

Comparisons of traditional electrocardiographic criteria for left and right ventricular hypertrophy in young Asian women

The CHIEF heart study

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Abstract

The performance of electrocardiographic (ECG) voltage criteria to identify left and right ventricular hypertrophy (LVH and RVH) in young Asian female adults have not been clarified so far.

In a sample of 255 military young female adults, aged 25.2 years on average, echocardiographic LVH was respectively defined as the left ventricular mass (LVM) indexed by body surface area (BSA) (\geq 88 g/m²) and by height^{2.7} (\geq 41 g/m^{2.7}), and RVH was defined as anterior right ventricular wall thickness >5.2 mm. The performance of ECG voltage criteria for the echocardiographic LVH and RVH were assessed by area under curve (AUC) of receiver operating characteristic (ROC) curve to estimate sensitivity and specificity.

For the Sokolow-Lyon (the maximum of SV₁ or SV₂ + RV₅ or RV₆) and Cornell (RaVL + SV₃) voltage criteria with the LVM/BSA \geq 88 g/m², the AUC of ROC curves were 0.66 (95% confidence intervals [CI]: 0.52–0.81, *P* = .039) and 0.61 (95% CI: 0.44–0.77, *P* = .18), respectively. For these 2 ECG voltage criteria with the LVM/height^{2.7} \geq 41 g/m^{2.7}, the AUC of ROC curves were 0.64 (95% CI: 0.52–0.75, *P* = 0.11) and 0.73 (95% CI: 0.61–0.85, *P* = 0.0074), respectively. The best cut-off points selected for the Sokolow-Lyon and Cornell voltage criteria with echocardiographic LVH in young Asian females were 26 mm and 6 mm, respectively. In contrast, all the AUC of ROC curves were less than 0.60 and not significant according to the Sokolow-Lyon (the maximum of RV1 + SV5 or V6) and Myers' voltage criteria (eg, the voltage of R wave in V1 and the ratios of R/S in V1, V5 and V6) with echocardiographic RVH.

There was a suggestion that the ECG voltage criteria to screen the presence of LVH should be adjusted for the young Asian female adults, and with regard to RVH, the ECG voltage criteria were found ineffective.

Abbreviations: AUC = area under curve, BSA = body surface area, CHIEF = cardiorespiratory fitness and hospitalization events in armed forces, ECG = electrocardiography, LVH = left ventricular hypertrophy, LVM = left ventricular mass, ROC = receiver operating characteristic, RVH = right ventricular hypertrophy, RVWT = right ventricular wall thickness.

Keywords: echocardiography, electrocardiographic criteria, left ventricular hypertrophy, right ventricular hypertrophy, young female adults

1. Introduction

The traditional electrocardiographic (ECG) voltage criteria in screening of the presence of left (LVH) and right ventricular hypertrophy (RVH) in the general population have been used for

decades.^[1–4] Most of the previous studies using Sokolow-Lyon and Cornell ECG voltage criteria to relate to LVH which was diagnosed by echocardiography or cardiac magnetic resonance imaging (MRI) showed consistent results that the sensitivity was

Editor: Michael Masoomi.

The study was supported by the grant from Hualien Armed Forces General Hospital (No. 805C-109-07).

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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How to cite this article: Su FY, Lin YP, Lin F, Yu YS, Kwon Y, Lu HS, Lin GM. Comparisons of traditional electrocardiographic criteria for left and right ventricular hypertrophy in young Asian women: the CHIEF heart study. Medicine 2020;99:42(e22836).

Received: 2 July 2020 / Received in final form: 10 September 2020 / Accepted: 19 September 2020

http://dx.doi.org/10.1097/MD.00000000022836

very low, estimated merely 20%-30%, whereas the specificity was extremely high, estimated over 95%.^[5,6] Similarly, using the ECG voltage criteria for the imaging-based RVH such as the Myers et al and Sokolow-Lyon revealed low sensitivity, commonly lower than 20% and high specificity which was up to 95% or more.^[7,8]

It is notable that most studies examining the performance of the ECG voltage criteria to relate to the imaging-based LVH and RVH were carried out in White and Black, and middle to old aged persons of the Western world.^[9–12] For the Asian individuals, the studies reporting the ECG criteria performance were relatively rare,^[13–15] and in the same situation, most of these studies were aimed for the middle to old aged populations with several cardiovascular risk factors such like hypertension.^[13,14] To our knowledge, since there have not established standard references with regard to the echocardiographic or other imaging based LVH or RVH for young Asian adults, only a few ECG studies were carried out to investigate the performance of the ECG voltage criteria in this population, particularly a lack of young Asian female adults so far.^[8,15]

Military personnel are mainly composed of young adults, who have to receive regular exercise training. They are good samples to set standard references of imaging based LVH and RVH for the young adults. Therefore, the purpose of the study was firstly to clarify the standard references of echocardiographic LVH and RVH and then to examine the performance of ECG voltage criteria in a military young Asian female cohort in Taiwan.

2. Method

2.1. Study population

The ancillary cardiorespiratory fitness and hospitalization events in armed forces (CHIEF) Heart study included 1526 military young female adults, aged 18 to 42 years, in eastern Taiwan in 2014 to 2018.^[16] All participants carried out a comprehensive health examination, and self-reported a questionnaire for their experience regarding toxic substances use and physical activity in the Hualien Armed Forces General Hospital of Taiwan. Of these, there were 265 subjects receiving a 12-lead ECG and a transthoracic echocardiography on the same day to ensure their cardiac health for the rank promotions and military awards, which were the inclusion criteria in this study, Those with hypertension (systolic/diastolic blood pressure ≥140/90 mm Hg, or on antihypertensive therapy) or an ECG finding of bundle branch block (n=10) were excluded, leaving a sample of 255 females for the final analyses. The study design of CHIEF study has been described in detail previously.^[17-21]

2.1.1. Measurements of 12-lead surface ECG. All 12-lead surface ECGs (Philips PageWriter Trim III) which were recorded at 25 mm/s paper speed and 1 mV/cm were prospectively performed by an experienced technician (Yu YS). The ECG variables including amplitudes of R and S waves in all limb and precordial leads and were retrospectively validated by 2 well-trained technicians (Yu YS and Lin F) and confirmed by a cardiologist (Lin GM) at the Hualien-Armed Forces General Hospital. For female adults, the Sokolow-Lyon voltage criterion for LVH was defined as the maximum of the amplitude (SV₁ or SV₂+RV₅ or RV₆) \geq 35 mm,^[1] and the Cornell voltage criterion for LVH was defined as the amplitude (RaVL+SV₃) \geq 20 mm.^[2] In addition, the Sokolow-Lyon voltage criterion for RVH was defined as the amplitudes (RV₁+SV₅ or SV₆) >

10.5 mm,^[3] and the Myers et al voltage criterion for RVH was defined as the R/S ratio of lead $V_1 > 1$ or the R/S ratio of lead V_5 or $V_6 < 1$ or the R amplitude in lead $V_1 > 6$ mm.^[4]

2.1.2. Measurements of transthoracic echocardiography. All procedures of echocardiography using a 1 to 5 MHz transducer (iE33; Philips Medical Systems, Andover, MA) were performed by the same experienced technician (Yu YS) after the ECG and verified by a cardiologist (Lin GM) at the Hualien-Armed Forces General Hospital. All participants were examined using parasternal long-axis and short-axis approaches for the apical four and 2-chamber views in supine and left lateral positions. According to the suggestions of American Society of Echocardiography,^[22] quantification of left ventricular wall thickness (interventricular septal and posterior walls) and chamber dimension were measured approximately at the onset of the QRS complex of end diastole and tips of the mitral valve by Mmode and 2-dimensional measurements in parasternal long axis view. Left ventricular mass (LVM) was thus calculated according to the corrected formula proposed by Devereux et al.^[23] LVM= $0.8 \times \{1.04 \times [(left ventricular end diastolic diameter (LVIDd) +$ end diastolic posterior wall thickness + end diastolic interventricular septal thickness]³ – left ventricular end diastolic diameter³+ 0.6. In addition, LVM was indexed for body surface area (LVM/BSA, g/m²), according to the Dubois formula,^[24] and alternatively for height^{2.7} (LVM/height^{2.7}, g/m^{2.7}) suggested by de Simone et al.^[25] The cut-off value for echocardiographic LVH was set as LVM/BSA $\geq 88 \text{ g/m}^2$ and LVM/height^{2.7} $\geq 41 \text{ g/m}^{2.7}$ which were the 95th percentile in the military young female adults in CHIEF study and according to another study finding for the young Asian female adults.^[26,27] Measurements of anterior right ventricular wall thickness (RVWT) were by M-mode and 2dimensional windows at the onset of the QRS complex of end diastole via the parasternal long-axis approaches.^[28] Echocardiographic RVH was defined as RVWT > 5.2 mm, which was the 95th percentile in our young female cohort.^[29]

2.2. Statistical analysis

Baseline characteristics of the CHIEF military female cohort were expressed as mean±standard deviation (SD) for continuous variables and number (%) for categorical variables, respectively. Pearson correlation coefficient was used to determine the correlation of each ECG voltage criterion with the LVM indexes and RVWT, and was compared by the Fisher *z* test. Area under curves (AUC) of the receiver-operating characteristics (ROC) curves were used to evaluate and compare the performance of ECG voltage criteria for echocardiographic LVH and RVH. In addition, using the ROC curve to find the maximal sum of sensitivity and specificity was reclassified for each ECG criterion. A two-tailed value of P < .05 was considered significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

2.2.1. Ethic statement. This study was reviewed and approved by the Institutional Review Board of the Mennonite Christian Hospital (No. 16-05-008) in Taiwan, and written informed consent was obtained from all participants.

3. Results

The baseline characteristics including ECG and echocardiographic data of the military female cohort are shown in Tables 1 and 2, respectively. Ages in the study subjects were between 18 and 42

Table 1

Baseline characteristics of demographic, anthropometric, and electrocardiographic measurements of the military female population.

Variables	Military female participants (n=255)
Age (yrs)	25.22 ± 5.26
Height (cm)	161.01 ± 5.01
Weight (kg)	59.13 ± 9.29
Waist (cm)	74.76 ± 8.00
Body mass index (kg/m ²)	22.79 ± 3.28
Underweight (<18.5) (%)	15 (5.88)
Normal (18.5–24.9) (%)	175 (68.63)
Overweight (25-29.9) (%)	59 (23.14)
Obesity (≥30) (%)	6 (2.35)
Body surface area (m ²)	1.57 ± 0.13
Systolic blood pressure (mm Hg)	107.12±11.19
Diastolic blood pressure (mm Hg)	64.31 ± 8.46
Heart rate (beats/min)	68.68 ± 23.51
Sokolow-Lyon V (mm)	24.72±6.45
Cornell V (mm)	6.87 ± 3.85
QRS duration (ms)	89.56 ± 11.42
R/S (V1)	0.49 ± 0.45
R-S (V1)	-4.33±3.76
R/S (V5 or 6) minimum	6.16±5.81
R-S (V5 or 6) minimum	9.14 ± 5.42
R (V1) (mm)	2.76 ± 1.58
Sokolow-Lyon RVH (mm) R(V1) + S(V5 or 6) maximum	5.24 ± 2.56

Continuous variables are expressed as mean ± standard deviation and categorical variables as number (percentage).

V=the voltage criterion, RVH=right ventricular hypertrophy.

years and averaged 25.2 years. The prevalence of echocardiographic LVH was 5.49% as LVM/BSA \geq 88g/m² and 4.71% as LVM/height^{2.7} \geq 41g/m^{2.7}, respectively. In addition, the prevalence of echocardiographic RVH was 4.95% as RVWT > 5.2 mm.

3.1. Correlation of each ECG criterion with the LVM indexes and RVWT

Table 3 reveals that there was a correlation of the Cornell criterionbased voltage (RaV+SV₃) with the LVM indexes for BSA and LVM/height^{2.7} (r=0.209 and 0.181, respectively), whereas there

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Baseline echocardiographic parameters of the military population.

Echocardiographic variables	Military female participants (n=255)			
Interventricular septum (mm)	7.59 ± 0.84			
LV posterior wall (mm)	7.33 ± 0.80			
LV end-diastolic dimension (mm)	45.62±3.19			
LVM/BSA (g/m ²)	68.14 ± 10.84			
LVM/height ^{2.7} (g/m ^{2.7})	29.65 ± 5.65			
RVWT (mm)	4.30 ± 0.57			
Prevalence of LVH				
By LVM/BSA, n (%)	14 (5.49)			
By LVM/height ^{2.7} , n (%)	12 (4.71)			
Prevalence of RVH				
RVWT > 5.2 mm, n (%)	11 (4.95)			

Continuous variables are expressed as mean ± standard deviation and categorical variables as number (oercentage).

LV = left ventricle, LVM/BSA = left ventricular mass indexed by body surface area, LVM/height^{2,7} = left ventricular mass indexed by height^{2,7}, RVH = right ventricular hypertrophy, RVWT = right ventricular wall thickness.

were no correlations between the Sokolow-Lyon criterion–based voltage (the maximal sum of SV₁ or SV₂+RV₅ or RV₆) and the 2 LVM indexes (r=0.045 and 0.025, respectively). In addition, there were no correlations between RVWT and each ECG voltage criterion for RVH. The greatest correlation coefficients with RVWT were observed in the Myers' voltage criteria for the R/S ratio in lead 5 or 6 (r=-0.124), and in the Sokolow-Lyon criterion-based voltage (the maximum of RV₁+SV₅ or SV₆) (r=0.017).

3.2. Performance of the ECG voltage criteria for LVH and RVH using ROC curves

Figure 1A reveals the AUC of ROC curve using the Sokolow-Lyon voltage criterion for LVH \geq 35 mm to detect the LVM/BSA index \geq 88 g/m² higher than that using the Cornell voltage criterion \geq 20 mm for LVH (0.66 vs 0.61) in the young Asian females. On the contrary, Figure 1B shows the AUC of ROC curve using the Cornell voltage criterion \geq 20 mm for LVH to identify the LVM/height^{2.7} index \geq 41 g/m^{2.7} greater than that utilizing the Sokolow- Lyon voltage criterion \geq 35 mm for LVH (0.73 vs 0.64) in the young Asian females. Figure 1C reveals the AUC of ROC curves using the Myers et al and Sokolow-Lyon

Table 3

Pearson correlation coefficient (r) of electrocardiographic criteria with the left ventricular mass indexes and right ventricular wall thickness in the military female population.

	LVM/I	BSA	LVM/height ^{2.7}	
Electrocardiographic criteria with left ventricular mass indexes	r	P value	r	P value
Sokolow-Lyon V (mm)	0.045*	.4707	0.025 [†]	.6883
Cornell V (mm)	0.209	.0008	0.181	.0038
Electrocardiographic criteria with right ventricular wall thickness	RVWT(mm)			
	r	P value		
R/S (V1)	0.010	.8801		
R/S (V5, 6) minimum	-0.124	.1062		
R (V1) (mm)	0.037	.5863		
Sokolow-Lyon RVH (mm) R(V1)+S(V5 or 6) maximum	0.117	.0812		

LVM/BSA = left ventricular mass indexed by body surface area, LVM/height²⁻⁷ = left ventricular mass indexed by height²⁻⁷, V = the voltage criterion, RWT = right ventricular wall thickness, RVH = right ventricular hypertrophy.

*P=.030 vs Cornell V.

 $^{\dagger}P$ =.038 vs Cornell V.

 $^{*}P$ =.035 vs R (V1).

||P=.0033 vs R(V1) + S(V5 or 6) maximum.

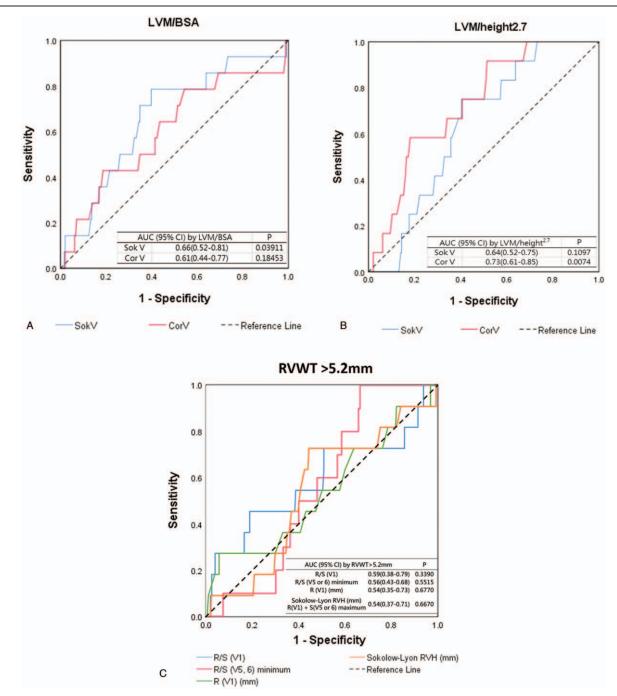


Figure 1. The ROC curve with ECG criteria for identifying LVH and RVH in the military female population in Taiwan. (A) The ROC curve with 2 ECG criteria [the Sokolow-Lyon voltage (Sok V) and the Cornell voltage (Cor V)] for identifying LVH using left ventricular mass (LVM)/body surface area (BSA) \geq 88 g/m²; (B) The ROC curve with 2 ECG criteria [the Sok V and the Cor V] for defining LVH using LVM/height^{2.7} \geq 41 g/m^{2.7}; (C) The ROC curve with the four ECG criteria [R/S (V1) and the minimum of R/S (V5 or V6), R(V1), and the maximum of R(V1) + S(V5 or V6) of Sokolow-Lyon RVH] for identifying RVH which was defined by the right ventricular wall thickness >5.2 mm. BSA = body surface area, ECG = electrocardiography, LVH = left ventricular hypertrophy, LVM = left ventricular mass, ROC = receiver operating characteristic, RVH = right ventricular hypertrophy.

voltage criteria for RVH to identify the RVWT > 5.2 mm (0.54-0.59) where all were nonsignificant in the young Asian females.

3.3. Performance of the ECG voltage criteria for LVH and RVH using traditional and revised cut-off values

Table 4 demonstrates that the prevalence, sensitivity and positive predictive value of the ECG voltage criteria using traditional cut-

off values to identify the presence of LVH and RVH in the young Asian females were extremely low, all estimated far less than 20%. In contrast, the specificity and negative predictive value of the ECG voltage criteria to identify the presence of LVH and RVH were extremely high, all estimated much greater than 92% in the young Asian females. When using the AUC of RUC curves to select the best cut-off points for echocardiographic LVH in the young Asian females, the Sokolow-Lyon voltage criterion was

Table 4

The prevalence, sensitivity, specificity, predictive values and best cut-off point of each electrocardiographic criterion for echocardiographic left ventricular hypertrophy and right ventricular hypertrophy.

Electrocardiographic criteria	Prevalence (%)	Sen (%)	Spe (%)	PPV (%)	NPV (%)	Best cut-off point	Sen (%)	Spe (%)
LVM/BSA \geq 88 g/m ²	5.49							
Sokolow-Lyon V \geq 35 mm	4.31	14.29	96.27	18.18	95.08	26.25	78.57	60.17
Cornell V≥20 mm	0.39	0.00	99.59	0.00	94.49	5.95	78.57	45.64
LVM/height ^{2.7} \geq 41 g/m ^{2.7}	4.71							
Sokolow-Lyon V \geq 35 mm	4.31	0.00	95.47	0.00	95.08	26.25	75.00	25.00
Cornell V \geq 20 mm	0.39	0.00	99.59	0.00	95.28	6.05	91.67	48.56
RVWT > 5.2 mm	4.95							
R/S (V1)>1	7.66	9.09	92.42	5.88	95.12	0.19	45.45	54.55
R/S (V5 or V6) < 1	7.21	9.09	92.89	6.25	95.15	6.46	100.00	33.33
R (V1)>6 mm	4.95	9.09	95.26	9.09	95.26	0.75	27.27	94.31
Sokolow-Lyon RVH $\!>\!10.5$ mm	4.05	9.09	96.21	11.11	95.31	5.15	72.73	55.45

NPV=negative predictive value, PPV=positive predictive value, LVM/BSA=left ventricular mass indexed by body surface area, LVM/height^{2.7}=left ventricular mass indexed by height^{2.7}, V=the voltage criterion, RVWT=right ventricular wall thickness, RVH=right ventricular hypertrophy, Sen=sensitivity, Spe=specificity.

reclassified as $\geq 26 \text{ mm}$ and the Cornell voltage criterion was $\geq 6 \text{ mm}$, respectively. In addition, the best cut-off point of Sokolow-Lyon criterion for echocardiographic RVH was reclassified as >5.2 mm.

4. Discussion

Our principal findings were that firstly for the young Asian female adults, we established a standard of echocardiographic LVH as defied by the LVM/BSA index \geq 88 g/m² and by the LVM/ height^{2.7} index \geq 41 g/m^{2.7}, respectively. In addition, we established a standard of echocardiographic RVH as defined by the RVWT > 5.2 mm. Second, using traditional ECG voltage criteria for LVH and RVH in the young Asian females consistently yielded low sensitivity and high specificity which were in line with the finding of previous studies. Finally, the best cut-off points for the ECG voltage criteria for LVH and RVH in the young Asian females should be lowered to obtain the maximal sum of sensitivity and specificity.

It is notable that among the premenopausal women in Asia, the prevalence of metabolic abnormalities such as obesity and hypertension, which are the risk factors of cardiac hypertrophy, is low.^[20] In a previous study in Taiwan, the LVM and LVM index were lower in the female adults as compared with the male adults and the values decreased with younger ages.^[30] The mean of LVM/ BSA index was 63.6 g/m² in women aged \leq 30 years and 67.4 g/m² in women aged 31 to 40 years. In addition, in another study for a multiethnic southeast Asian women cohort,^[26] those aged <50 years had a mean LVM/BSA index with 64 (standard deviation = 14) g/m² and the 95th percentile of the LVM/BSA index was 86 g/m², close to our finding of 88 g/m² as the cut-off point for echocardiographic LVH. Moreover, this is the first study clarifying the RVWT > 5.2 mm as echocardiographic RVH for the young Asian females.

As compared with the previous ECG studies for the middleaged females,^[14,28] Our findings revealed relevant results that there were low sensitivity and high specificity with regard to using the traditional ECG criteria to identify imaging-based LVH and RVH among the young Asian female adults. These findings were likely due to a very low prevalence of ECG-defined LVH, less than 5% in our subjects, reflecting a need to revise the cut-off values of ECG criteria-defined voltage for LVH. In addition, the correlation coefficients of the Cornell criterion-based voltage were found consistently better than that of the Sokolow-Lyon criterion-based voltage against the two LVM indexes in the young Asian female adults. Unlike the previous study findings for the middle-aged females, ^[14,31] the AUC of ROC curve was greater for the Sokolow-Lyon voltage criterion to detect the LVM/BSA index \geq 88 g/m² in the young Asian females, which might be due to a selection of different cut- off value for echocardiographic LVH. On the contrary, neither the Sokolow-Lyon nor the Myers et al criterion-based voltage to correlate with RVWT or to detect echocardiographic RVH was significant in the young Asian female adults. Although the ECG studies for the relationship with RVH in females were rare, the findings in our study were in line with that for males.

Our study had several strengths. First, both the ECG and echocardiographic examinations were performed in a strict manner and the procedures were standardized. Second, the military young females had to participate regular physical training that would modestly increase the level of 95th percentile to define the echocardiographic LVH and RVH compared with that of the age- matched general population of young females and avoid the selection bias. In contrast, this study had some limitations. First, this study was conducted on athletic military young Asian females and thus the results might not be appropriately applied to the general population of young females. Second, the female breast size might be a potential confounder for technicians to put the ECG precordial leads on the standard locations of chests wall, possibly leading to a bias. Third, there might be different results using other imaging diagnostic modalities such as cardiac magnetic resonance imaging for LVH and RVH.

5. Conclusion

There was a suggestion that the ECG voltage criteria to identify the presence of LVH as defined by echocardiographic LVM indexes should be adjusted for young Asian females, and for RVH as defined by echocardiographic RVWT, the ECG voltage criteria were found ineffective.

Author contributions

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