved by combining repolarisation abnormalities with high ECG voltage criteria.[16] However, our data from a community-based healthy population has a very low incidence of repolarisation abnormalities (only 10 cases of T-wave inversions), so this was not included in the current analyses.

Two recent studies in East Asian populations also lend weight to this notion. In a study by Xie et al[17] of hypertensive Chinese patients, Cornell product and voltage criteria were good predictors of LVH (sensitivity of 28% and 30.1% in men and women respectively; specificity of 95.9% and 91.4% in men and women respectively) based on LVMI cut-off values of >125 g/m^2 men and >110 g/m^2 women which was similar to those in Western cohorts.[6] Of note, these cut-off values for echocardiographic LVH were higher than the ASE[13] recommended cut-offs (>115 mg/m^2 men; >95 mg/m^2 women) used in this present study. The selected population of only hypertensive subjects as compared to our study population of healthy community-based adults may also have increased the number of patients with LVH in their cohort compared to our study.

In contrast, a study of Korean patients by Park et al[18] that diagnosed echocardiographic LVH using the same ASE guidelines as our study, found that the sensitivity of Cornell voltage criteria in Korean men was much lower (and similar to our findings) at 1.4% and 9.7% in women. The ROC AUC for the Cornell voltage criteria against LVMI was 0.648 in men and 0.735 in women, which was similar to the AUC for our cohort at 0.644. Park et al proposed reducing the cut-off values to 20 mm in men and 16 mm in women leading to a markedly improved sensitivity of 19.7% in men and 22.6% in women at a fixed specificity of 95%. This again was similar to our recommendation of 22 mm in men and 20 mm in women. These studies not only highlight the potential limitations of applying conventional ECG cut-off values in the Asian population but also suggest that the apparent performance of these ECG voltage criteria could well be affected by which standard of echocardiographic LVH they are compared against. This is especially since standard ASE criteria for echocardiographic LVH has not been validated in Asian populations. Although different LVMI cutoff values for LVH has been proposed for Southeast Asian populations (106 g/m^2 for men and 96 g/m^2 for women),[14] it should be noted that these defined LVH by 95th percentile partition values rather than by the probability of future clinical outcomes in a "normal" population. In the present paper, we have chosen to use these arbitrary cut-off values because they are the only available echocardiographic LVH criteria derived from Southeast Asian populations. These have yet

to be validated against clinical outcomes. It is likely that further validation of these echocardiographic LVH criteria will allow us to more accurately define patients who have LVH and allow us to further refine ECG LVH criteria.

Previous studies have shown that Sokolow-Lyon voltage and Cornell voltage parameter correlated well with LVM or LVMI in Western populations.[6,19] These were clinic-based cohorts and had higher rates of hypertension than in our community-based cohort. Nonetheless, our data from a community-based cohort also showed that the Sokolow-Lyon voltage and Cornell voltage parameters correlated with LVMI in an Asian cohort. Even when adjusted for age, BMI and hypertension, the correlation persisted. This suggests that the poor performance of conventional voltage criteria in our cohort may be due to the fact that these cut-off values were not suitable for our population rather than a lack of correlation with LVH. It is also likely that cut-off values more tailored to specific ethnic groups may make these voltage criteria more accurate in our Asian population.

Recent studies by Bacharova et al[20,21] based on the solid angle theory[22,23] found that LVM is not the only determinant of QRS voltage changes in LVH. Instead, it is a combination of anatomic and electric remodelling that result in the altered ECG voltage. In other words, the creation of the QRS voltage depends on spatial (the size and anatomy of the heart) and non-spatial (the electrical properties of myocardium) factors, which challenges of the traditional conceptual model that the QRS voltage reflects increased LVM. However, these studies were based on computer modelling of underlying myocardial changes and its effect on the ECG. Hence, the clinical implications of these findings are uncertain. In this paper, we chose a more simplistic view of relating ECG voltage criteria to echocardiographic LVH defined by LVM as the latter has been used in the past to define LVH. The aim was to allow us to refine the ECG criteria for diagnosing LVH in Asian patients without the added expense and complexity of echocardiography.

Gender Specific Cut-offs May Be More Appropriate in Asians

In keeping with earlier studies in both Western and Asian cohorts,[6,8,17,18] men and women in this present study had significantly different LVMI, and Sokolow-Lyon and Cornell voltage parameters. Moreover, the sensitivity and specificity of both criteria varied when assessed by gender. This is particularly true for the Sokolow-Lyon criterion that has conventionally used the same cut-off for both genders. In our women subjects, this resulted in a sensitivity of only 3.5%, but this was increased to 14% by reducing the cut-off to 31 mm, while preserving specificity at 94%. In contrast, the cut-off of 35 mm resulted in acceptable sensitivity and specificity in men in our study (14.7% and 92.0% respectively). These could be further improved by raising the cut-off to 36 mm in our cohort (14.7% and 95.5% respectively) and we propose that this cut-off is optimal in Asian men.

It is expected that different cut-offs are required in men and women because previous studies, as well as ours, have found that men have significantly higher LVMI, absolute LV mass, LV diastolic and systolic dimensions, height, weight and BSA.[8,18] Significant sex-specific voltage differences in the S wave in lead V3 were also noted (13.2 mm ± 8.2 mm males; 7 mm ± 4.4 mm females; P <0.001).[6] Widely accepted explanations for this observation include the larger distance between precordial leads and myocardium due to the presence of breast tissue in women[24] and smaller ventricular mass in women leading to smaller S wave amplitude in V3 which measures posteriorly directed myocardial electrical activity.[6] Despite this, Casale et al[6] showed that S in V3 correlated best with LVMI in both genders and hence it was proposed as part of the Cornell voltage criteria, but importantly, with different cut-off values for men and women.

In a study comparing cardiac MRI diagnosed LVH with ECG voltage criteria for LVH in a group of hypertensive patients and healthy controls, Alfakih et al[8] demonstrated that the Sokolow-Lyon criteria had non-significantly higher sensitivity (32% vs 23.3%) but lower specificity (90.5% vs 94.2%) in men compared to women. The reverse was true of the Cornell criteria which had lower sensitivity (18.5% vs 25.6%) but higher specificity (99.2% vs 89.3%) in men. The authors proposed new cut-offs that would fix specificity at 95% but that resulted in reduced sensitivity of the Sokolow-Lyon criteria in men (18.5% from 32%), and also reduced sensitivity of the Cornell criteria in women (16.3% from 25.6%). Hence, using gender-specific cut-offs may not necessarily improve the sensitivity of ECG criteria when adequate specificity is targeted. This is in contrast with our study, where the ECG criteria generally had higher specificities but lower sensitivities. As a result, our proposed cut-offs (which stipulated a specificity of 95%) had higher sensitivities than conventional cut-off values. For Cornell voltage criteria, a new cut-off value (RaVL + SV3 >22 mm for men; >18 mm for women) increased sensitivity (0% to 14.7% for men; from 8.8% to 17.5% for women), while maintaining a high specificity (>94%). Likewise, introducing sex-specific cut-offs (SV1 + RV5 or V6 >36 mm for men; >31 mm for women) for Sokolow-Lyon voltage criteria increased its sensitivity in women from 3.5% to 14% and an overall improved sensitivity of 14.2% (as compared to the initial 7.7%) while still maintaining a high specificity (>94%).

Our findings suggest that revised gender-specific cut-off values for both Cornell and Sokolow-Lyon voltage criteria are appropriate.

Limitations

The study subjects in this study were community-dwelling individuals and are very likely to differ significantly from some previous studies that only examined patients with hypertension or cardiovascular disease in a hospital or clinic setting. It is likely that this may affect the sensitivity and specificities of these ECG criteria derived from a different population. Criteria derived in this study may also not be applicable to younger adults. Nonetheless, these are the first available combined ECG and echocardiographic data from a large random sample of older Asian adults from the general community. These findings warrant validation in larger Asian cohorts across the full range of age.

ECG LVH voltage criteria can vary significantly due to lead placement variability, hence reproducibility of this test may be low.[25] Furthermore, we used echocardiographic-LVH as the gold standard rather than CMR, and the former may be affected more by inter-operator variability. Nonetheless, we found that there was still significant correlation between the ECG voltage criteria and LVMI. Given the wider availability and lower costs of these tests compared to CMR, it can be argued that our findings may be more easily applicable.

Conclusion

Conventional ECG voltage criteria for LVH developed and validated in Western populations perform poorly in Asian patients. However, tailoring cut-off values to ethnicity and gender improves the ability of ECG voltage to detect LVH in our multi-ethnic Asian cohort. We propose the use of modified Cornell voltage criteria (R in aVL + S in V3 >22 mm men; >18 mm women) and modified Sokolow-Lyon voltage criteria (S in V1 + R in V5 or V6 >35 mm men; >31 mm women) to improve detection of LVH in the Asian population.

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