

Electro- and echocardiographic features of left ventricle hypertrophy in patients with hypertrophic cardiomyopathy

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Abstract

Background: Standard 12-lead electrocardiogram (ECG), next to medical history and physical examination, is a basic screening tool for hypertrophic cardiomyopathy in General practice. There are many electrocardiographic criteria of left ventricular hypertrophy, but their accuracy is usually weak in patients with systemic hypertension or aortic stenosis. Sensitivity of these criteria in patients with HCM has not been well described.

Aim: To assess the prevalence of electrocardiographic criteria for LVH in patients with HCM and their relationship with echocardiographic parameters.

Material and methods: A total of 49 patients with HCM (mean age 53.2 ± 15.4 years; men/women: 31/18) were enrolled to study. Eight electrocardiographic criteria for LVH were evaluated and correlated with echocardiographic parameters.

Results: The ECG features of LVH were found in 36 (73.5%) subjects. These patients had increased thickness of intraventricular septum (20.5 ± 4.7 vs. 17.3 ± 3.2 mm, $p = .03$), LVM (340.5 ± 104.8 vs. 264.0 ± 61.5 g; $p = .02$), and LVMI (178.9 ± 48.8 vs. 125.9 ± 22.5 ; $p = .002$). All of ECG criteria for LVH had low sensitivity (14.3%–40.8%) for LVH diagnosis confirmed by echocardiography. The most common positive criterion was Cornell Voltage (20 patients; 40.8%). A total of 41 (83.4%) patients had T-wave inversion in limb and/or precordial leads. LVMI correlated positively with R-wave amplitude in aVL ($R = 0.34$; $p = .03$), Gubner-Ungerleider voltage ($R = 0.4$; $p = .009$), and Cornell Voltage ($R = 0.31$; $p = .04$).

Conclusion: ECG criteria for LVH are characterized by poor sensitivity in patients with HCM. Cornell Voltage and criteria based on limb leads correlate positively with LVMI.

KEYWORDS

electrocardiography, hypertrophic cardiomyopathy, left ventricular hypertrophy

Hypertrophic cardiomyopathy (HCM) is one of the leading cause of sudden cardiac death (SCD) in individuals below 35 years old (Corrado et al., 1998; Harmon et al., 2015; Maron et al., 1986; Papadakis et al., 2009). Patients with HCM often may be asymptomatic at the time of diagnosis (Maron, 2018). Medical societies and sport associations recommend screening programs for athletes to prevent SCD (Corrado et al., 2005; Drezner et al., 2016; Fritsch et al., 2017; Maron et al., 2014; Maron et al., 2015; Mont et al., 2017; Wang et al., 2021). Standard 12-lead electrocardiogram (ECG), next to medical history and physical examination, is included in all guidelines as a basic screening tool. Abnormal ECG patterns may be found even in 75%–95% of patients with HCM (Maron, 2002). Features of left ventricular hypertrophy and inverted T waves are the most common abnormality, which may be found in ECG in patients with HCM (Dohy et al., 2020; Morimoto et al., 2020; Sharma et al., 2018). There are many electrocardiographic criteria of left ventricular hypertrophy, but their sensitivity is usually weak in patients with systemic hypertension or aortic stenosis (Greve et al., 2012; Narayanan et al., 2014; Pewsner et al., 2007; Sundström et al., 2001).

Thus, the primary aim of this study was to assess the prevalence of electrocardiographic criteria for LVH in patients with HCM. Secondly, the relationship between electrocardiographic hypertrophy criteria and the most used echocardiographic parameters and measures were evaluated.

1 | METHODS

1.1 | Study population

Eighty-nine consecutive, adult patients with HCM hospitalized in I Department of Cardiology Medical University of Silesia in years 2015 to 2020 were studied retrospectively. Clinical data, transthoracic echocardiography (TTE), and 12-lead electrocardiogram were assessed. Patients with lysosomal storage diseases, amyloidosis, complete and incomplete bundle branch blocks, nonspecific intraventricular conduction disturbances (NIVCD), paced rhythm, treated with digoxin were excluded. To final analysis, 49 patients were enrolled.

1.2 | Transthoracic echocardiography

All subjects were evaluated in TTE by experienced cardiologists. The diagnosis of HCM was based on the presence of a left ventricular wall thickness ≥ 15 mm in absence of severe hypertension and valvular or congenital heart diseases (Elliott et al., 2014). The presence of left ventricular outflow tract obstruction (LVOTO) at rest and during exercise and systolic anterior of the mitral valve (SAM) were assessed in all individuals. Left ventricular mass (LVM) was calculated according to formula: $0.8 \times 1.4 \times [(IVSd + LVIDd + PWTd)^3 - LVIDd^3] + 0.6$ g (Lang et al., 2015). Left ventricular mass index (LVMI) was defined as LVM/ body surface area (g/m^2).

1.3 | Electrocardiography

Standard 12-lead ECGs were obtained in all patients in supine position using Mortara ELI 250c electrocardiograph (paper speed 25 mm/s, 10 mm/mV). All ECG recordings were evaluated by two experienced cardiologists. ECGs were consulted with another cardiologist if there was any doubt. More than one ECG was available in all cases, so there was possibility to assess electrocardiographic abnormalities in consecutive ECGs if the first assessment was inconclusive.

Several electrocardiographic parameters including heart rate, heart rhythm, axis, QRS duration and amplitude, presence of T wave inversion (TWI) in limb, and precordial leads were analyzed. Heart rate and QRS complex duration were measured using the algorithm in device software. The remaining features were evaluated manually. LVH features were assessed in ECG using eight selected criteria: amplitude of R in aVL > 1.1 mV (Sokolow & Lyon, 1949); Gubner-Ungerleider voltage: sum of R wave in I and S wave in III lead > 2.5 mV (Gubner & Ungerleider, 1943); Sokolow-Lyon index: sum of S wave in V1 and R wave in V5 or V6 > 3.5 mV (Sokolow & Lyon, 1949); sum of S wave in V2 and R wave in V5 or V6 > 4.5 mV (Romhilt et al., 1969); amplitude of R wave in V5 or V6 > 2.6 mV (Sokolow & Lyon, 1949); comparison of amplitude of R wave in V5 and V6: $R V6 > R V5$ (Holt & Spodick, 1962); sum of largest amplitude of R wave and largest amplitude of S wave in precordial leads > 4.5 mV (McPhie, 1958); Cornell Voltage: sum of R wave in aVL and S wave in V3 > 2.0 mV for women and > 2.8 mV for men (Casale et al., 1987). The ECG was considered as positive for LVH if at least one of LVH criteria was met.

1.4 | Statistical Analysis

Continuous variables are presented as mean \pm standard deviation or median 1 to 3 quartile boundaries. Categorical variables are expressed as number or percentage of subjects. Comparison of unpaired normally distributed samples was performed with Student's *t*-test, while non-normal data was compared with the Mann-Whitney *U* test. The differences between categorical variables were assessed with the chi-squared test. The strength of correlation between two variables was tested with Spearman's rank correlation coefficient. A *p*-value of $< .05$ was considered as statistically significant. All statistical analyses were conducted using Statistica 14.

2 | RESULTS

2.1 | Demographic and clinical characteristics

A total of 49 patients with HCM (mean age 53.2 ± 15.4 years; men/women: 31/18) were eligible to study analysis. The median time from diagnosis was 2 years. The mean LVMI was 167.3 ± 49.4 g/m^2 . Apical cardiomyopathy was present in three patients (6.1%). The ECG features of LVH were found in 36 (73.5%) subjects. Those patients had greater diameter of intraventricular septum (20.5 ± 4.7

vs. 17.3 ± 3.2 mm, $p = .03$), LVM (340.5 ± 104.8 vs. 264.0 ± 61.5 g; $p = .02$) and LVMI (178.9 ± 48.8 vs. 125.9 ± 22.5 ; $p = .002$). There was no difference in prevalence of comorbidities, value of Sudden Cardiac Death Risk Score and presence of left ventricular outflow tract obstruction. The overview of demographic and clinical data of patients is highlighted in Table 1.

2.2 | ECG characteristics

Sinus rhythm was present in majority of patients (46; 93.9%). Left axis deviation was found in 13 ECGs. Eight electrocardiographic criteria for LVH were evaluated. All of those criteria were characterized by low sensitivity (14.3%–40.8%). The most common positive criterion was Cornell Voltage (20 patients). To obtain higher sensitivity, we combined Cornell Voltage with R wave $V_6 > V_5$ and Sokolow-Lyon. It allowed to identify 34 (69.4%) patients with LVH.

LVH in ECG was accompanied by TWI in almost all cases (91.7%). A total of 41 (83.4%) patients had TWI in limb and/or precordial leads. Normal ECG was found in three patients (age: 57–68 years old). Detailed characteristics of ECG findings is shown in Tables 2 and 3.

LVMI correlated positively with amplitude of R in aVL ($R = 0.34$; $p = .03$), Gubner-Ungerleider voltage ($R = 0.4$; $p = .009$) and Cornell Voltage ($R = 0.31$; $p = .04$). Such correlation was not found between LVMI and criteria based on precordial leads (Table 4). There was no correlation between body mass index (BMI) and any of ECG criteria for LVH.

3 | DISCUSSION

The main finding of this study is low sensitivity (14.3%–40.8%) of each respective ECG criteria of LVH. This may be surprising in presence of extensive hypertrophy confirmed in TTE; however, it is consistent

TABLE 1 Clinical characteristic and echocardiographic assessment of study population

	All patients (n = 49)	Positive ECG for LVH (n = 36)	Negative ECG for LVH (n = 13)	p-value
DEMOGRAPHIC AND CLINICAL DATA				
Age (years)	53.2 ± 15.4	52.9 ± 14.5	54.0 ± 18.1	NS
Sex (men/women)	31/18	21/15	10/3	NS
BMI	28.3 ± 4.2	28.4 ± 4.3	27.9 ± 4.1	NS
Arterial Hypertension	26 (54.2%)	19 (52.8%)	7 (53.8%)	NS
History of CAD	14 (29.2%)	11 (30.6%)	3 (23.1%)	NS
Diabetes mellitus	7 (14.6%)	6 (16.7%)	1 (7.8%)	NS
History of VT/VF	22 (45.8%)	17 (47.2%)	5 (38.5%)	NS
Time from diagnosis (years) ^a	2 (0;11)	2.5 (0;10.5)	2.0 (0; 11)	NS
SCD Risk Score [%] ^a	3.1 (2.1;5.9)	3.7 (2.2; 6.1)	2.4 (2.1; 3.7)	NS
ECHOCARDIOGRAPHY				
LA diameter [mm]	43.4 ± 6.5	44.2 ± 6.7	41.2 ± 6.5	NS
IVSd [mm]	19.6 ± 4.5	20.5 ± 4.7	17.3 ± 3.2	0.03
PWTd [mm]	12.2 ± 2.5	12.4 ± 2.6	11.5 ± 1.8	NS
LVESD [mm]	26.0 ± 6.0	25.8 ± 6.1	26.6 ± 5.8	NS
LVEDD [mm]	46.1 ± 6.4	46.4 ± 6.6	45.3 ± 5.9	NS
LVEF [%]	59.1 ± 8.6	58.8 ± 9.4	59.7 ± 6.0	NS
Presence of resting LVOTO (N)	16 (33.3%)	14 (38.9%)	2 (15.4%)	NS
Presence of exercise-induced LVOTO	22 (45.8%)	17 (47.2%)	5 (38.5%)	NS
Apical hypertrophic cardiomyopathy	3 (6.1%)	1 (2.8%)	2 (15.4%)	NS
LVM [g]	319.3 ± 100.3	340.5 ± 104.8	264.0 ± 61.5	0.02
LVMI [g/m ²]	167.3 ± 49.4	178.9 ± 48.8	125.9 ± 22.5	0.002
RWT [cm]	0.54 ± 0.15	0.56 ± 0.17	0.51 ± 0.09	NS

Abbreviations: AVA, aortic valve area; AS, aortic stenosis; BMI, body mass index; CAD, coronary artery disease; IVSd, intraventricular septum diameter; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVH, left ventricular hypertrophy; LVM, left ventricular mass; LVMI, left ventricular mass index; LVOTO, left ventricular outflow tract obstruction; MI, myocardial infarction; NS, not significant; PWTd, posterior wall thickness diameter; RWT, relative wall thickness; SCD, sudden cardiac death; TTE, transthoracic echocardiography.

^anon-normal distribution.

TABLE 2 ECG findings in HCM patients

Variable	HCM patients [n = 49]
Sinus rhythm [n]	46 (93.9%)
Atrial fibrillation [n]	3 (6.1%)
Normal axis [n]	36 (73.5%)
Left axis deviation [n]	13 (26.5%)
QRS complex [ms]	100.4 ± 15
Positive ECG for LVH [n]	36 (73.5%)
TWI in any leads [n]	41 (83.4%)
TWI in precordial leads [n]	33 (67.3%)
TWI in limb leads [n]	34 (69.4%)
LVH + TWI [n]	33 (67.3%)

Abbreviations: ECG, electrocardiogram; LVH, left ventricular hypertrophy; TWI, T wave inversion.

TABLE 3 Sensitivity of eight ECG criteria for LVH compared to echocardiographic- based LVH

ECG Criteria	Positive results [n]	Sensitivity [%]
Amplitude of R in aVL	13	26.5
Gubner-Ungerleider voltage	13	26.5
Sokolow-Lyon index	15	30.6
Sum of S in V2 and R in V5 or V6	7	14.3
Amplitude of R in V5 or V6	10	20.4
R in V6 > R in V5	18	36.7
Sum of the largest R and largest S in precordial leads	9	18.4
Cornell Voltage	20	40.8
Cornell Voltage or R in V6 > R in V5	28	57.1
Cornell Voltage or Sokolow-Lyon index	27	55.1
Cornell Voltage or R in V6 > R in V5 or Sokolow Lyon index	34	69.4

Abbreviations: ECG, electrocardiogram; LVH, left ventricular hypertrophy.

with results of several studies (Dohy et al., 2020; Erice et al., 2009; Grall et al., 2014; Tangwiwat et al., 2019). Majority of those analyzes took into consideration only Sokolow-Lyon Index and Cornell Voltage. Interestingly, at least one ECG criterion was met in 73.5% of patients in our study, which showed significant variability in distribution of QRS complexes with high amplitude. Dohy et al. suggested that fibrosis of myocardium may be connected with lower QRS amplitude in corresponding leads (Dohy et al., 2020). Conversely, Grall et al. did not find relation between LGE and QRS amplitude (Grall et al., 2014). We showed that combination of two or three criteria highly increases sensitivity. Similar findings presented Erice et al., who combined Cornell

TABLE 4 Correlation between value of ECG criteria for LVH and echocardiographic parameters

		LVM	LVMI	RWT
Amplitude of R in aVL	r	0.25	0.34	0.26
	p	NS	.03	NS
Gubner-Ungerleider voltage	r	0.33	0.40	0.22
	p	.02	.009	NS
Sokolow-Lyon index	r	-0.07	0.02	0.25
	p	NS	NS	NS
Sum of S in V2 and R in V5 or V6	r	-0.01	0.04	0.26
	p	NS	NS	NS
Sum of largest R and largest S in precordial leads	r	0.12	0.11	0.33
	p	NS	NS	.02
Cornell Voltage	r	0.31	0.34	0.41
	p	.04	.03	.004

Abbreviations: ECG, electrocardiogram; LVH, left ventricular hypertrophy; LVM, left ventricular mass; LVMI, left ventricular mass index; RWT, relative wall thickness.

Voltage and the Lewis or Gubner-Ungerleider criteria, what resulted in high sensitivity up to 80% (Erice et al., 2009).

Another interesting finding was positive correlation of LVMI with value of ECG criteria of LVH based on limb leads, but not on precordial leads. We cannot find explanation of this phenomenon. Dohy et al. found significant relationship between LVMI and both Cornell and Sokolow-Lyon criteria (Dohy et al., 2020). Similar results were presented in research of Fronza et al. (2016). LVMI was calculated on the basis of cardiac magnetic resonance in both mentioned studies in contrast to our research. Many factors may influence on lowering amplitude of QRS complex, such severe chronic obstructive pulmonary disease, obesity, pericardial effusion or infiltrative cardiomyopathy (Madias, 2008). The body mass index (BMI) might be the only disturbing factor in present study. However, we did not find correlation between BMI and amplitude of QRS complex. BMI was similar in both group.

TWI was common abnormality in ECG of our HCM patients and was present in almost all ECG with features of LVH. Fronza et al. showed that the presence of negative T waves in specific leads of ECG corresponded with localization of late gadolinium enhancement in magnetic resonance (Fronza et al., 2016). TWI is almost always an alarming sign, which required further investigation according to International Recommendations for Electrocardiographic Interpretation in Athletes (Sharma et al., 2018).

3.1 | Study Limitation

This is a retrospective, single-center study with small number of patients. The time since diagnosis of HCM varied among patients. The impact of ECG findings on prognosis and clinical outcome was not assessed.

3.2 | Summary

Electrocardiographic criteria for left ventricular hypertrophy are characterized by rather poor sensitivity even in patients with HCM. Cornell Voltage criteria seems to be the most efficient criterion, especially combined with Sokolow-Lyon index. Cornell Voltage and criteria based on limb leads correlate positively with LVMI. Based on result on the present study the lack of amplitude features of LVH in ECG should not discourage of further diagnostics towards HCM. It seems reasonable to calculate more than one of ECG criteria for LVH in HCM screening. TWI may be more useful in screening tests for HCM than voltage criteria of LVH.

AUTHOR CONTRIBUTIONS

All authors contributed to the work. They were involved in data collection, data analysis, writing and revising the article prior to submission. All authors have given final approval of the version to be published.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding this article. The study was neither funded nor supported by any external company or organization.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL

The study has been conducted according to the standards of the Declaration of Helsinki and the study protocol was approved by the local institutional review board.

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