

ORIGINAL ARTICLE

Evaluating the performance of electrocardiography and immunological markers (IL-6, TNF- α , and C-Reactive protein) in the diagnosis of left ventricular hypertrophy using echocardiography as the gold standard

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ABSTRACT

Aim: To evaluate the diagnostic performance of ECG criteria and inflammatory markers—interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and C-reactive protein (CRP)—in detecting LVH.

Materials and Methods: A total of 241 patients with concentric LVH confirmed by ECHO were included and categorised into ECG-positive and ECG-negative groups. Additionally, 50 age-matched controls without LVH were recruited. The diagnostic performance of Sokolow–Lyon, Cornell voltage, and Peguero–Lo Presti ECG criteria was assessed using sensitivity, specificity, and accuracy. Serum levels of IL-6, TNF- α , and CRP were analysed across different levels of left ventricular mass index (LVMI).

Results: Significant differences were observed between ECG groups in interventricular septal thickness, left ventricular diameter, and LVMI ($p < 0.05$). ECG criteria demonstrated low sensitivity (10.37%–20.75%) but high specificity (up to 100%), with limited overall accuracy. In contrast, IL-6, TNF- α , and CRP levels were significantly elevated in patients with severe LVH ($p < 0.001$).

Conclusions: ECG criteria show high specificity but limited sensitivity in diagnosing LVH. Elevated inflammatory markers correlate strongly with disease severity, suggesting their potential role in improving diagnostic accuracy.

KEY WORDS: IL-6, TNF- α , Echocardiography, Electrocardiography, left ventricular hypertrophy (LVH), and C-Reactive Protein

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INTRODUCTION

Left ventricular hypertrophy (LVH) is a cardiac condition characterized by an increase in the size and mass of the left ventricle, often resulting from chronic pressure overload due to hypertension, aortic stenosis or other cardiovascular disease. The presence of LVH is associated with increases risk of adverse cardiovascular outcomes, including heart failure, arrhythmias and sudden cardiac death [1]. Early and accurate diagnosis of LVH is crucial for timely intervention and managing event of the underlying causes, hence diagnosis of LVH has become a vital area of research in the field of cardiology [2]. Electrocardiography (ECG) is a widely used, non-invasive tool for the initial assessment of LVH. Over the years, different criteria have been developed for the identification of LVH on ECG, these include

Sokolow–Lyon voltage criteria, the Cornell voltage criteria and the Romhilt–Estes score [3]. Age, sex, and BMI can affect the accuracy of LVH criteria, which vary in sensitivity and specificity [4, 5]. Although ECG is widely used to diagnose LVH, echocardiography (ECHO) remains the gold standard because it directly assesses cardiac structure and function. Therefore, comparing different ECG criteria with ECHO findings is important to improve diagnostic accuracy [6]. The Sokolow–Lyon criteria, based on the S wave in V1 and the R wave in V5 or V6, have been widely studied [7]. In a meta-analysis, You et al. (2020) [8] found that the Sokolow–Lyon criteria have a sensitivity of 50–70% and a specificity of 70–80% for detecting LVH when compared to ECHO. The Cornell criteria including QRS voltage and duration have higher sensitivity but may have lower specificity

in some populations [8]. The Romhilt-Estes score, which includes various ECG findings and clinical factors and may improve diagnostic accuracy but requires a more complex scoring system [9]. On the other hand, ECHO provides a more complete assessment of the LVH by measuring the thickness and mass of the left ventricle. LVH was defined according to the American Society of Echocardiography as left ventricular mass index (LVMI) >115 g/m² in men and >95 g/m² in women [10]. However, although ECHO is the gold standard, its cost and limited availability in some settings highlight the need for reliable ECG criteria that can be easily used in routine practice [11]. Several immunological markers have been found to be associated with LVH, indicating that inflammation is also involved in heart remodeling. These include IL-6, TNF- α , and CRP, which have been implicated in left ventricular hypertrophy, diastolic dysfunction, and other cardiovascular conditions [12, 13]. Also, CRP is a known marker of systemic inflammation and has been linked with LVH and other adverse cardiovascular events [14]. These results imply that inflammation markers can be used not only for diagnostic purposes but also as predictors in LVH patients. Understanding how they interact with LVH could help us better understand the pathophysiology of LVH and develop new treatment targets. In this study, the diagnostic ability of the three voltage criteria, namely Peguero-Lo Presti, Sokolow-Lyon, and Cornell criteria in LVH, is evaluated based on ECHO test, which is the gold standard for the diagnosis of LVH. The factors involved in assessing the diagnostic ability of the three voltage criteria include sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

AIM

To evaluate the diagnostic performance of ECG criteria and inflammatory markers—interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and C-reactive protein (CRP)—in detecting LVH.

MATERIALS AND METHODS

This study employs a cross-sectional and retrospective design that examines medical files of patients referred to Al-Hussain Medical City in Kerbala. The Pulmonology and Cardiology Department supplied the patient records, which had information on demographics, body mass index (BMI), smoking habits, and chronic disease history and medication. The Research and Ethics Committee of Al-Hussain Medical City and the college of Medicine at the University of Kerbala granted approval for the study, and informed consent was obtained from

the participants. All patient information was kept confidential and managed by the researchers.

STUDY POPULATION

A total of 241 patients diagnosed with concentric LVH via ECHO analysis were selected for the study. Additionally, 50 age-matched participants without LVH, confirmed through ECHO, were recruited as the control group. All participants underwent ECG evaluations after which they were categorized into two groups: (1) those with positive ECG findings for LVH and (2) those with negative ECG results. The inclusion criteria required that patients had an ECHO conducted within three months prior to the ECG. Only adults 20 years and older, as defined by the World Health Organization (WHO), were included. Patients were excluded if they had LVH due to congenital conditions, factors that could prevent appropriate LVH analysis (like left bundle branch block), deposition diseases, incomplete or inadequate medical records or if they were under the age of 20 years of age.

ECHOCARDIOGRAPHIC EVALUATION

The ECHO assessment included measuring the left ventricular diastolic diameter (LVDD), interventricular septal thickness (IVST), posterior wall thickness (PWT), and ejection fraction (EF). These metrics were used to identify the geometric pattern of the left ventricle based on the formulas proposed by Devereux et al [15]. The left ventricular mass calculation was performed using the formula.

The cut-off values for classifying LVH based on left ventricular mass index (LVMI) were set at 95 g/m² for women and 115 g/m² for men [10]. All ECHO tests were conducted using GE Vivid E9 BT12 Ultrasound System, (USA). For the classification of LVH into mildly, moderately, or severely increased LVMI, the following criteria were utilized (Table 1).

ELECTROCARDIOGRAPHIC EVALUATION

The performance of ECG is according to international standards using graph paper, a thermosensitive machine set to 25 mm/s, and an amplitude of 10 mm/mV, included 12 leads (aVF, aVR, aVL, DI, DII, DIII, V1, V2, V3, V4, V5, and V6). The ECGs of all 241 patients and 50 participants of the control group were evaluated to calculate the ECG criteria for LVH. The diagnostic criteria employed included: (1) Sokolow-Lyon criterion ($SV1 + RV5$ or $V6 \geq 35$ mV) [7]; (2) Cornell voltage criterion ($RaVL + SV3 \geq 20$ mV for women and ≥ 28 mV for men) [16]; and (3) Peguero-Lo Presti criterion (deeper S + $SV4 \geq 2.3$ mV in women and ≥ 2.8 mV in men) [17].

Table 1. LVMI classification (g/m²)

Classification	Males (g/m ²)	Females (g/m ²)
Normal	< 115	< 95
Mildly Increased	115 – 130	95 – 105
Moderately Increased	131 – 149	106 – 120
Severely Increased	≥ 150	≥ 120

Source: compiled by the authors of this study

Table 2. General features of the patients with LVH by ECHO and positive ECG

	LVH (ECHO) - Positive ECG			
	All	Male	Female	p-value
	(n = 93)	(n = 44)	(n = 49)	
Age, years (mean±SD)	56.06±13.59	55.07±14.41	56.96±12.91	0.253
BMI Categories, n (%)				
Underweight	2 (2.2)	2 (4.5)	0 (0)	0.061
Normal	35 (37.6)	19 (43.2)	16 (32.7)	
Overweight	28 (30.1)	16 (36.4)	12 (24.5)	
Obese	28 (30.1)	7 (15.9)	21 (42.9)	
Smoking status, n (%)				
Smokers	22 (23.7)	17 (38.6)	5 (10.2)	0.001*
Non-smokers	71 (76.3)	27 (61.4)	44 (89.8)	
Chronic Disease, n (%)				
Yes	85 (91.4)	39 (88.6)	46 (93.9)	0.368
No	8 (8.6)	5 (11.4)	3 (6.1)	
Medication, n (%)				
No	30 (32.3)	19 (43.2)	11 (22.4)	0.033
Yes	63 (67.7)	25 (56.8)	38 (77.6)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index

*Statistical significance at $p < 0.05$

Source: compiled by the authors of this study

SERUM CYTOKINE ANALYSIS

Blood samples were drawn for all the participants using anticoagulant free vacutainers were allowed rest at room temperature for 15 – 30 minutes. Serum was prepared by centrifugating the blood samples at 10000 g for 10 minutes after that the supernatant was transferred into Eppendorf tubes and stored at -70 °C, thawed under standardized conditions simultaneously. Serum levels of TNF- α , IL-6, and CRP were measured using commercial ELISA kits: the human TNF-alpha ELISA kit (CytImmune Sciences Inc., Rockville, MD), the human IL-6 ELISA kit (Cell Sciences Inc., Canton, MA), and the Human C-Reactive Protein ELISA Kit (CRP) from Sigma-Aldrich (Massachusetts, United States), adhering to the manufacturers' protocols.

STATISTICAL ANALYSIS

Descriptive statistics regarding age, sex, smoking status, presence of chronic diseases, use of medication and the incidence of LVH were analyzed using the Shapiro-Wilk test to examine normality, followed by the Chi-Squared test. One way ANOVA test and Kruskal Wallis test was used to determine statistical significance between the study groups with respect to ECHO findings, serum cytokine levels respectively. For each ECG criterion in the study, sensitivity, specificity, PPV, NPV, and accuracy were assessed in three contexts: mildly increased LVMI, moderately increased LVMI, and severely increased LVMI, utilizing IBM SPSS Statistics v.25.0 (IBM Corporation, Armonk, New York). Statistical significance was set at $p < 0.05$.

Table 3. Patients with negative ECG

	LVH (ECHO) - Negative ECG			
	All	Male	Female	p-value
	(n = 148)	(n = 57)	(n = 91)	
Age, years (mean±SD)	57.18±10.37	58.49±11.08	56.34±9.78	0.109
BMI Categories, n (%)				
Underweight	0 (0)	0 (0)	0 (0)	
Normal	71 (48.0)	35 (61.4)	36 (39.6)	0.016*
Overweight	36 (24.3)	13 (22.8)	23 (25.3)	
Obese	41 (27.7)	9 (15.8)	32 (35.2)	
Smoking status, n (%)				
Smokers	39 (26.4)	22 (38.6)	17 (18.7)	0.007*
Non-smokers	109 (73.6)	35 (61.4)	74 (81.3)	
Chronic Disease, n (%)				
Yes	116 (78.4)	40 (70.2)	76 (83.5)	0.055
No	32 (21.6)	17 (29.8)	15 (16.5)	
Medication, n (%)				
No	60 (40.5)	30 (52.6)	30 (33.0)	0.018*
Yes	88 (59.5)	27 (47.4)	61 (67.0)	

General features of the patients with LVH by ECHO but negative ECG, LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index

*Statistical significance at p < 0.05

Source: compiled by the authors of this study

ETHICS

This work complies with the principles of the Declaration of Helsinki.

AI STATEMENT

The author states that no AI tools were used in writing this article.

RESULTS

GENERAL CHARACTERISTICS SUBJECTS

Out of the 241 patients included in the study, 93 (38.6%) showed positive ECG outcome, while the remaining 148 patients (61.4%) had negative ECG result. Table 2 shows the general features of the patients with positive ECG which comprised of 44 males and 49 females with the mean age of 55.07±14.41 years and 56.96±12.91 years respectively. Table 3 shows the general features of the patients with negative ECG which comprised of 57

males and 91 females with the mean age of 58.49±11.08 years and 56.34±9.78 years respectively. The general features if the 50 participants that constitute the control group is presented in Table 4. The comprised of 23 males and 27 females, with the mean age of 53.95±8.37 years and 57.55±14.82 years respectively. Table 5 however, shows the distribution of the study participants with respect to the presence of chronic disease(s).

ECHOCARDIOGRAPHIC PARAMETERS OF THE LVH PATIENTS

The ECHO parameters comparing patients with LVH, categorized based on their ECG results is presented in Table 6. In patients with positive ECG findings for LVH, the IVST was 14.09±1.89 mm, which was slightly lower in those with negative ECG results, i.e. 13.65±1.64 mm. The difference is statistically significant with a p-value of 0.027. For PWT, LVH patients with positive had a mean value of 14.09±1.62 mm, compared to 13.92±1.87 mm in the negative ECG group; however, this difference did

Table 4. General features of the non-LVH participants

Control group				
	All	Male	Female	p-value
	(n = 50)	(n = 23)	(n = 27)	
Age, years (mean±SD)	55.23±11.27	53.95±8.37	57.55±14.82	1.153
BMI Categories, n (%)				
Underweight	2 (4.0)	0 (0)	2 (7.4)	0.178
Normal	29 (58.0)	12 (52.2)	17 (63.0)	
Overweight	15 (30.0)	10 (43.5)	5 (18.5)	
Obese	4 (8.0)	1 (4.3)	3 (11.1)	
Smoking status, n (%)				
Smokers	11 (22.0)	8 (34.8)	3 (11.1)	0.044*
Non-smokers	39 (78.0)	15 (65.2)	24 (88.9)	
Chronic Disease, n (%)				
Yes	8 (16.0)	3 (13.0)	5 (18.5)	0.599
No	42 (84.0)	20 (87.0)	22 (81.5)	
Medication, n (%)				
No	44 (88.0)	22 (95.65)	22 (81.5)	0.124
Yes	6 (12.0)	1 (4.35)	5 (18.5)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; BMI: body mass index

*Statistical significance at $p < 0.05$

Source: compiled by the authors of this study

not reach statistical significance. The LVDD was greater in the positive ECG group, (44.75 $\pm$ 4.98 mm) versus the negative ECG group (43.39 $\pm$ 5.51 mm), with a p-value of 0.026, indicating a statistically significant difference at $p < 0.05$. The EF was similar between the two groups with the positive ECG group and negative ECG group having an EF value of 67.00 $\pm$ 6.87% and 66.90 $\pm$ 5.82%, respectively. The LVMI was significantly higher in patients with positive ECG findings (134.82 $\pm$ 26.19 g/m²) compared to those with negative ECG result 124.42 $\pm$ 23.50 g/m²), ($p = 0.001$). Regarding diastolic function, the majority of both groups exhibited diastolic dysfunction with 91.4% of the positive ECG group and 90.4% of the negative ECG group reporting the condition. The proportion of participant with normal diastolic function was low in both groups (8.6% in positive ECG and 9.6% in negative ECG), and this difference was not statistically significant (0.961).

DIAGNOSTIC PERFORMANCE OF THE ECG CRITERIA

Diagnostic performance of the ECG criteria was described in Table 6.

Table 7 shows the performance of each ECG criteria in the assessment of concentric LVH as well as the different categories of LVH based on sensitivity, specificity, PPV, NPV and accuracy. In diagnosis of concentric LVH (Table 7A), Sokolow-Lyon criteria showed a sensitivity of 13.69% and perfect specificity of 100%. The PPV was also 100%, while NPV was 19.38%, resulting to an overall accuracy of 28.52%. Cornell criteria exhibited a sensitivity of 10.37%, specificity of 92%, with a PPV of 86.21%, an NPV of 17.55% and an accuracy of 24.4%. Peguero-Lo Presti criteria presented a higher sensitivity of 20.75%, an 86% specificity, a PPV of 87.72%, an NPV of 18.37%, and an accuracy of 31.96%.

Regarding diagnosis of mildly increased LVMI (Table 7B), Sokolow-Lyon sensitivity was 10.09% with 100% specificity, a PPV of 100%, NPV of 33.78%, and accuracy of 38.36%. The Cornell criteria indicated a sensitivity of 9.34%, 88.46% specificity, a PPV of 62.5%, an NPV of 32.17%, and an accuracy of 35.22%. Peguero-Lo Presti showed a sensitivity of 18.35%, specificity of 88%, a PPV of 76.9%, an NPV of 33.08%, and an accuracy rate of 40.25%.

Table 5. Distribution of the study subjects with respect to presence of chronic diseases

	Positive ECG (n = 85)	Negative ECG (n = 116)	Control (n = 8)
Hypertension (HT)	47	49	0
Diabetes (DM)	9	9	0
Cardiovascular accident (CVA)	0	1	3
Cancer (breast)	0	2	0
Asthma	0	0	0
Rheumatoid arthritis	0	0	2
Hypothyroidism	0	5	2
Systemic lupus erythematosus	0	1	0
Valvular heart disease	2	0	1
HT + DM	16	40	0
HT + CKD	3	2	0
HT + CVA	1	0	0
HT + Hypothyroidism	0	1	0
HT + Hyperthyroidism	1	0	0
HT + Hyperlipidemia	1	0	0
HT + Rheumatoid arthritis	0	1	0
HT + DM + CKD	1	1	0
HT + DM + CVA	1	1	0
HT + DM + Asthma	0	1	0
HT + DM + Hypothyroidism	0	1	0
HT + CVA + Cancer (Non-Hodgkin lymphoma)	1	0	0
HT + DM + Cancer (pancreas)	1	0	0
HT + DM + Cancer (breast)	1	0	0
HT + DM + CVA + Hypothyroidism	0	1	0

Source: compiled by the authors of this study

In the assessment of moderately increased LVMI (Table 6C), Sokolow-Lyon with the sensitivity of 12.72%, maintained a 100% specificity, a PPV of 100%, an NPV of 51.02%, and an accuracy of 54.29%. While for Cornell, the sensitivity dropped to 5.45%, specificity remained high at 92%, PPV was 42.86%, NPV was 46.94%, resulting in an accuracy of 46.67%. The Peguero-Lo Presti demonstrated a sensitivity of 20.83%, specificity at 85.96%, a PPV of 55.56%, an NPV of 56.32%, and an accuracy of 56.19%.

In diagnosis of severely increased LVMI (Table 7D), Sokolow-Lyon criteria indicated a sensitivity of 19.74% with 100% specificity, PPV of 100%, NPV of 45.5%, leading to an accuracy of 54.59%. Cornell showed a sensitivity of 14.47%, specificity of 90%, PPV of 68.75%, NPV of 40.91%, and an accuracy of 44.44%. Lastly, Peguero-Lo Presti criteria reported a sensitivity of 26.32%, specificity of 76%, a PPV of 62.5%, an NPV of 40.43%, yielding an accuracy of 46.03%.

SERUM LEVELS OF INFLAMMATORY MARKERS IN RELATION TO CATEGORIES OF LVH

Fig. 1 is the graphical presentation of the mean values for serum IL-6, TNF- α and CRP of the study groups with respect to their LVH categories. For IL-6, the control group showed a mean level of 3.26 ± 0.42 pg/mL. Patients with mildly increased LVMI had a mean IL-6 level 8.11 ± 1.64 pg/mL for those with a positive ECG and 6.14 ± 1.22 pg/mL for those with a negative ECG. Moderately increase LVMI patients exhibited higher levels of IL-6 levels, with averages of 11.20 ± 2.82 pg/mL for positive ECG and 9.47 ± 2.77 pg/mL for negative ECG. In patients with severely increased LVMI, IL-6 levels were 17.23 ± 3.58 pg/mL for positive ECG group and 18.26 ± 3.02 pg/mL for negative ECG. The p-values for both ECG groups ($p < 0.001$) indicated that the differences were statistically significant (Table 8A).

Regarding TNF- α , the control group had a mean level of 4.54 ± 1.15 pg/mL, and in those with mildly increased LVMI, TNF- α levels averaged at 11.51 ± 1.24 pg/mL for

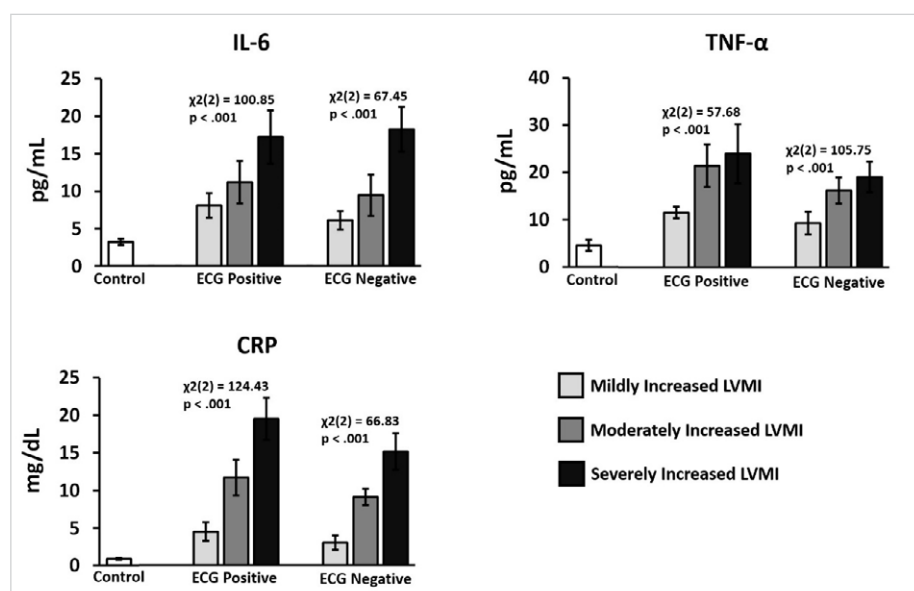


Fig. 1. Serum Levels of IL-6, TNF- α , and CRP in Different LVH Categories
Picture taken by the authors

Table 6. ECHO parameters of the study subjects

ECHO Parameters	LVH (ECHO)		p-value
	Positive ECG	Negative ECG	
IVST (mm)	14.09 $\pm$ 1.89	13.65 $\pm$ 1.64	0.027*
PWT (mm)	14.09 $\pm$ 1.62	13.92 $\pm$ 1.87	0.228
LVDD (mm)	44.75 $\pm$ 4.98	43.39 $\pm$ 5.51	0.026*
EF (%)	67.00 $\pm$ 6.87	66.90 $\pm$ 5.82	0.456
LVMI (g/m ²)	134.82 $\pm$ 26.19	124.42 $\pm$ 23.50	0.001*
Diastolic Function, n (%)			
Normal	8 (8.6)	13 (9.6)	0.961
Diastolic dysfunction	85 (91.4)	135 (90.4)	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; IVST: interventricular septum thickness; PWT: posterior wall thickness; LVDD: left ventricular diastolic diameter; EF: ejection fraction; LVMI: left ventricular mass index

*Statistical significance at $p < 0.05$

Source: compiled by the authors of this study

the positive ECG group and 9.33 ± 2.41 pg/mL for the negative ECG group. Patients with moderately increased LVMI presented higher TNF- α levels, with mean values of 21.47 ± 4.52 pg/mL for positive ECG and 16.25 ± 2.78 pg/mL for negative ECG. In patients categorized with severely increased LVMI, TNF- α levels are 24.03 ± 6.27 pg/mL for the positive ECG group and 19.09 ± 3.24 pg/mL for the negative ECG group. The p-values (< 0.001) confirm that the differences among groups were statistically significant (Table 8B).

Bar graphs illustrating the mean serum levels of IL-6 (top left), TNF- α (top right), and CRP (bottom left) across three groups: Control, ECG Positive, and ECG Negative. Each bar represents the mean $\pm$ standard deviation for each group. The colour coding indicates the degree of left ventricular mass index (LVMI): white for Mildly Increased LVMI, light grey for Moderately Increased LVMI, and black for Severely Increased LVMI.

For CRP levels, the control group showed a mean CRP level of 0.88 ± 0.13 mg/dL. For the mildly increased LVMI group, mean CRP levels were 4.51 ± 1.24 mg/dL for those with positive ECG and 3.03 ± 0.95 mg/dL for those with negative ECG. Moderately increased LVMI patients presented even higher CRP levels averaging 11.71 ± 2.38 mg/dL for positive ECG and 9.12 ± 1.08 mg/dL for negative ECG. In the severely increased LVMI category, CRP levels were significantly heightened, with mean values of 19.54 ± 2.78 mg/dL for the positive ECG group and 15.18 ± 2.41 mg/dL for the negative ECG group (Table 7C); the differences among groups were statistically significant with p-value < 0.001 .

DISCUSSION

Our study evaluated the characteristic and diagnostic utility of ECG and serum inflammatory markers in pa-

Table 7. Performance of ECG criteria in the assessment of LVH

A.		Concentric LVH			
ECG Criteria	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Sokolov - Lyon	13.69	100	100	19.38	28.52
Cornell	10.37	92	86.21	17.55	24.4
Peguero-Lo Presti	20.75	86	87.72	18.37	31.96
B.		Mildly Increased LVMI			
ECG Criteria	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Sokolov - Lyon	10.09	100	100	33.78	38.36
Cornell	9.34	88.46	62.5	32.17	35.22
Peguero-Lo Presti	18.35	88	76.9	33.08	40.25
C.		Moderately Increased LVMI			
ECG Criteria	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Sokolov - Lyon	12.72	100	100	51.02	54.29
Cornell	5.45	92	42.86	46.94	46.67
Peguero-Lo Presti	20.83	85.96	55.56	56.32	56.19
D.		Severely Increased LVMI			
ECG Criteria	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Sokolov - Lyon	19.74	100	100	45.05	54.59
Cornell	14.47	90	68.75	40.91	44.44
Peguero-Lo Presti	26.32	76	62.5	40.43	46.03

LVH: left ventricular hypertrophy; ECG: electrocardiography; PPV: positive predictive value; NPV: negative predictive value

Source: compiled by the authors of this study

tients with LVH using ECHO as the gold standard. The findings revealed significant differences in the demographic and clinical features between patients with positive and negative ECG outcomes, particularly in smoking status, BMI and use of medication(s). Notably, smoking status emerged as a statistically significant differentiator, with a higher proportion of smokers in the positive ECG group compared to non-smoking ($p = 0.001$). This aligns with numerous researches that indicate smoking as a known contributor to cardiovascular disease and LVH development [18]. In the control group, smoking was significantly more common among males than females, reflecting sex-related differences in smoking behavior. Additionally, the higher prevalence of obesity in the patients with positive ECG results suggests a correlation between LVH and increase body weight, consistent with findings from previous studies [19, 20], which emphasized the impact of obesity on cardiac load and hypertrophy. Medication use was more common among patients with positive ECG findings than those with negative ECG findings (67.7% vs. 59.5%, $p = 0.033$). This likely reflects the higher burden of underlying cardiovascular comorbidities, particularly

hypertension and diabetes, which require long-term pharmacological treatment and are themselves major risk factors for LVH, rather than indicating that medication use is directly associated with the development of LVH. Previous studies have demonstrated that appropriate antihypertensive therapy may improve cardiac remodeling and clinical outcomes in patients with LVH [21].

The control group in this study had a markedly lower prevalence of chronic diseases, while LVH groups exhibited high rates, with the ECG positive group having a higher prevalence than the ECG negative group. This highlights the importance of considering comorbidities in the assessment of LVH, aligning with the meta-analyses conducted by Cuspidi et al. (2018) [22] and Bouthoorn et al. (2018) [23], which respectively highlighted the complicity of hypertension and diabetes in significantly increasing the risk of developing LVH [22, 23].

The IVST was significantly greater in patients with positive ECG results compare to those with negative ECG results. This is in agreement with a previous study which suggested that IVST is one of the key echocardiographic markers for assessing LVH, supporting its role in

Table 8. Mean serum cytokine levels in relation to LVH categories

A. IL-6 (pg/mL)			
LVH (ECHO)			
LVH categories	Positive ECG	Negative ECG	Control
			3.26 $\pm$ 0.42
Mildly Increased LVMI	8.11 $\pm$ 1.64	6.14 $\pm$ 1.22	
Moderately Increased LVMI	11.20 $\pm$ 2.82	9.47 $\pm$ 2.77	
Severely Increased LVMI	17.23 $\pm$ 3.58	18.26 $\pm$ 3.02	
p-value	< 0.001	< 0.001	
B. TNF-α (pg/mL)			
LVH (ECHO)			
	Positive ECG	Negative ECG	Control
			4.54 $\pm$ 1.15
Mildly Increased LVMI	11.51 $\pm$ 1.24	9.33 $\pm$ 2.41	
Moderately Increased LVMI	21.47 $\pm$ 4.52	16.25 $\pm$ 2.78	
Severely Increased LVMI	24.03 $\pm$ 6.27	19.09 $\pm$ 3.24	
p-value	< 0.001	< 0.001	
C. CRP (mg/dL)			
LVH (ECHO)			
	Positive ECG	Negative ECG	Control
			0.88 $\pm$ 0.13
Mildly Increased LVMI	4.51 $\pm$ 1.24	3.03 $\pm$ 0.95	
Moderately Increased LVMI	11.71 $\pm$ 2.38	9.12 $\pm$ 1.08	
Severely Increased LVMI	19.54 $\pm$ 2.78	15.18 $\pm$ 2.41	
p-value	< 0.001	< 0.001	

LVH: left ventricular hypertrophy; ECHO: echocardiography; ECG: electrocardiography; LVMI: left ventricular mass index

Source: compiled by the authors of this study

the diagnostic process of the disease [24]. These findings highlight the importance of comprehensive ECHO assessment for accurate evaluation of cardiac structure and function. Although PWT did not differ significantly between the groups, its higher value in the positive ECG group supports the role of both IVST and PWT as markers of concentric remodeling, consistent with the findings of Barbieri et al. (2019) [25]. These variables are important to know when trying to understand the pathophysiology of hypertensive heart disease as well as LVH. Moreover, there was a significant difference between the two groups in terms of LVDD, which is higher among those with ECG than those without ECG. This finding is consistent with other literature regarding LVDD [26]. This indicates that patients with positive ECG results may be at an advanced stage of cardiac remodeling. It is interesting to note that while there was

no difference in the EF levels between the two groups, our study results corroborate other studies which have shown diastolic dysfunction with normal systolic function [27, 28]. The presence of diastolic dysfunction in the two groups (91.4% of those with positive ECG and 90.4% with negative ECG) indicates that diastolic dysfunction is a common feature in individuals with LVH [28].

Our study indicated that despite the fact that Sokolow-Lyon, Cornell, and Peguero-Lo Presti had very high specificity, sensitivity was still low in all three methods, which raises questions regarding the usefulness of ECG as a means of detecting LVH, especially where there is a need to diagnose LVH accurately. The Sokolow-Lyon criteria exhibited a specificity of 100%, which is in line with earlier studies, as this test is noted for its excellent capability to exclude LVH. Its sensitivity, however, at 13.69%, is quite low, which is

in accordance with other studies [29]. The low NPV of 19.38% and accuracy of 28.52% further accentuate the issue of misdiagnosis, especially among high-risk patients where depending only on ECGs can lead to missing cases of LVH. Also, the Cornell criteria had a low sensitivity of 10.37% but had a comparatively higher specificity of 92%. These results are also supported by a meta-analysis conducted by Zhang et al. (2020) showing that even though the Cornell criteria help in detecting LVH, low sensitivity continues to be an issue [24]. In terms of sensitivity, the Peguero-Lo Presti criteria achieved the highest value (20.75%). Even though it had relatively higher sensitivity compared to the other criteria, its PPV and NPV values were still lower than clinically acceptable values. This means that although the Peguero-Lo Presti criteria have a relatively high sensitivity in diagnosing LVH, it still lacks usefulness because of low PPV and NPV values. This is in line with the study conducted by Grogan et al. (2021) [30]. Likewise, similar trends were identified when assessing the increment in LVMI, where sensitivity was found to improve as the severity of LVH rose. In particular, the Sokolow-Lyon criteria revealed perfect 100% specificity among all categories of LVMI, while sensitivity remained relatively low, illustrating the challenges in recognizing early LVH. The data on mildly and moderately increased LVMI indicate that ECG is more likely to be effective in diagnosing severe LVH but has limited overall effectiveness. This conclusion is supported by the meta-analysis conducted by You et al. (2020) and suggesting that while ECG has good specificity, it cannot be used as a sole diagnostic technique [8]. Additionally, the differences between the criteria used for diagnosing LVH by ECG and the results of ECHOs show the necessity to use a combination of methods for making the diagnosis. The low sensitivity of ECGs is another reason to work on enhancing existing diagnostic criteria or utilizing new technology.

In this study, we also investigated the levels of inflammatory markers - IL-6, TNF- α , and CRP - in relation to LVH and ECG findings. Our results demonstrate a clear association between elevated levels of these inflammatory markers and the severity of LVH which agrees with reports that highlights the relationship between inflammation and cardiac remodeling. IL-6 levels significantly increased with severity of LVMI, as the control participants had normal levels, while patients with mildly increased LVMI demonstrated an increase in the serum levels of the cytokine which increase persisted with moderate and severe LVMI categories. These findings are consistent with previous studies that have illustrated a correlation between IL-6

and cardiac hypertrophy, suggesting that IL-6 might play a role in pathological cardiac remodeling due to its proinflammatory properties. Similarly, TNF- α levels also demonstrated a robust relationship with LVMI severity, starting from a control group mean of 4.54 pg/mL which is slightly above to normal reference range to 24.03 pg/mL in patients with severely increased LVMI with positive ECG results. This finding is paralleled by findings of previous research indicating that TNF- α levels is implicated in myocardial hypertrophy, contributing to the process of cardiac remodeling and dysfunction. The consistently elevated TNF- α levels across all LVMI categories, together with statistically significant p-values, support its potential role as a biomarker for identifying patients at increased risk of progressive cardiovascular disease. The consistently high TNF- α levels among all LVMI groups coupled with significant p-values indicate that TNF- α can be used as a marker to identify individuals who are at a higher risk of developing cardiovascular disease. The clear relationship between increased CRP levels and greater LVH severity further supports the role of inflammation in the pathogenesis of LVH. Although elevated IL-6, TNF- α , and CRP levels were associated with LVH severity, these biomarkers may also be affected by comorbid conditions such as diabetes mellitus, rheumatoid arthritis, systemic lupus erythematosus, and malignancy. Nevertheless, these conditions were present in only a small proportion of the study population and were therefore unlikely to have materially influenced the overall findings. Collectively, the elevated inflammatory marker levels observed in patients with LVH support a close association between inflammation and cardiac hypertrophy, highlighting their potential value as adjunctive biomarkers for diagnosis and risk stratification. Previous studies have also suggested that IL-6, TNF- α , and CRP are not only markers of cardiac stress but may also represent potential therapeutic targets in hypertensive heart disease.

CONCLUSIONS

In conclusion, our findings demonstrate significant clinical and demographic differences among patients with LVH according to ECG findings, highlighting the important role of smoking and obesity in the development and management of cardiac hypertrophy. The high prevalence of chronic diseases in both LVH groups further emphasizes the need for comprehensive patient management that addresses underlying cardiovascular risk factors. The study also highlights the limited diagnostic accuracy of ECG criteria for LVH, particularly in clinical settings with high disease prevalence. Although ECG may be useful

as a screening tool because of its high specificity, its low sensitivity emphasizes the need for comprehensive ECHO evaluation for accurate diagnosis. Furthermore, the higher ECHO parameters observed in ECG-positive patients support the importance of advanced imaging in assessing LVH. In addition, the observed association between elevated inflammatory markers and LVH suggests that these biomarkers may serve as useful adjuncts in diagnosis and future patient management strategies.

Future research should focus on clarifying the molecular mechanisms linking inflammatory markers to the progression of LVH, as our findings suggest that these markers may provide additional insight into the underlying pathophysiology of the condition and help improve diagnostic strategies. Further investigation in this field may contribute to better patient outcomes and more effective management of individuals at risk of LVH.

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CONFLICT OF INTEREST

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