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2

3 **TITLE:** Left ventricular hypertrophy in hypertensive patients; prevalence and
4 diagnosis

5

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26 **Short Running Title:** Left ventricular hypertrophy in hypertensive patients

27

28 **Guarantor of Submission:** The corresponding author is the guarantor of
29 submission.

30

31

32

33 **ABSTRACT**

34

35 **Aims**

36 Left ventricular hypertrophy is an important predictor of cardiovascular risk, and its
37 detection contributes to risk stratification. The aims of the study were to evaluate the
38 prevalence of left ventricular hypertrophy in hypertensive patients and to assess the
39 accuracy of electrocardiography in its diagnosis.

40

41 **Methods**

42 A single center based, prospective, cross sectional study was carried out for a period
43 of 8 months. The data were collected through direct interview and fulfilling of a
44 prepared questionnaire. Beside these all patients were sent to do
45 electrocardiography and echocardiography.

46

47 **Results**

48 Mean age was 62.7 ± 7.8 years, females (58%) were more than males (42%). mean
49 BMI of $(28.38 \pm 2.9 \text{ kg/m}^2)$, (30%) of the patients with hypertension found to have left
50 ventricular hypertrophy. Sensitivity/specificity of Sokolow-Lyon voltage, Cornell
51 voltage and strain pattern were 30/89, 25/93, 20/96 respectively.

52

53 **Conclusion**

54 Prevalence of left ventricular hypertrophy was 30% in hypertensive patients,
55 Electrocardiography cannot be used as the screening tool for the diagnosis of Left
56 Ventricular Hypertrophy.

57

58 **Keywords:** Hypertension, Left Ventricular hypertrophy, Electrocardiography,
59 Echocardiography.

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65 INTRODUCTION

66 LVH is defined by the increased left ventricular (LV) mass; with myocardial cell
67 hypertrophy and an increase in collagen within myocardium [1]. Multifactor etiology
68 for LVH has been implicated including, age, sex, body size, blood pressure and
69 diabetes [2].

70 Age, race, gender and body size can influence cardiac mass; this might occur
71 through cardiac load [3]. Hypertensive LVH is a risk factor for high insulin level and
72 insulin resistance. Significant correlation between LV mass, insulin-like growth
73 factor-I (IGF-I) and insulin was observed in a cohort study [4]. Correlation between
74 LVH in first-degree relatives than in second- degree relatives or couples is shown in
75 analyzing of LV mass heritability in the Framingham Heart Study, suggesting that
76 about 30% of LV mass variance is determined by genetic [5].

77 Pathological changes induced by chronic pressure overload include an increase in
78 the size of the cardiac myocytes, changing composition of the extracellular matrix
79 with increase of collagen fibers and abnormal changes in intramyocardial coronary
80 vessels [6]. However, most attention has been put on risk factors associated with
81 LVH, and on the beneficial effects of pharmacological treatment, as there is
82 detrimental contribution of LVH to cardiovascular events and survival [7].

83 Physical examination may show signs of hypertension and LVH like high blood
84 pressure measurement, augmented aortic sound on auscultation and displaced
85 cardiac impulse palpation. Yet, ECG may be an effective tool in the diagnosis of LVH
86 [8]. Precordial leads may show a negative P wave, anterior leads may have Large
87 QRS amplitudes while lateral leads demonstrating deep S and high R as a
88 consequence of LVH. The most popular ECG criteria are the Cornell voltage, the
89 Cornell product, the Sokolow-Lyon index and the Romhilt-Estes point score system
90 [8][9][10][11]. ECG limitations are; first, variable diseases present with near similar
91 changes. Second, inaccuracy in some patients like morbid obesity and
92 emphysematous chest. Echo, if available, should be the test of choice to assess for
93 LVH and detect other abnormalities such as left ventricular dysfunction and valvular
94 disease [12].

95 Cardiac MRI is more accurate for measuring LV mass and is assessed in well-
96 designed epidemiological and clinical studies but ECG and Echo are the cheapest
97 and most readily available tests for LVH [13].

98 The development of LVH leads to LV diastolic dysfunction, an important factor in the
99 evolution of congestive heart failure. Furthermore, interstitial myocardial fibrosis and
100 an increased myocardial mass reduce coronary flow reserve leading to impaired
101 tolerability and myocardial ischemia [14]. Also there is enough evidence showing
102 that LVH causes arrhythmia [15].

103 The aim of this study is to evaluate and show the prevalence of LVH in hypertensive
104 cases and to assess the accuracy of ECG in diagnosing LVH.

105

106 **MATERIALS AND METHODS**

107

108 **Study design & settings**

109 A cross sectional study was carried out at in single center for a period of 8 months,
110 from 1st of February 2016, to 1st of October 2016, all patients underwent ECG and
111 transthoracic Echo.

112

113 **Inclusion criteria**

114 All hypertensive patients, free from exclusion criteria, during the study period, were
115 included.

116

117 **Exclusion criteria**

118

119 **The followings are excluded**

120 Cor pulmonale, myocardial infarction, valvular heart disease, bundle branch blocks,
121 pre-excitation syndrome and cardiomyopathy.

122

123 **Intervention and Data collection**

124 The data were obtained from the patient's case notes and through direct questioning.
125 Physical examination of each patient was carried out including precordial
126 examination and taking blood pressure in a proper way. All patients underwent ECG

127 and Echo. The estimation of left ventricular mass (LVM) was based on the formula
128 derived by Devereux and colleagues [16]. $LVM = 0.8(1.04 [(LVIDd + PWTd +$
129 $IVSTd)^3 - (LVIDd)^3]) + 0.6 \text{ gm}$

130 Where LVIDd =left ventricle internal dimension in diastole,
131 PWTd= posterior wall thickness in diastole,
132 IVSTd = interventricularseptal thickness in diastole, 1.04 = specific
133 gravity of the myocardium.

134 Also by incorporating height and weight, LVM index calculated, LVM index was
135 defined as LVM divided by body surface area (LVM/BSA, g/m²). BSA was calculated
136 according to the formula: $BSA = 0.6 \times \text{height (m)} + 0.0128 \times \text{weight (kg)} - 0.1529$.

137 LVH was defined by LVM of ≥ 162 gram for women and ≥ 224 grams for men, or LVM
138 index of ≥ 95 gram/m² for women and ≥ 115 grams/m²for men and graded according
139 to the table 2.

140

141 **Ethical considerations:**

- 142 ▪ Approval was taken from Kurdistan Board of Medical Specialty & Sulaimany
143 Directorate of Health.
- 144 ▪ Oral consent was taken from each patient and they were assured about their
145 Confidentiality.

146

147 **Statistical analysis:**

148 Data analysis was done by computerized statistical software; Statistical Package for
149 Social Sciences (SPSS) version 22. Descriptive statistics presented as (mean \pm
150 standard deviation) and frequencies as percentages. Normality of the data set was
151 verified. Multiple contingency tables conducted and appropriate statistical tests were
152 performed, Chi-square test was used for categorical variables and independent t-test
153 was used to compare between means. In all statistical analysis, level of significance
154 (p value) was set at ≤ 0.05 .

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157

158

159 **RESULTS**

160

161 **Clinical and demographic characteristics**

162 The study included 200 patients, 84 (42%) cases were male and 116 (58%) patients
163 were female, the age ranged between 50-80 years with mean age of 62.7 ± 7 . Table
164 3 gives information about socio-demographic characteristic and risk factors of the
165 patients.

166

167 **Echo findings**

168 Sixty patients (30%) revealed LVH, among them 39 patients (65%) were female and
169 21 patients (35%) were male. Eighteen (9%) patients had LV systolic dysfunction, 54
170 patients (27%) had LV diastolic dysfunction. Table 4 shows details of ECG findings
171 of the patients.

172 The prevalence of LVH was significantly higher in female, and eccentric type was
173 significantly more prevalent in female as shown in table 5.

174

175 **ECG findings of patients in the study**

176 Thirty-three patients (16.5%) had voltage criteria of Sokolow-Lyon voltage, 25
177 patients (12.5%) had voltage criteria of Cornell voltage, and 18 patients (9%) had left
178 ventricular strain pattern.

179 The calculated sensitivity/specificity for the ECG findings in patients with LVH for
180 Sokolow-Lyon criteria was 30% / 89%, for cornel voltage was 25% / 93% and for
181 left ventricular strain pattern was 20% / 96% respectively (Table 6 and 7).

182

183 **DISCUSSION**

184 LVH is associated with increased cardiovascular morbidity and mortality, so its
185 diagnosis is critical, especially for hypertensive patients [17]. Echo criteria for LVH
186 have been shown to have excellent sensitivity, specificity and accuracy when
187 compared with postmortem LV mass, and its reliability has been confirmed
188 angiographically [18]. Based on the population studied and the criteria used for LVH,
189 the prevalence of LVH in hypertensive cases varies from 20% to 70% in most
190 studies worldwide [19-21]. In one meta- analysis of Cuspidi et al of 30 studies

191 published in the last decade provides one of the largest data base on Echo LVH
192 prevalence in a hypertensive population of 37700 patients from different
193 hypertensive cohorts and from the hypertensive fraction of the general population.
194 LVH is present in approximately 36% of the pooled population according to more
195 restrictive diagnostic criteria. In another meta-analysis by Pewsner D et al who
196 analyzed 5608 patients in 21 studies, the median prevalence of LVH was 33%
197 (interquartile range 23-41%). In the current study, the prevalence of LVH was 30%,
198 this result is very close to the results of de Simone et al and Fesler et al which were
199 31% and 33% respectively [22-25]. Majority of our patients were female. The data
200 were taken consecutively. Whether it occurred by chance or hypertensive is more
201 prevalent among female in our locality is not known.

202 As for LV geometric patterns, the eccentric pattern was more prevalent than the
203 concentric one in 14 out of 18 studies in the prementioned meta-analysis, the same
204 proportion was also obtained in this study in which eccentric LVH was 20% while
205 concentric LVH was 10% [22].

206 There are too much controversies regarding relationship between gender and LVH
207 [25-27]. There are studies that showed that females have a positive association with
208 LVH [28-30]. However, other studies confirmed the reverse of this [25][26][27]. At the
209 same time, another series showed that there is no difference between gender and
210 LVH [31]. This current series showed that the female gender is a predictor for the
211 development of LVH with an Odd ratio of 1.182.

212 Many studies found that patients with obesity are at risk of developing LVH [32-34].
213 This study supports these findings with odd ratio of 1.2 for patients with BMI more
214 than 25 compared with a patient who has normal weight at a 95% confident interval
215 of 0.07-2.08. The remodeling process in long-standing hypertension consists of
216 hypertrophy, fibrosis and impaired microvascular circulation with arterial stiffness is
217 accompanied by higher pulse pressure and systolic blood pressure, which are well-
218 known risk factors for cardiovascular diseases[35]. Few studies have assessed the
219 relationship between LVH and cigarette smoking. In the LIFE Study, smoking was
220 more common among LVH patients in comparison to control [36]. In the current
221 study, there was no association between LVH and smoking. For the last decade,
222 many studies have been conducted regarding ECG diagnosis of LVH based on ECG

223 criteria [37-45]. The criteria were used to increase the accuracy of the method for
224 diagnosing LVH. In this study, sensitivity of all criteria was low (20—30%).

225 In the present study, three applicable ECG criteria for LVH diagnosis in
226 hypertensive cases with Echo as the diagnostic standard. Sokolow-Lyon criteria are
227 the oldest criteria revised by Sokolow M. and Lyon in 1949. It is the oldest, quickest
228 and simplest method for diagnosis of LVH by ECG. According to this study, it has
229 sensitivity of 30%, specificity of 89 %, PPV of 55%, NPV of 75% and accuracy of
230 71%.

231 The specificity and sensitivity of Sokolow-Lyon criteria showed different results in
232 different studies, in our study it was very close to the sensitivity/ specificity of
233 Norman et al. (1995) and Lallijiet al. (2007) which were 30% / 86% and 31% / 86%
234 respectively [37][38].

235 In assessing Cornell voltage criteria, sensitivity of 25%, specificity of 93%, PPV of
236 60%, NPV of 74% and accuracy of 72%.

237 The sensitivity / specificity of Cornell voltage criteria in the current study was close to
238 Salles et al which were 24% / 89% respectively while the sensitivity of our study was
239 far more than the results of Fragolaw which was 8% and a higher score obtained in
240 Calacaw which was 41% [39-41].

241 In assessing the scores for LV strain pattern, sensitivity of 20%, specificity of 96%,
242 PPV of 67%, NPV of 73%, accuracy of 73%.

243 There is wide range among studies in evaluation of sensitivity of LV pattern,
244 sensitivity ranging from 11.9% to 38.6%. Our study took a median position among
245 them and it was very close to Sundströmet al in which sensitivity was 21% and
246 specificity was 92%.

247 Alfakih et al analyzed the value of gender specific partition for ECG criteria of LVH
248 recalibrated against cardiac MRI, and evaluated that Cornell voltage criterion had
249 highest sensitivities in males (26.2%) as compared to females (16.3%), while the
250 reverse was found in Sergio et al, who assessed both the specificity and sensitivity
251 of Sokolow –Lyon and Cornell voltage criteria for LVH. In their study, the sensitivity
252 of Cornell voltage criterion was 22.5% for males and 28% for females, Rodrigues et
253 al reported a similar finding, our results go with Sergio et al in which sensitivity of
254 Cornell voltage criterion was higher for female [42-44].

255 There are limitations for this study; the sample size is small, the duration of the study
256 was short and finally, although we assessed risk factors at the time, we could not
257 reliably measure how long the risk factors had been present before, as patients may
258 not seek medical attention.

259

260 **CONCLUSION**

261 This study found that the prevalence of LVH was 30% among hypertensive
262 population. Effort should be made for early detection and treatment of LVH since it
263 carries bad prognosis. LVH was more prevalent in female, especially eccentric type.
264 Because their sensitivity is, unacceptably low, ECG cannot be used as a substitute
265 of Echo in detecting LVH.

266

267 **CONFLICT OF INTEREST**

268 None to be declared.

269

270 **AUTHOR'S CONTRIBUTIONS**

271 Amanj A. Khaznadar

272 Group 1 -Substantial contribution to the concept and design.

273 Group 2- Revising the article

274 Group 3- Final approval of the article

275

276 Kawa T. Rahim and Farman J. Ahmed

277 Group 1- Substantial contribution to the concept and design

278 Group 2- Drafting and revising the manuscript

279 Group 3- Final approval of the manuscript.

280

281 Fahmi H. Kakamad

282 Group 1- Substantial contribution to the concept and design, Acquisition of the data

283 Group 2- Revising the manuscript

284 Group 3- Final approval of the manuscript.

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286

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447 **TABLES**

448

449 Table 1: Common ECG criteria for the diagnosis of LVH [8][9][10].

450

Cornell voltage criteria	SV3 + RaVL ≥ 2.8 mV (28 mm) in men SV3 + RaVL ≥ 2.0 mV (20 mm) in women
Cornell product criteria	SV3 + RaVL (+8 in women a) x QRS duration ≥ 2,440 mm x ms
Sokolow-Lyon voltage criteria	SV1 + RV5 or RV6 ≥ 3.5 mV (35 mm) b or RaVL ≥ 1.1 mV (11 mm)
Romhilt-Estes (point score system)	(a score ≥ 5 is diagnostic of LVH, a score of 4 is “probable” LVH) Voltage criteria (3 points): Any S or R in limb leads ≥ 20 mm SV1, SV2, RV5, or RV6 ≥ 30 mm ST-T wave changes of LVH (3 points, 1 point on digitalis) Left atrial abnormality (3 points): Terminal component of the P wave in V1 ≥ 1 mm and ≥ 40 ms Left axis deviation (2 points): QRS axis of -30 degrees or more negative Prolonged QRS duration (1 point): ≥ 90 ms Delayed intrinsicoid deflection time (1 point): ≥ 50 ms in V5 or V6

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457 Table 2: LVH grading [16]

458

	Mild	Moderate	Severe
LV mass/BSA (g/m ²) Women	96–108	109–121	≥122
LV mass/BSA (g/m ²) Men	116–131	132–148	≥149

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482 Table 3: Demographic characteristics of patients

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Variable	No.	%
Age		
50-59	62	31
60-69	94	47
≥ 70	44	22
Male	84	42
Female	116	58
Weight mean±SD (76.34±10 kg)		
Height mean±SD (162± 7.2 cm)		
BMI mean±SD (28.38± 2.9 kg/m2)		
Anti-hypertensive treatment	140	70
Duration of hypertension		
1-5 years	62	31
6-10 years	94	47
11-15 years	32	16
≥16 years	12	6
Mean systolic blood pressure	158.45	
Mean diastolic blood pressure	87.67	
Mean MAP	110.76	
Diabetes mellitus	26	13
Smoking history	42	21

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493 Table 4: Echo findings of the patients

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Echocardiographic finding	No	%
No LVH on echocardiography	140	70
LVH on echocardiography	60	30
Systolic dysfunction	18	9
Diastolic dysfunction	54	27
Eccentric LVH	40	20
Concentric LVH	20	10
Mild LVH	38	19
Moderate LVH	15	7.5
Severe LVH	7	3.5

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514 Table 5: Gender –specific difference in geometry of LVH

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Type of LVH	Gender				P-value
	Male		Female		
	No.	%	No.	%	
LVH (ALL)	21	10.5	39	19.5	<0.05
Eccentric LVH	14	7	26	13	<0.05
Concentric LVH	12	6	8	4	>0.05

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539 Table 6: Sensitivity, specificity, positive predictive value, negative predictive value
 540 and accuracy of ECG in comparison to Echo regarding diagnosis of LVH
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Criteria	Sensitivity %	Specificity %	Accuracy %	Positive predictive value	Negative predictive value
Sokolow-Lyon voltage	30	89	71	55	75
Cornell voltage	25	93	72	60	74
strain pattern	20	96	73	67	73

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560 Table 7. Gender difference in sensitivity, specificity of ECG

Criteria	Female			Male		
	Sensitivity %	Specificity %	p- value	Sensitivity %	Specificity %	p- value
Sokolow- Lyon voltage	35.9	87	0.007	19	90.5	0.2
Cornell voltage	28.2	90.9	0.032	19	95.2	0.062
strain pattern	20.5	93.5	0.013	19	98.4	0.013

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