The Accuracy of Electrocardiographic Criteria for Predicting Left Ventricular Hypertrophy in adult Patients with Systemic Hypertension

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ABSTRACT:

BACKGROUND:

Left ventricular hypertrophy is a significant risk factor for cardiovascular complications such as ischemic heart disease, heart failure, sudden death, atrial fibrillation, and stroke. A proper non-expensive tool is required for detection of this pathology. Different electrocardiographic (ECG) criteria were investigated; however, the results were conflicting regarding the accuracy of these criteria.

OBJECTIVE:

To assess the accuracy of three electrocardiographic criteria in diagnosis of left ventricular hypertrophy in adult patients with hypertension using echocardiography as a reference test.

PATIENTS AND METHODS:

This is a hospital-based cross sectional observational study which included 340 adult patients with a history of hypertension (240 patients with left ventricular hypertrophy and 100 patients without depending on Echocardiographic results). Three electrocardiographic criteria including Sokolow Lyon Voltage, Cornell voltage, and Cornell voltage duration were evaluated for their sensitivity and specificity in detection of left ventricular hypertrophy in those patients.

RESULTS:

Each of older ages (over 50 years) (OR= (OR=6.25, 95%CI=3.75-10.39, p<0.001), male gender (OR=0.58, 95% CI= 0.36-0.93, p= 0.018) and type 2 diabetes mellitus (OR=8.14, 95%CI= 4.04-16.41, p<0.001) were significantly associated with development of left ventricular hypertrophy in patients with hypertension. The sensitivity and specificity of Sokolow Lyon Voltage, Cornell voltage, and Cornell voltage duration were 17.5% and 96%; 13.33% and 97%; and 10% and 98%, respectively.

CONCLUSION:

Older ages, male gender, and type 2 diabetes mellitus can increase the risk of left ventricular hypertrophy in hypertensive patients. All the studied criteria have low sensitivity and high specificity in recognition of the left ventricular hypertrophy in patients with hypertension, with no advantage of definite criterion over the others.

KEYWORDS:Electrocardiographic (ECG) Criteria, Left ventricular hypertrophy (LVH), Hypertension.

INTRODUCTION:

Left ventricular hypertrophy (LVH) is defined as an increase in the mass of the left ventricle in response to a disease state, which can be secondary to an increase in the wall thickness of the left ventricular (LV), an increase in cavity size, or both [1]. LVH is caused by a constantly increased workload on the heart. This predominantly results from a chronic increase in afterload of the left ventricle caused by the hypertension, and also in aortic stenosis.

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Another important cause is increased filling of the left ventricle (ie, diastolic overload), which is the causal mechanism for LVH in the presence of aortic or mitral regurgitation and dilated cardiomyopathy. Ischemic heart disease can also have a role in the pathogenesis of LVH, in an attempt of the normal myocardium to compensate for the ischemic or infarcted tissue [2, 3].

Both casual office blood pressure (BP) readings and 24-hour ambulatory blood pressure monitoring (ABPM) have a direct association with LVM/LVH: the higher BP measured in office, the higher average BP documented during the day and night, or the higher ABPM loads (prevalence

of abnormal elevated BP records), the greater possibility for LVH [4].

A fundamental factor in the development of LVH is myocardial fibrosis which impairs cardiac function, manifested initially as diastolic dysfunction, and with progressive disease systolic dysfunction occurs. Pathophysiologically the myocardial fibrosis appears to be related to the renin-angiotensin-aldosterone system (RAAS). Specifically, in the hypertensive patients the angiotensin II has a profibrotic effect on the myocardium [5, 6].

Detection Methods

Electrocardiography

LVH causes electrocardiographic changes in the QRS complex, the ST segment, and the T wave. QRS changes comprise increased QRS amplitudes usually with prolonged durations, notching or slurring of R waves, left axis deviation, and patterns suggesting intraventricular conduction defects. The most distinctive association is increased amplitude of the QRS complex. R waves in leads I, aVL, V5, and V6 (leads facing the left ventricle) are taller than normal, and S waves in V1 and V2 leads (leads overlying the opposite side of the heart) are deeper than normal [7].

The ST segment could be within normal limit or somewhat elevated in tall R waves leads. In many patients, however, the ST segment is depressed and followed by an inverted T wave in leads I, II, aVL, and V5 -V6. In these cases the depressed ST segment is typically either flat or slopes downward from a depressed J point, and the T wave is asymmetrically inverted. Usually these LVH-related repolarization abnormalities occur in association with QRS changes but may appear alone. Further changes may include prolongation of the QT interval and changes associated with left atrial abnormality [8].

Diagnostic Criteria

According to these ECG abnormalities, many sets of criteria to detect anatomic LVH have been developed.

The reported diagnostic accuracies of these ECG criteria to detect structural LVH are highly variable, differing with the specific criteria tested, the imaging method utilized to detect the anatomical measurements, and the population studied. Most studies, including those relying on cardiac MRI have reported low sensitivity and high specificity. Different studies have reported a median sensitivity for six commonly used criteria ranging from 10.5% to 21% and a median specificity of 89% to 99% [9].

Because of the variability in the accuracy of the various criteria from one trial to another, no single criterion can be established as the preferred method. Accuracy also varies with sex (with women having lower QRS amplitudes than men), race (with African Americans having higher QRS amplitudes than whites), age (increasing age associated with lower voltages), and body habitus (obesity associated with reduced QRS amplitudes) [10].

Although the electrocardiographic criteria characterized by low sensitivities, The clinical importance of ST-T wave abnormalities has been established, for example, the presence of ST-T changes by the Sokolow-Lyon or Cornell voltage criteria among hypertensive patients increased the 5-year risk of heart failure by more than threefold and the risk of heart failure–linked mortality by more than fourfold. In addition, the onset of ST-T changes during the first year of follow-up was associated with a three- to five-fold increase in clinical events [11].

Echocardiography

Assessment of the left ventricular mass by cardiovascular magnetic resonance imaging (CMR) is more precise and reproducible than echocardiography, but the last modality has lower cost and is a more accessible test compared with CMR. Echocardiography is an imaging technique that creates pictures of the heart utilizing high-frequency ultrasound waves. Echocardiography, whether it is two-dimensional, three-dimensional, or M-mode, is used to evaluate target organ damage (TOD) and measure LVM. Echocardiographic studies find out the myocardial volume by subtracting the left ventricular cavity volume from the volume of the correspondent epicardium. When the myocardial volume obtained, multiplication by the myocardial density results in the LVM [12]. The LVM can then be indexed to body surface area, or height$^{2.7}$ to assess LVH. One of the difficulties in assessing LVH by echocardiography is accurately finding the limit between the cardiac blood pool and the endocardium [13]. If this step was improper (due to, for example, poor acoustic window, or excessive fat tissue in the chest), there would be incorrect assessment of the LV cavity volume and the epicardial volume, leading to imprecise measurement of myocardial volumes when performing calculations and thus, incorrect LVM

and LVH indicators. According to a study by Havranek et al, an adult with a LVM index ≥51 g/$m^{2.7}$ is considered to have LVH, this study showed that LVMI above this threshold is associated with more than four times increased risk of morbidity and mortality [14], so left ventricular mass must be indexed to normalize the relationship without neglecting obesity.

Foster et al. revealed that normalizing LVM to the body surface area or to the height results in either underestimation or overestimation of LVM, respectively [15], so they suggested using lean body mass (LBM) as the ideal scaling variable for normalization.

Three-dimensional echocardiography was also employed to estimate LVM and allows for LVM estimation using the same principles used in CMR. LVM is determined by taking the difference between epicardial and endocardial volumes and may better account for ventricular morphology. Using three-dimensional echocardiography to quantify LVM has been shown to be used in the adult group, but remains limited in pediatrics at this time [16].

PATIENTS AND METHODS:

Setting and Design

This is a hospital-based cross sectional observational study which was conducted at Baghdad Teaching Hospital/ Echocardiography department. The study involved a total of 240 adults aged 18 years and older for an interval ranged from March/ 2019 till March/ 2020. All patients had systemic hypertension and had left ventricular hypertrophy based on echocardiographic criteria. One-hundred patients with hypertension and without LVH by echocardiography were included as a control group.

Patients included had the criteria of being ≥ 18-year-old; with history of hypertension on treatment or with blood pressure of ≥140 mmHg systole and/or ≥ 90 mmHg diastole.

Athletics patients and patients with congenital heart disease, hypertrophic obstructive cardiomyopathy, amyloidosis, valvular heart disease, ischemic heart disease, right ventricular hypertrophy, sinus node diseases, dilatation or aneurysm of left ventricle, Wolff-Parkinson White syndrome ,ventricular or supraventricular tachycardias or conduction abnormalities, and patients with ECG or echocardiography of inadequate technical quality had been excluded from this study.

Ethical consideration

A written consent from each participant was obtained prior to data collection after explaining the aim of study. Each patient was given the complete unconditioned choice to withdraw anytime. The confidentiality of data throughout the study was guaranteed and the patients were assured that data will be used for research purpose only.

Echocardiography

Transthoracic echocardiography (using Vivid S6/ USA) was performed by experienced echocardiographer with the patient in a partial left lateral decubitus position. The American Society of Echocardiography guidelines [17] were adopted in all measurements and calculation . For obtaining the left ventricular end-diastolic and end-systolic measurements, the long axis view was used. Frames with optimal visualization of interfaces and having concurrent imagining of the septum, left ventricular internal diameter, and posterior wall were used.

Devereux formula was used to calculate left ventricular mass as following:

Left ventricular mass (g) = 0.8 × {1.04× [(septal thickness+ internal diameter+ posterior wall thickness) 3-(internal diameter)3)]} +0.6g. Then the resulted number was indexed based on body surface area.

According to Echocardiographic features, LVH defined as LVM index >125 g/m^2 in male subjects or >110 g/m^2 in female subjects [18].

Electrocardiography

ECGs had been registered using (MAC1600/USA) using standard calibrations. The following criteria were applied to all ECG records to define LVH by ECG as follows :

Sokolow-Lyon Voltage Criteria: SV1 + RV5 > 3.5 mV, RaVL > 1.1 mV.

Cornell voltage criteria: SV3 + RaVL > 2.8 mV (for men) and SV3 + RaVL > 2.0 mV (for women).

Cornell voltage duration: QRS duration × Cornell voltage > 2436 mm-sec. [7]

Data Collection

Each participant was subjected to clinical examination after taking the sufficient history. Data including age, sex, weight, height, co-morbidities such as diabetes mellitus (DM) and chronic obstructive pulmonary diseases (COPD), systolic and diastolic pressure, heart rate, and the body surface area were obtained through direct interview.

The following formula was used to calculate the body surface area:
Body surface area BSA $^{(m2)}$ = 0.007184 × (weight in kg) 0.425 × (height in cm) 0.725
Blood pressure measurement was obtained according to the of European Society recommendations for Hypertension using well calibrated mercurial sphygmomanometers [19].

RESULTS:

Demographic and Clinical Characteristics of Study Population

The mean age of the participants was 54.71±13.6 years (range 18 to 85 years), among whom 190(55.88%) were males and 150(44.12%) were females (Table 1).

About one-fourth of the participants were ex/current smokers. Diabetes mellitus was reported in a total of 124 subjects (36.47%). The mean BMI and BSA were 32.4±6.2 kg/m^2 and 1.935±0.47m^2 respectively (Table 1).
Three factors showed significant association with the presence of LVH. Patients with LVH had a significantly higher mean age than non LVH patients (58.24±13.81 years versus 43.06±14.7 years). Likewise, male sex was more frequent among patients than controls (60% versus 46%). Finally, the frequency of type-2 DM was much higher in patients (47.5%) than non LVH patients (10%) as shown in table 1. Although mean BMI and BSA were higher in patients than controls, the difference was not statistically significant.

Table 1: Demographic and clinical risk factors for left ventricular hypertrophy in patients with hypertension.

Variables	Total (n=340)	Patients with LVH (n=240)	Patients without LVH (n=100)	P-value
Age (years)	54.71±13.6	58.24±13.81	43.06±14.7	0.029
Sex	190 (55.88%)	144 (60%)	46 (46%)	0.018
Male				
Female	150 (44.12%)	96 (40%)	54 (54%)	
Diabetes Mellitus	216 (63.53%)	126 (52.5%)	90 (90%)	<0.001
No				
Yes	124 (36.47%)	114 (47.5%)	10 (10%)	
Smoking	226(63.53%)	179(74.58%)	78 (78%)	0.504
Never				
Ex/current Smoker	124 (36.47%)	61(25.42%)	22(22%)	
BMI (Kg/m^2)	32.4±6.2	32.8±3.81	31.2±6.6	0.122
BSA (m^2)	1.935±0.47	1.94±0.5	1.92±0.4	0.152

Predictors of Left Ventricular Hypertrophy

Risk factors which showed significant association with LVH were entered into logistic regression model to find out their predictive power for LVH. The results are shown in table 2. Out of 240 patients with LVH, 185 patients (77.08%) were older than 50 years compared with 35% controls who were older than 50 years (OR=6.25, 95%CI=3.75-10.39, p<0.001). In contrast, female sex have lower incidence of LVH (OR=0.58, 95% CI= 0.36-0.93, p= 0.018). However, the most powerful predictor in this study was DM (OR=8.14, 95%= 4.04-16.41, p<0.001).

Table 2: Predictors of left ventricular hypertrophy.

Variables	Patients with LVH(n=240)	Patients without LVH (n=100)	P-value	OR (95% CI)
Age (years)	55(22.92%)	65(65%)	<0.001	1.0
≤ 50				6.25(3.75-10.39)
>50	185(77.08%)	35(35%)		
Sex	144(60%)	46(46%)	0.018	1.0
Male				0.58(0.36-0.93)
Female	96(40%)	54(54%)		
Diabetes Mellitus	126(52.5%)	90(90%)	<0.001	1.0
No				8.14(4.04-16.41)
Yes	114(47.5%)	10(10%)		

Assessment of Different ECG Criteria in Detection of LVH

Sokolow-Lyon Voltage Criteria

In this study, out of these 240 patients with evidence of LVH, Sokolow-Lyon voltage criteria detected 42 patients. On the other hand, only 4 control subjects were positive for this criterion. Accordingly, the sensitivity and specificity of Sokolow-Lyon Voltage are 17.5% and 96%, respectively. The positive and negative predictive values were 91.3% and 32.6%, respectively (Table 3).

Table 3: Sensitivity and specificity of Sokolow-Lyon Voltage criteria in detection of LVH.

		Echo		Total
		Positive	Negative	
ECG	Positive	42	4	46
	Negative	198	96	284
	Total	240	100	340

Sensitivity = 42/(42+198) X 100 = 17.5%.
Specificity= 96/ (96+4) X 100 = 96%.
Positive predictive value= 42(42+4) X 100 = 91.3%.
Negative predictive value= 96/(96+198)X100= 32.6%.

Cornell Voltage Duration Criteria

According to this criterion, 24 (out of 240 of patients) were positive for LVH, while 2 subjects (out of 100 controls) were positive for LVH in this criterion (Table 4). Thus, the sensitivity and specificity of the criterion were 10% and 98% respectively. The positive and negative predictive values were 96% and 31.21%, respectively.

Table 4: Sensitivity and specificity of Cornell voltage duration criteria in detection of LVH.

		Echo		Total
		Positive	Negative	
ECG	Positive	24	2	26
	Negative	216	98	314
	Total	240	100	340

Sensitivity= 24/ (24+216) X 100 = 10%.
Specificity = 98/ (98+2) X 100 = 98%.
Positive predictive value= 24/ (24+2) X 100 = 96%.
Negative predictive value= 98/ (98+216) X100= 31.21%.

Cornell Voltage Criteria

In this criterion, 32 out of 240 patients were positive for LVH, while 3 subjects among controls were also positive. The sensitivity and specificity of the criterion were 13.33% and 97% respectively. The positive predictive value was 91.43% and negative predictive value was 31.8% (Table 5).

Table 5: Sensitivity and specificity of Cornell Voltage criteria in detection of LVH.

		Echo		Total
		Positive	Negative	
ECG	Positive	32	3	35
	Negative	208	97	305
	Total	240	100	340

Sensitivity = 32/ (32+208) X 100 = 13.33%.
Specificity = 97/ (97+3) X 100 = 97%.
Positive predictive value= 32/(32+3)X 100 = 91.43%.
Negative predictive value= 97/(97+208)X100= 31.8%.

DISCUSSION:

Predictors of Left Ventricular Hypertrophy (LVH)

The present study revealed that only 3 out of 6 demographic and clinical risk factors significantly associated with the incidence of LVH. The first risk factor was the age where older age (>50 years) patients were more prone for LVH (OR=6.25, 95%CI= 3.75-10.39, p< 0.001). This implies that hypertensive patients older than 50 years will be at 6.25-time greater risk to have LVH compared with hypertensive patients with younger ages. In a Spanish study, Lazano et al. [20] assessed 15798 patients with hypertension to establish the prevalence of LVH in those patients. Multivariate analysis showed that LVH was associated in an independent manner with older ages. In another study, Gredts et al. [21] assessed 560 Norwegian hypertensive patients for LVH. At baseline assessment, patients with older age (>65 years) displayed greater pulse pressure, LV mass, and prevalence of concentric hypertrophy than younger patients. This propensity may be elucidated by the extended period that elderly patients experiencing hypertension which ultimately increases the load of left ventricle and causes LVH .

The second risk factor for LVH in the present study was male gender (OR= 0.58, 95%CI= 0.36-0.93, p=0.018). This implies that female gender can reduce the risk of LVH to about a half. Internationally, two large studies addressed this issue with conflicting results. The first one, the Losartan Intervention for Endpoint reduction in hypertension (LIFE) trial performed on 177 female patients and 242 male patients. The incident of cardiovascular death, stroke, LVH and MI was lower in women than in men [22] .

The other study involved 12329 hypertensive patients who were followed for a median of about 4 years. Left ventricular hypertrophy was more common in women than in men (43.4 vs. 32.1%, p<0.01). Furthermore, women had higher left ventricular ejection function than men irrespective of presence of LVH [23].

In between, Ruebner et al. [24] did not find a significant effect of sex on LVH among USA patients .

The inconsistent results are possibly clarified by differences in the characteristics of the study population and the differences in criteria that were used for sex-specific cut off values of LV mass index .

It is well stated that women in general have a lifetime lower incidence of cardiovascular illness compared with men. The prevalence of subclinical cardiac damage such as LVH is more common amongst hypertensive women than men [25]. This may be explained at least in part by the greater impact of visceral lipid mass on LV mass and geometry in women than men. This was evident in studies that used either echocardiography or cardiac MRI [26] .

Under pressure overload (PO), women are more predisposed to develop concentric hypertrophy involving thickening of the LV wall owing to sarcomeres addition and an upturn in myocyte width. Men are more likely to have eccentric hypertrophy with less thick ventricular walls and greater cavities because of addition of sarcomeres. Sex variation in cardiac pathology is most

commonly observed in elderly patients suffering from aortic stenosis. Women usually have a more concentric type of hypertrophy associated with relatively small diameters of ventricle as well as less ventricular dilatation and better systolic ventricular contraction as compared with men [27]. As age progresses, the left ventricular mass as well as arterial stiffness increases. This was noted in both sexes. However, it is more obvious in female patients, particularly in the postmenopausal years [28] .

The last risk factor which was significantly associated with LVH in the present study was DM (OR=8.14,95%= 4.04-16.41, p<0.001) which implies that diabetic patients will be at 8.14-fold higher risk for developing LVH compared to non-diabetic patients. A large number of previous studies were in accordance with this result. In an American study [29], a total of 1932 hypertensive patients (443 DM and 1489 non-DM) were investigated for LVH. The LV mass (189±60g vs. 174±59g; p<0.001), body mass index, and systolic blood pressure were higher in the DM group than in the non-DM group. Furthermore, the multivariate analysis revealed that type 2 diabetes mellitus (T2DM) can be an independent factor that is associated with increased LV mass (P=0.03), with a significantly association between T2DM and increased risk of LVH (OR= 1.46; 95%CI, 1.13–1.88, P=0.004).

In a Japanese study, the LVH was evaluated in 400 uncomplicated hypertensive patients and compared between diabetic (n =161) and nondiabetic (n= 239) patients. Patients with diabetes had higher relative ventricular wall thickness (0.50 v 0.44, P<0.001) and higher prevalence of concentric LV hypertrophy (39.4% v 26.8%, P< 0.001) than nondiabetic patients. The presence of diabetes increases the OR by 2.76 (95%CI=1.73– 4.41, P< 0.001) [30]. Almost similar results were obtained by some other studies [31, 32].

The effect of T2DM on left ventricular mass may at least be partly elucidated by its interaction with central obesity. It may be explained by the possible direct effects of different types of adipocytokines contained in visceral fat on LV mass [33].

Assessment of Different ECG Criteria in Detection of LVH

Sokolow-Lyon Voltage Criteria

According to the outcome of the available study, the sensitivity and specificity of Sokolow-Lyon Voltage in detection of LVH in hypertensive patients were 17.5% and 96%, respectively, with 91.3% PPV and 32.6% NPV. In a similar recent Brazilian study, Burgos et al. [34] assessed this criterion in 2240 patients with hypertension. The recorded sensitivity was 22.2% and specificity was 88.3%, while a higher sensitivity (58.62%) and lower specificity (60.66%) were noted by Ogunlade et al. [35] among Nigerian study with hypertensive patients .

Elffers et al. [36] included 1091 participants of the Netherlands Epidemiology of Obesity Study (NEO) who underwent cardiac echocardiography and demonstrated almost similar sensitivity (16%) and lower specificity (90%). Furthermore, a systematic review of 21 studies and data on 5608 patients showed that in primary care settings, sensitivity of Sokolow–Lyon voltage criteria ranged from 8 to 40% and specificities ranged from 53 to 100%. These facts signify the relatively low sensitivity and high specificity of this criterion in detection of LVH [37] .

Cornell Voltage Criteria

The present study reveals that the sensitivity and specificity of this criterion were 13.33% and 97% respectively. The positive and negative PV were 91.43% and 31.8%, respectively. In accordance with this result is the study of Elffers et al. [36] who revealed 28% sensitivity and 90% specificity for this criterion.

A much better result was suggested by Casale et al. [38], who recorded a sensitivity of 41% and a specificity of 98% for this criterion among American patients. The authors interpreted high performance by the actuality that the increased ventricular mass directs the electric forces both horizontally (corresponding to the R wave in aVL) and posteriorly (S wave in V3). In addition, the V3 lead is closer to the left ventricle and is probably less influenced by variations in the distance between the myocardium and the leads.

Cornell Voltage Duration Criteria

The sensitivity and specificity of the criterion in the present study were 10% and 98% respectively, with PPV of 96% and NPV of 31.21% .

In a Dutch study, Buchner et al. [39] employed 120 patients with LHV and 30 healthy volunteers to evaluate different ECG criteria including Cornell duration in diagnosis of LVH. The sensitivity, specificity, PPV and NPV of this criterion were

found to be 56%, 87%, 96% and 48% respectively. In the Elffers's study the sensitivity was 25% and the specificity was 90% [39].

Thus, it is obvious that none of these criteria could be used as a reliable diagnostic tool for detection of LVH. Moreover, all these criteria have high specificity and PPV with low sensitivity and NPV which indicate their association with different cardiac pathologies rather than only LVH .

CONCLUSION:

Older ages (over 50 years), male gender, and T2DM are associated with the development of LVH in hypertensive patients. All included criteria have low sensitivity and high specificity in detection of LVH in hypertensive patients, with no advantage of certain criterion over the other criteria. It is recommended to use echocardiography for detection of LVH in high-risk hypertensive patients and study the sensitivity and specificity of a combination of two or more ECG criteria compared with echocardiography.

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