Accuracy of ECG Criteria for the Diagnosis of Left Ventricular Hypertrophy: A Comparison with Magnetic Resonance Imaging

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Background: *There are many ECG criteria for the diagnosis of left ventricular hypertrophy (LVH). There are, however, limited data on the accuracy of these criteria in comparison with cardiac magnetic resonance (CMR).*
Objective: *To determine the accuracy of ECG criteria for the diagnosis of LVH using CMR as the gold standard and to assess gender-specific data.*
Material and Method: *Patients who were referred for CMR for clinical purposes were studied. ECG and CMR were performed on the same day. Functional CMR protocol was performed for the assessment of cardiac volume, function and mass. CMR variables were indexed by the adjustment of body surface area. The following ECG criteria were used: Romhilt-Estes criteria (score at least 4 or 5 points were used in the present study), Sokolow-Lyon and Sokolow-Lyon-Rappaport, Cornell voltage and Cornell product, and sum of QRS voltage of all 12 leads. CMR of 184 subjects (120 females, 64 males) free of cardiovascular disease was used as controls. Patients with left ventricular mass index above 95 percentile of gender specific left ventricular mass in control group were considered LVH. Diagnostic yield of ECG criteria for LVH was calculated for the whole group and each gender.*
Results: *There were a total of 1,882 patients, 994 males and 888 females. Average age was 64.6 $\pm$ 11.3 years. LVH was diagnosed by CMR in 23.3% in female and 25.4% in male. ECG criteria for the diagnosis of LVH had a relatively low sensitivity (0.25-0.61), and high specificity (0.75-0.95). Female had a lower sensitivity, higher specificity, higher PPV, similar NPV, and higher overall accuracy than male. Cornell product, Romhilt-Estes (at least 4 points) and Sokolow-Lyon were the ECG criteria with the best accuracy, sensitivity and specificity, respectively.*
Conclusion: *ECG criteria for the diagnosis of LVH had a relatively low sensitivity, and high specificity. The accuracy was in the range of 0.71-0.80. Cornell product had the highest accuracy.*

Keywords: *ECG, Left ventricular hypertrophy, Sokolow-Lyon, Cornell voltage, Cornell product, Romhilt-Estes*

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Left ventricular hypertrophy (LVH) is an important and independent factor contributing to an increased risk for cardiovascular event in general population[1] and in patients with hypertension[2,3]. It reflects an increased left ventricular mass which contributes to an increased myocardial oxygen demand and, in certain conditions, may cause an inadequate blood supply to the myocardium and may also cause myocardial ischemia or infarction[4]. In patients with hypertension, it reflects inadequate blood pressure control, thereby increased the risk of coronary artery disease and may lead to progressive heart failure[5]. Increased myocardial mass, by itself, can increased risk of cardiac arrhythmia and sudden cardiac death[6].

Twelve-lead ECG is by far the most conventional and simplest investigation for the assessment of LVH[7]. Many clinical trials used different ECG criteria for the assessment of LVH and have shown that LVH by ECG is a useful tool for the prediction of those who carryincreased risk of a cardiovascular event[8]. Moreover, they showed that treatments that can reduce LVH are associated with a risk reduction[9].

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There are many standard ECG criteria for the diagnosis of LVH, e.g., Sokolow-Lyon[10], Sokolow-Lyon-Rappaport[11], Romhilt-Estes[12], Cornell voltage[13], Cornell product[14], and sum of 12 leads QRS voltage[15]. However, previous reports have shown that they lack accuracy for the diagnosis of LVH[16,17]. These reports were based on the comparison of 12-lead ECG with echocardiography. Echocardiogram is a standard investigation that can assess LVH. However, LVH by echocardiogram isusually calculated by a formula based on a geometric assumption[17,18]. Multi-dimensional echocardiography can assess LVH directly and should be more accurate for the assessment of LVH[19]. Cardiac magnetic resonance (CMR) is an investigation that has been used as a gold standard for the assessment of left ventricular volume, mass and left ventricular ejection fraction (LVEF) due to its high image resolution and 3-dimensional image acquisition[19-21].

The objective of the present study was to determine diagnostic accuracy of LVH by different ECG criteria compared to CMR and assess gender-specific data.

Material and Method

Study population

The authors studied patients over 18 years of age who were referred for CMR for clinical purposes during 2005-2009. Patients with the following conditions were excluded; unable to complete CMR examination, indicating unstable clinical conditions, known contraindication for CMR such as intracranial clip, using pacemakers or internal defibrillators, suffer from claustrophobia. Patients with Wolff-Parkinson-White syndrome, complete left bundle branch block or right bundle branch block were also excluded. CMR was also performed in 184 healthy volunteers as control group. Data in the control group was used to determine the cut off value for the diagnosis of LVH by CMR.

The present study was approved by the Ethics committee of Siriraj Hospital. Written informed consent was obtained prior to participation. Twelve-lead ECG was performed on the same day prior to CMR examination.

CMR protocol

All patients underwent CMR for the assessment of cardiac function, left ventricular volume and mass. CMR was performed by a 1.5 T Gyroscan NT Philips scanner (Philip Medical System, Best, the Netherlands). After a brief survey, spin echo image was acquired. Functional images was subsequently performed by a steady-state free-precession (SSFP) technique in horizontal long axis, vertical long axis, 4-chamber and multiple slice short axis series. Parameters for functional images were as follows: repetition time/ echo time/number of excitations = 3.7/1.8/2, 390 x 312 mm field of view, 256 x 240 matrix, 1.52 x 1.21 reconstruction pixel, 8 mm slice thickness and 70 degree flip angle.

Analysis of CMR images

CMR analysis was performed by the View Forum workstation (Philip Medical System, Best, the Netherlands). Functional data were analyzed for volume, mass and ejection fraction of the left ventricle. The endocardial and epicardial border of the left ventricle during diastole and endocardial detection for images during systole was automatically detected. Additional manual adjustment was performed by an experienced technician. Left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular mass (LVMASS) and LVEF were calculated. Calculation of indices of LVEDV (LVEDVI), LVESV (LVESVI) and LVMASS (LVMASSI) was performed for the adjustment of body surface area. Intra- and inter-observer variability presented as percentages of the mean of 2 repeated measurements averaged $\pm$ standard deviations were 3 $\pm$ 4% and 4 $\pm$ 4% for LVEDV, 4 $\pm$ 5% and 6 $\pm$ 6% for LVESV and 3 $\pm$ 4% and 5 $\pm$ 5% for LVMASS. Segmental wall motion was also assessed.

Patients were considered to have LVH when LVMASSI above 95% of LVMASSI in control group[22].

Analysis of 12-lead ECG

Standard 12-lead ECG was recorded at a 25 mm/sec paper speed and a 1 mV/cm calibration made with the patients in the supine position and quiet respiration. Twelve-lead ECG was interpreted by an experienced investigator with the use of calipers and blinded to clinical information. The following ECG criteria were used in the present study; 1) Sokolow-Lyon (S in V1 + R in V5 or V6 > 3.5 mV or R in V5 or V6 > 2.6 mV)[10] 2) Sokolow-Lyon-Rappaport (S in V1 or V2 + R in V5 or V6 > 3.5 mV or R in V5 or V6 > 2.6 mV)[11] 3) Romhilt-Estes point score system (5 points or more for LVH, 4 points for probable LVH) of at least 4 points or 5 points 4) Cornell voltage (R in aVL + S in V3 > 2.0 mV in female and > 2.8 mV in male)[13] 5) Cornell product (the product of QRS duration times the Cornell voltage combination with 6 mV added in women > 2,440 mm)[14] and 6) Sum QRS 12 leads (sum QRS amplitude. In all

leads > 175 mm) (15). Details of each ECG criteria were measured.

Statistical analysis

Continuous data were presented as mean and standard deviation (SD) whereas categorical data were presented as number and percentages. Comparison of continuous data was made by the student t-test for unpaired data and comparison of categorical data was made by the Chi-square test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive and negative likelihood ratio and accuracy were calculated. A p-value of < 0.05 was considered statistically significant.

Results

A total of 1,882 patients were studied. There were 994 male (52.82%) and 888 female (47.18%) with an average age of 64.6 $\pm$ 11.3 years. We used 95 percentile of LVMASSI in control group as a cut off value for the diagnosis of LVH by CMR. LVH was diagnosis when LVMASSI above 69.09 g/m^2 in male and above 55.96 g/m^2 in female. Among 1,882 patients, LVH was diagnosed in 459 patients (24.39%); 252 (25.35%) in male and 207 (23.31%) in female. Baseline characteristics of patients with and without LVH are shown in Table 1. Patients with LVH are more likely to have underlying risk factors, cardiovascular disease, to beon more cardiovascular medications and have

Table 1. Baseline characteristics of patients with and without left ventricular hypertrophyby CMR

Characteristics	LVH (n = 459)	No LVH (n = 1423)	p-value
Male gender	252 (54.9)	742 (52.1)	0.303
Age (year)	63.3 $\pm$ 12.4	65.0 $\pm$ 11.0	0.013
Weight (kg)	62.4 $\pm$ 12.6	66.1 $\pm$ 12.1	< 0.001
Height (cm)	160.1 $\pm$ 8.2	160.5 $\pm$ 8.5	0.391
Body surface area (m^2)	1.66 $\pm$ 0.19	1.17 $\pm$ 0.18	< 0.001
Body mass index (kg/m^2)	24.3 $\pm$ 4.2	25.6 $\pm$ 4.0	< 0.001
Systolic blood pressure (mmHg)	145.8 $\pm$ 28.8	135.6 $\pm$ 21.8	< 0.001
Diastolic blood pressure (mmHg)	77.4 $\pm$ 15.4	75.2 $\pm$ 12.6	0.016
Smoking	119 (25.9)	255 (17.9)	< 0.001
Hypercholesterolemia	280 (61.0)	926 (65.1)	0.114
Diabetes mellitus	189 (41.2)	474 (33.3)	0.002
Hypertension	313 (68.2)	864 (60.7)	0.004
History of myocardial infarction	101 (22.0)	171 (12.0)	< 0.001
History of coronary revascularization	84 (18.3)	202 (14.2)	0.033
History of dyspnea on exertion	257 (56.0)	606 (42.6)	< 0.001
History of angina	226 (49.2)	791 (55.6)	0.018
Medications			
Beta blocker	239 (52.1)	705 (49.5)	0.347
Calcium channel blocker	100 (21.8)	324 (22.8)	0.661
Nitrate	218 (47.5)	461 (32.4)	< 0.001
Aspirin/clopidogrel	330 (71.9)	874 (61.4)	< 0.001
Angiotensin converting enzyme inhibitors or angiotensin receptor blockers	237 (51.6)	538 (37.8)	< 0.001
Statins	269 (58.6)	788 (55.4)	0.225
CMR variables			
LVEDVI (ml/m^2)	106.1 $\pm$ 47.7	65.9 $\pm$ 22.7	< 0.001
LVESVI (ml/m^2)	63.2 $\pm$ 48.9	26.5 $\pm$ 24.5	< 0.001
LVMASSI (gm/m^2)	82.4 $\pm$ 22.6	47.0 $\pm$ 10.1	< 0.001
LVEF (%)	47.5 $\pm$ 21.8	64.7 $\pm$ 15.2	< 0.001
Abnormal wall motion	308 (67.1)	378 (26.6)	< 0.001

Values are number (percentages) or mean $\pm$ SD

LVH = left ventricular hypertrophy, CMR = cardiac magnetic resonance, LVEDVI = left ventricular end-diastolic volume index, LVESVI = left ventricular end-systolic volume index, LVMASSI = left ventricular mass index, LVEF = left ventricular ejection fraction

abnormal CMR results. Comparisons of ECG variables in patients with and without LVH are shown in Table 2. Patients with LVH had an increased voltage in every item of the ECG criteria in both genders.

Sensitivity, specificity, PPV, NPV, positive and negative likelihood ratio and accuracy of different ECG criteria for the diagnosis of LVH are shown in Table 3. Overall accuracy was 0.71-0.80. Cornell product had

Table 2. ECG variables used for different LVH criteria in patients with and without LVH by CMR

ECG characteristics	Mean ± SD		p-value
	LVH (n = 459)	No LVH (n = 1,423)	
Romhilt-Estes score			
All	4.24 ± 2.77	2.16 ± 2.15	< 0.001
Male	4.54 ± 2.79	2.50 ± 2.25	< 0.001
Female	3.89 ± 2.70	1.79 ± 1.96	< 0.001
SV1 + RV5			
All	25.41 ± 12.11	19.55 ± 7.98	< 0.001
Male	25.48 ± 12.92	19.95 ± 8.68	< 0.001
Female	25.32 ± 11.08	19.11 ± 7.13	< 0.001
SV1 + RV6			
All	24.30 ± 10.89	17.83 ± 7.25	< 0.001
Male	24.25 ± 11.09	18.05 ± 7.71	< 0.001
Female	24.35 ± 10.67	17.58 ± 6.71	< 0.001
SV1 + RV5 or 6			
All	26.90 ± 12.05	20.00 ± 7.90	< 0.001
Male	27.17 ± 12.62	20.46 ± 8.53	< 0.001
Female	26.59 ± 11.35	19.51 ± 7.13	< 0.001
SV1 or 2 + RV5 or 6			
All	31.9 ± 12.9	23.2 ± 8.5	< 0.001
Male	33.5 ± 13.5	24.6 ± 9.2	< 0.001
Female	30.1 ± 12.0	21.7 ± 7.2	< 0.001
RV5			
All	15.07 ± 9.20	12.90 ± 6.20	< 0.001
Male	15.13 ± 9.95	13.17 ± 6.80	0.004
Female	14.99 ± 8.23	12.61 ± 5.47	< 0.001
RV6			
All	13.95 ± 7.75	11.18 ± 5.19	< 0.001
Male	13.89 ± 7.74	11.27 ± 5.54	< 0.001
Female	14.02 ± 7.79	11.08 ± 4.77	< 0.001
RV5 or 6			
All	16.55 ± 9.08	13.35 ± 6.06	< 0.001
Male	16.80 ± 9.54	13.68 ± 6.56	< 0.001
Female	16.26 ± 8.51	13.00 ± 5.44	< 0.001
RaVL + SV3			
Male	22.46 ± 10.47	14.76 ± 6.80	< 0.001
Female	18.12 ± 8.23	11.72 ± 5.19	< 0.001
QRSD x (RaVL + SV3)			
Male	2,280 ± 1,157	1,415 ± 702	< 0.001
Female	1,719 ± 847	1,034 ± 503	< 0.001
Sum QRS			
All	159.20 ± 46.64	126.73 ± 33.58	< 0.001
Male	162.96 ± 43.30	132.10 ± 33.71	< 0.001
Female	154.94 ± 49.92	120.98 ± 32.50	< 0.001

LVH = left ventricular hypertrophy, QRSD = QRS duration

Table 3. Yield of various criteria of 12-lead ECG for the diagnosis of LVH (including 95% confidence interval)

Both sex	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	LH+	LH-	Accuracy
Cornell voltage	131	1,344	79	328	0.29 (0.25-0.33)	0.94 (0.93-0.96)	0.62 (0.56-0.69)	0.80 (0.78-0.82)	5.14 (3.97-6.66)	0.76 (0.71-0.80)	0.78 (0.76-0.80)
Cornell product	170	1,327	96	289	0.37 (0.33-0.42)	0.93 (0.92-0.94)	0.64 (0.58-0.69)	0.82 (0.80-0.84)	5.49 (4.37-6.89)	0.68 (0.63-0.73)	0.80 (0.78-0.81)
Romhilt -5	170	1,263	160	289	0.37 (0.33-0.42)	0.89 (0.87-0.90)	0.52 (0.46-0.57)	0.81 (0.79-0.83)	3.29 (2.73-3.98)	0.71 (0.66-0.76)	0.76 (0.74-0.78)
Romhilt -4	280	1,062	361	179	0.61 (0.56-0.65)	0.75 (0.72-0.77)	0.44 (0.40-0.48)	0.86 (0.84-0.87)	2.40 (2.14-2.70)	0.52 (0.46-0.59)	0.71 (0.69-0.73)
Sokolow	113	1,353	70	346	0.25 (0.21-0.29)	0.95 (0.94-0.96)	0.62 (0.55-0.68)	0.80 (0.78-0.81)	5.00 (3.79-6.61)	0.79 (0.75-0.84)	0.78 (0.76-0.80)
Rappaport	169	1,280	133	284	0.37 (0.33-0.42)	0.91 (0.89-0.92)	0.56 (0.50-0.61)	0.82 (0.80-0.84)	3.96 (3.24-4.85)	0.69 (0.64-0.74)	0.78 (0.76-0.79)
Sum QRS	140	1,314	109	319	0.31 (0.26-0.35)	0.92 (0.91-0.94)	0.56 (0.50-0.62)	0.80 (0.78-0.82)	3.98 (3.17-5.00)	0.75 (0.71-0.80)	0.77 (0.75-0.79)

(TP = true positive, TN = true negative, FP = false positive, FN = false negative, PPV = positive predictive value, NPV = negative predictive value, LH+ = positive likelihood ratio, LH- = negative likelihood ratio)

the highest accuracy and also highest PPV and positive likelihood ratio. Romhilt-at least 4 points-had the highest sensitivity and NPV and lowest negative likelihood ratio. Sokolow-Lyon had the highest specificity.

Analysis by gender

Diagnostic yields of different ECG criteria for the diagnosis of LVH in male and female are shown in Fig. 1 and 2. Female had a lower sensitivity, higher specificity, higher PPV, similar NPV, and higher overall accuracy than male.

Discussion

Results of the present study demonstrated that ECG criteria for the diagnosis of LVH had a relatively low sensitivity (0.25-0.61), and high specificity (0.75-0.95). The accuracy was in the range of 0.71-0.80. Cornell product had the highest accuracy (0.80). Female had a lower sensitivity, higher specificity, higher PPV, similar NPV and higher overall accuracy than male.

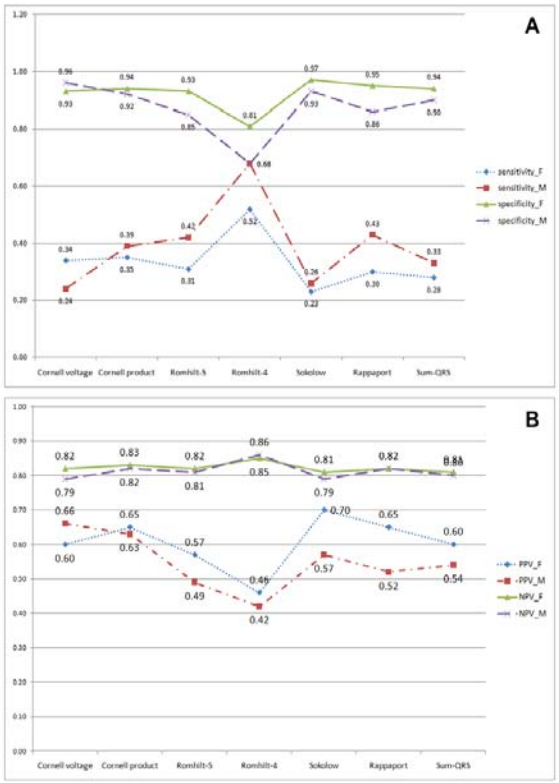

Fig. 1 Sensitivity, specificity (A), positive predictive value and negative predictive value (B) of different ECG criteria for the diagnosis of LVH in male and female (M = male, F = female, PPV = positive predictive value, NPV = negative predictive value)

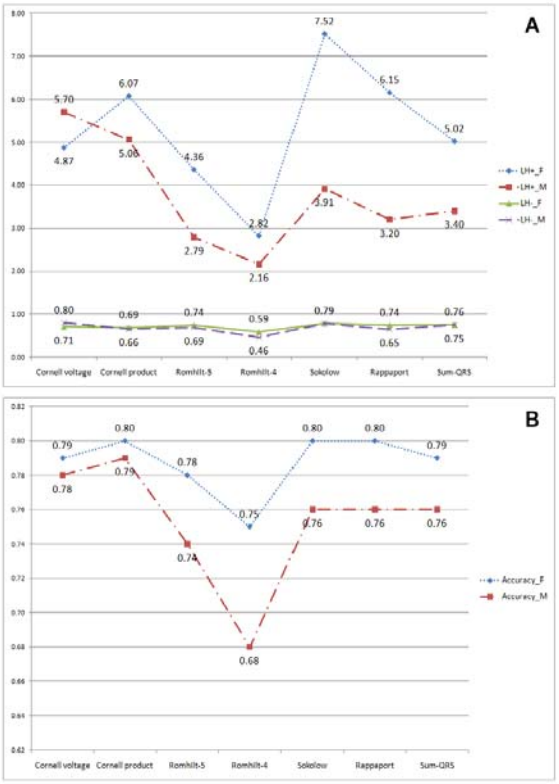

Fig. 2 Positive and negative likelihood ratio (A) and accuracy (B) of different ECG criteria for the diagnosis of LVH in male and female (M = male, F = female, LH = likelihood ratio)

There have been many ECG criteria for the diagnosis of LVH. However, there are little data on the validation of these ECG criteria. In general, ECG diagnosis of LVH had a relatively low sensitivity and high specificity[7,23]. Sokolow-Lyon criteria used the summation of QRS voltage in leads V1, and V5 or V6 for the diagnosis of LVH[10]. Sokolow-Lyon-Rappaport used voltage in V1 or V2 and V5 or V6[11]. Previous report showed that Sokolow-Lyon-Rappaport criteria had a higher sensitivity with lower specificity compared to Sokolow-Lyon criteria[24]. Cornell voltage criteria, through the use of summation of voltage of R wave in lead aVL and S wave in lead V3, has been shown to have a good diagnostic accuracy[13], especially with adjustment for gender[25]. R wave in lead aVL and S wave in lead III has been shown to have prognostic value in hypertensive patients[26]. The accuracy may be improved by the product of voltage and QRS duration[14,27]. Romhilt-Estes criteria calculated point score system from QRS voltage, ST segment pattern, left atrial abnormality, QRS axis, QRS duration and intrinsicoid deflection[12,28]. ST segment and T wave changes may improve the diagnostic yield and prognostic value in patients with LVH[29].

Many studies used postmortem left ventricular mass as the gold standard of LVH[30,31]. However, it is difficult to validate different ECG criteria with the postmortem study. Echocardiography and CMR are non-invasive investigations for the assessment of left ventricular mass[20,32]. Echocardiography is more widely used due to its availability and ease ofuse. Formula for the calculation of left ventricular mass derived from the M-mode image has been developed[17,18,32]. It has been validated with postmortem study to have a good accuracy[31]. 3-D echocardiography can acquire left ventricular mass without the need for ageometric formula[19]. It has been validated to have a better accuracy than 2-D echocardiography with the use of CMR as the gold standard[19]. CMR has many potential advantages over echocardiography especially better image quality and higher reproducibility[20]. In a comparative study of echocardiography and CMR, CMR has been shown to be a more precise and reliable method for the assessment of LVH in hypertensive patients[33]. Study using CMR therefore needs a smaller sample size comparing to echocardiography[20]. LVH assessed by echocardiography or CMR has been shown to be a prognostic marker for the occurrence of cardiovascular events both in patients with hypertension[2,3] and patients suspected of coronary artery disease[34].

Results from the present study confirmed the findings from previous studies that ECG had a low sensitivity (0.25-0.61) and high specificity (0.75-0.95) for the diagnosis of LVH. The overall accuracy was 71 to 80%. Cornell product had the highest accuracy and Romhilt-Estes-at least 4 points- had the lowest accuracy. Romhilt-Estes -at least 4 points-had the highest sensitivity but lowest specificity whereas Sokolow-Lyon had the lowest sensitivity but highest specificity of 0.95. Cornell product had the highest PPV and Romhilt-Estes-at least 4 points-had the highest NPV. Our findings are in agreement with the finding from Bushner et al[21]. Our finding also confirmed findings from previous studies[14,27] that Cornell product can improve sensitivity and PPV compared well with Cornell voltage criteria.

Previous report showed gender differences in left ventricular anatomy[35]. Our findings demonstrated that female had a lower sensitivity, higher specificity, similar NPV, higher PPV, higher positive likelihood ratio, similar negative likelihood ratio and

higher overall accuracy than male. These findings are similar across various ECG criteria. These findings are different from findings from Alfakih et al[36] which showed that Cornell voltage and Cornell product are superior in male whereas Sokolow-Lyon is superior in female. Our findings agreed with reports from Barrios et al who demonstrated that Cornell product had a better diagnostic yield in women[27].

Potential conflicts of interest

None.

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ความแม่นยำของคลื่นไฟฟ้าหัวใจในการวินิจฉัยกล้ามเนื้อหัวใจห้องล่างซ้ายหนาโดยเทียบกับการตรวจหัวใจด้วยสนามแม่เหล็ก

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ภูมิหลัง: *ข้อมูลของความแม่นยำของการตรวจคลื่นไฟฟ้าหัวใจ (ECG) ในการวินิจฉัยภาวะกล้ามเนื้อหัวใจห้องล่างซ้ายหนา (LVH) โดยเปรียบเทียบกับการตรวจคลื่นหัวใจด้วยสนามแม่เหล็ก (MRI) มีจำกัด*

วัตถุประสงค์: *เพื่อศึกษาความแม่นยำของ ECG ในการวินิจฉัย LVH เทียบกับ MRI*

วัสดุและวิธีการ: *ผู้นิพนธ์ศึกษาผู้ป่วยที่ส่งมาตรวจหัวใจด้วย MRI และได้รับการตรวจ ECG ในวันเดียวกัน เกณฑ์ของ LVH จาก ECG ที่ศึกษา คือ Sokolow-Lyon, Sokolow-Lyon-Rappaport, Romhilt-Estes, Cornell voltage, Cornell product และ sum of 12 leads QRS voltage กลุ่มควบคุม 184 คน เกณฑ์การวินิจฉัย LVH ใช้มวลของหัวใจห้องล่างซ้ายเกิน 95 percentile ของกลุ่มควบคุม*

ผลการศึกษา: *มีประชากร 1,882 คน เป็นเพศชาย 994 คน เป็นเพศหญิง 888 คน อายุเฉลี่ย 64.6 ปี 23% ของเพศหญิง และ 25% ของเพศชาย ได้รับการวินิจฉัยว่ามี LVH จาก MRI เกณฑ์ของ ECG มีความไวต่ำ (0.25-0.61) และความจำเพาะสูง (0.75-0.95) ในเพศหญิงเมื่อเทียบกับเพศชายมีความไวต่ำกว่า แต่มีความจำเพาะและความแม่นยำสูงกว่า เกณฑ์ที่ทำให้ความแม่นยำสูงสุดคือ Cornell product เกณฑ์ที่มีความไวสูงสุดคือ Romhilt-Estes (4 points) ส่วนเกณฑ์ Sokolow-Lyon มีความจำเพาะสูงสุด*

สรุป: *เกณฑ์ของ ECG ในการวินิจฉัย LVH มีความไวต่ำ ความจำเพาะสูง ความแม่นยำอยู่ในช่วง 0.71-0.80 เกณฑ์ Cornell product ให้ความแม่นยำสูงสุด*