IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 5 Ser.8 (May. 2021), PP 19-26
www.iosrjournals.org

A Correlation of Different Electrocardiographic Criteria, Biochemical Indices, and Echocardiographic Left Ventricular Hypertrophy in Adult Nigerian Hypertensives

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ABSTRACT

Background

Echocardiographic left ventricular hypertrophy (LVH) is a powerful risk factor for sudden death, coronary events, stroke, cardiac arrhythmias and heart failure. Routine echocardiographic assessment in all hypertensive patients is worth carrying out but this is a challenge in resource poor regions like sub-Saharan Africa. The need arises to determine the electrocardiographic (ECG) criteria with adequate sensitivity and specificity for detection of LVH and also correlates strongly with echocardiographic left ventricular mass index (LVMI).

Method

The study was a retrospective analysis of prospectively collected data carried out at the cardiology clinic of the Benue State University Teaching hospital (BSUTH) Makurdi, Nigeria. The case records of patients were utilized to obtain demographic, clinical, biochemical, ECG and echocardiographic data. The gold standard for diagnosis of LVH was echocardiographic LVMI. Pearson's correlation coefficient test was used to determine the relationship between ECG, biochemical indices and echocardiographic LVMI.

Results

A total of 252 hypertensive subjects were enrolled in the study. The prevalence of echocardiographic LVH was 7.9%. The ECG criteria with the highest sensitivity was the strain pattern (30%) while the Cornell criteria had the highest specificity (93.5%). Combination of these improved sensitivity when compared to other criteria. The strongest ECG correlate of LVMI was the Wolff criteria ($r = 0.364$; $p < 0.001$), followed closely by the Cornell criteria ($r = 0.360$; $p < 0.001$).

Conclusion

In resource poor communities without echocardiography, either or combination of the strain pattern and Cornell criteria is recommended for diagnosis of LVH by ECG.

KEY WORDS – Left ventricular hypertrophy, Hypertensive, electrocardiography, echocardiography, correlation, Nigeria.

Date of Submission: 07-05-2021 Date of Acceptance: 22-05-2021

I. INTRODUCTION

Left ventricular hypertrophy (LVH) in hypertension is associated with severe cardiovascular risk and adverse prognosis, especially in the black race[1.] Although for many years, LVH was thought to be a beneficial compensatory mechanism for maintaining wall stress in left ventricular (LV) pressure and volume overloads, epidemiologic studies using electrocardiography (ECG) and more recently echocardiography have shown that LVH is the most powerful risk factor for sudden death, stroke, ventricular arrhythmias, myocardial ischemia, coronary artery disease, and congestive heart failure[2,3]. The risk of these conditions is also raised even among normotensive individuals with LVH.

To date several non-invasive imaging modalities, such as echocardiography, magnetic resonance imaging (MRI), and computed tomography (CT), have been performed to detect LVH[3,4]. Echocardiography is the cheapest and most convenient of these three imaging modalities but the availability is still limited in resource poor regions like sub-Saharan Africa. Studies have shown that echocardiographically determined LVH is a sensitive indicator of LVH having been shown to increase cardiac risk[5] and correlate with necropsy findings[6].

Although it is desirable for all hypertensive patients to undergo echocardiography, resource constraints limiting availability may make this impossible in many African countries. In general however, ECG is a more

widely used diagnostic tool for assessment of LVH[7]. ECG is a non-invasive, convenient, inexpensive, and easily reproducible test, but the clinical utility of traditional, purely voltage-based ECG criteria for the detection of LVH is limited due to poor sensitivity[8]. Therefore criteria based on the combination of the voltage and QRS duration [9,10] or the strain pattern[11] have been developed and have improved the sensitivity of LVH detection by ECG in hypertensive populations.

Several studies have elucidated the relationship between LVH based on different electrocardiographic criteria and echocardiographic LVH[12,13,14] in hypertensive patients. However few studies in Africa have assessed the relationship between the ECG criteria based on combination of the voltage and QRS duration (voltage-duration product) and the left ventricular mass index (LVMI) in hypertensives.

The aim of our study is to determine the relationship between different ECG criteria namely Sokolow-Lyon voltage criteria (SV) [15], Sokolow-Lyon voltage duration product (SP)[10], Cornell voltage criteria (CV)[7], Cornell voltage-duration product (CP)[10], Wolff voltage criteria (WV)[16], Araoye voltage criteria (AV)[17] and strain pattern[11] with echocardiographic LVH in hypertensive patients seen in BSUTH Makurdi North Central Nigeria. The sensitivity and specificity of the various ECG criteria would be determined using echocardiographic LVH as the gold standard for diagnosis of LVH. The relationship between echocardiographic LVH and baseline clinical and laboratory indices will also be determined. This will help identify the criteria to be used to determine electrocardiographic LVH in resource poor settings where echocardiography is not available and the clinical and laboratory indices which can be modified to regress LVH.

II. MATERIALS AND METHOD

This was a hospital based retrospective analysis of prospectively collected data carried out at the Cardiology clinic of the Medical Outpatient Department (MOPD) of Benue State University Teaching Hospital (BSUTH) Makurdi. Eligible subjects were male and female hypertensive patients aged 18 years and older attending the MOPD clinic from 1st January 2014 to 31st December 2019. The diagnosis of hypertension was based on a systolic blood pressure (SBP) ≥ 140mmHg and/or a diastolic blood pressure (DBP) ≥ 90mmHg on at least two clinic visits or being on antihypertensive therapy[18].

Subjects with established symptoms of congestive heart failure, Diabetes Mellitus, renal failure, history or symptoms of ischemic heart disease, human immunodeficiency virus (HIV) infection were excluded from the study. Ethical clearance was obtained from the Research Ethics Committee of BSUTH.

The estimated minimum sample size was 238 hypertensive patients. This was based on the prevalence of echocardiographic LVH in hypertensive subjects in a Nigerian study which ranged from 30.9% to 56.9% [19]depending on the partition value used. A total of 252 subjects were eventually enrolled for the study.

Baseline clinical and demographic characteristics

Baseline, clinical and demographic characteristics were obtained from the subjects' case notes. These include age, gender, duration of hypertension, family history of hypertension, history of diabetes. The blood pressure (BP), body weight and height were obtained at the time of echocardiography and body mass index calculated using the formula: weight /height^2. The weight was obtained in kilograms using a weighing scale and the height with a stadiometer in meters. The body surface area was calculated using the formula of Dubois[20].

Laboratory indices

Laboratory indices such serum sodium, potassium, urea, creatinine at presentation were obtained from subjects' case notes. Serum creatinine levels were used to calculate the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) equation[21]

Electrocardiography

A resting ECG using Mediana ECG machine model YM4121 was recorded in the supine position by a trained ECG technician according to the recommendations of American Heart Association[22]. This was obtained from patients' case records and analysed. The presence of LVH by ECG was determined using Sokolow-Lyon voltage criteria (SV1 + RV5 or RV6 > 35mm)[15]; Cornell voltage(SV3 + RaVL > 28mm in men and > 20mm in women)[7]; Wolff voltage criteria (SV2 + RV5 > 35mm)[16]; and Code 1 of Araoye Voltage criteria (SV2 + RV6 > 40mm for males and > 35mm for females)[17].The Sokolow-Lyon voltage duration product (≥ 3674mm.msec in men and ≥ 3224mm.msec in women[10]); and the Cornell voltage duration product (≥ 2440ms.msec)[10] in addition to the presence of LV strain pattern defined as asymmetrical ST – segment depression ≥ 1mm with asymmetrically inverted T-wave in leads I, aVL, V5 and V6[11] were also used to define ECG LVH. Participants with ECG evidence of bundle branch block or myocardial infarction were excluded from the study at this point.

Echocardiography

All echocardiograms were performed by the three trained cardiologists using Siemens Sonoline G50 echocardiography machine model 7474922 and a 3.5 MHz transducer. This was performed with each subject in the lateral decubitus position. Measurements were made from leading edge to leading as recommended by the American Society of Echocardiography[23].

Two-dimensionally guided M-mode end- diastolic measurements of the LV interventricular septum (IVSd), LV internal diameter (LVIDd), posterior wall thickness (PWTd) were obtained. The LV end systolic volume (LVESV) and LV end-diastolic volume (LVEDV), ejection fraction (EF) and fractional shortening (FS) were estimated using Teichholz formula[24]. Other parameters obtained included left atrial (LA) diameter and aortic root (AO) diameter. LV diastolic function was assessed using transmitral flow velocities. Participants with evidence of regional wall motion abnormalities were excluded from the study at this point.

The LV mass was calculated using the formula introduced by Devereux et. al[25] and indexed for body surface area to obtain the LVMI. Left ventricular hypertrophy was diagnosed when LVMI was > 134g/m^2 in men and > 110g/m^2 in women[6,26]. Relative wall thickness (RWT) was calculated as 2xPWTd/LVIDd. Increased RWT was present when RWT >0.44[27].

Statistical analysis

Statistical analysis was carried out using the Statistical Packages for Social Sciences (SPSS) version 23.0 (SPSS Inc, Chicago, IL, USA). Continuous variables were presented as mean and standard deviation and compared using student's t-test. Categorical variables were expressed as percentages and compared using chi-square test. Pearson's correlation coefficient was used to test the relationship between ECG, clinical and laboratory indices with echocardiographic LVH (LVMI). Values of $p < 0.05$ were considered statistically significant.

III. RESULTS

Baseline and biochemical characteristics of the study population by gender

A total of 252 subjects were enrolled in the study. This consisted of 125 males and 127 females. The mean age of the population was 52.38±12.42. There were no significant differences in the mean age or systolic blood pressure (SBP) of males and females. However the mean diastolic blood pressure (DBP), weight, height, body mass index (BMI), and body surface area (BSA) were significantly higher in the males than females. Furthermore, the mean serum sodium, serum urea, serum creatinine, total cholesterol (TC), triglycerides (TG), and high density lipoprotein cholesterol (HDL-C) were significantly higher in males than females. This is shown in table 1.

Echocardiographic characteristics of the study population by gender

There were significant differences in the mean LA, LVIDd, LVM, EF and E/A ratio between males and females. There were no significant differences in the mean IVSd, PWTd and LVMI between males and females. This is shown in table 2.

The prevalence of echo LVH and left ventricular geometric pattern of the study population

The prevalence of echocardiographic LVH in the study population was 7.9%. Their left ventricular geometric pattern was as follows: 40.5% had normal geometry, 51.6% has concentric remodelling, 1.6% had eccentric hypertrophy and 6.3% had concentric hypertrophy. This is shown in figure 1.

Sensitivity, specificity and predictive values of the various ECG criteria for detecting LVH

Using echocardiographic LVH as the gold standard for diagnosis of LVH, the ECG criteria with the highest sensitivity at detecting LVH was the strain pattern with a sensitivity of 30.0%. The criteria with the highest specificity was the Cornell criteria with a specificity of 93.5%. The highest positive predictive value was demonstrated by the Cornell criteria also being 20.0% and the highest negative predictive value was demonstrated by the strain pattern being 92.9%. These are shown in table 3. Combination of the strain pattern and Cornell criteria improved sensitivity (22.5%) compared to other criteria (15%).

Correlation between ECG voltage criteria, clinical and biochemical indices with LVMI

There were significant correlations between all ECG voltage criteria with LVMI and the strongest correlation was with the Wolff criteria ($r = 0.364$; $p < 0.001$). This was followed closely by the Cornell criteria ($r = 0.360$; $p < 0.001$). LVMI correlated significantly with SBP and DBP and negatively with BMI. There were no correlations between biochemical indices and echo LVH. This is shown in table 4.

IV. DISCUSSION

The results of this study showed that the prevalence of echo LVH in the population was 7.9% and that the most prevalent abnormal geometric pattern in the population was concentric remodelling seen in 51.6% of the population, followed by concentric hypertrophy seen in 6.3% of the population. The results also showed that using echocardiography as gold standard for the detection of LVH, the strain pattern was the most sensitive ECG criteria with a sensitivity of 30.0% to detect LVH and the Cornell criteria was the most specific with a specificity of 93.5% for LVH detection. The strongest correlation between ECG voltage criteria and LVMI was demonstrated by the Wolff criteria ($r = 0.364$; $p < 0.001$) followed closely by the Cornell criteria ($r = 0.360$; $p < 0.001$). There were significant correlations between SBP, DBP and LVMI. There were no correlations between LVMI and biochemical indices.

The prevalence of echo LVH in patients with essential hypertension in various studies range from 12% to70% [19,28,29,30] depending to a large extent on the criteria used for diagnosis. Several criteria, based on LV mass indexed to weight, height, height^2 or body surface area have been proposed [26]. The low prevalence of echo LVH in our study was probably due to the sex-specific cut off value we have used of $>134 g/m^2$ in men and $> 110 g/m^2$ in women. These were used because the prognostic value of these figures has been clearly shown in previous reports [6,26].

Echocardiographally determined LVH has been shown in a prospective study to increase the risk of new coronary events, new stroke and new congestive heart failure more than twice the ability of ECG derived LVH [31]. Echocardiographic LVH was also been shown to be 4.3 times more sensitive in predicting new coronary events and 4.0 times more sensitive in predicting new stroke than ECG LVH [31].

The most prevalent abnormal LV geometric pattern in our study was concentric remodelling, followed by concentric hypertrophy and then eccentric hypertrophy. Echocardiographic concentric remodelling has been shown to increase cardiovascular events 2.56 times compared with normal echocardiographic LV geometry [32]. In a study where echocardiograms were obtained in 9,771 patients older than 70 years with a normal LV ejection fraction, all-cause mortality was 15.9% in patients with concentric LVH, 15.5% in concentric remodelling, 13.7% in eccentric LVH and 11.5% in normal LV geometry [33].

Echocardiography is more sensitive than ECG in diagnosing LVH. In a blinded prospective study of 476 patients aged 62 years and older by Aronow et al[34] and Casale et al[7], echocardiographic LVH was 67% to 71% present in 167 patients (35%) [34]. The sensitivity of 5 different ECG criteria in diagnosing LVH varied from 12% to 29%, the specificity from 93% to 96%, the positive predictive value from 62% to 71%, and the negative predictive value from 67% to 71% [34]. The Cornell criteria[7] had the highest sensitivity (29%) in predicting LVH, a specificity of 93%, positive predictive value of 69%, and a negative predictive value of 71% [34].

The findings of Aronow et al.[33] and Casale et al.[7] are similar to that of our study where sensitivity of the various ECG criteria ranged from 15% to 30% with the Cornell criteria having the highest specificity of 93.5%. However it differed from our study in that the strain pattern had the highest sensitivity in our study. This finding in our study concerning the strain pattern agrees with that of Adegoke and Adebiyi[14] who found that ECG LVH identified using the strain pattern was associated with higher prevalence of echo LVH than other criteria [14].

Our study revealed that amongst the ECG voltage criteria, the Wolff criteria had the strongest correlation with LVMI ($r = 0.364$) followed by the Cornell criteria ($r = 0.360$). Our findings differ from that of Nkado et al. [13]who found the Araoye voltage criteria to have the strongest correlation ($r = 0.360$) in hypertensive males only. There were no correlations between LVMI and biochemical indices in our study. Data from the LIFE study (Lorsartan Intervention For Endpoint reduction in hypertension) revealed a close correlation between microalbuminuria and ECG-determined LVH [35].

It is well established that single ECG LVH criteria have low sensitivity and high specificity [34]. A combination of the Cornell criteria and the strain pattern improved sensitivity in our study. Some studies have suggested that combination of the Cornell product and Sokolow-Lyon voltage criteria increased sensitivity for the detection of LVH and coexistence of these two criteria further improved risk prediction for future cardiovascular events and all-cause mortality [36].

Loss of weight, reduction in sodium intake and aggressive blood pressure control are effective in reducing echocardiographic LVH [28,37]. There were significant correlations between SBP, DBP and echocardiographic LVMI in our study. However it showed a negative correlation with BMI and no correlations with biochemical indices. Reduction in sodium intake reduces LVH by reducing blood pressure levels. Results of a meta-analysis including 109 treatment studies consisting of 2,357 patients with hypertension revealed that the angiotensin-converting enzyme inhibitors were the most effective antihypertensive medications in reducing left ventricular mass[38].

In conclusion, since the strain pattern had the highest sensitivity for LVH detection and the Cornell criteria had the strongest specificity with next to strongest correlation with LVMI in this study, either or a

combination of both criteria is recommended for detection of LVH in resource poor countries where echocardiography is not available.

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RESULTS

Table 1 – Baseline and biochemical characteristics of the study population by gender

Characteristic	All subjects (n=252)	Males (n=125)	Females (n=127)	p-value
Age (years)	52.38 ± 12.42	53.74 ± 12.68	51.04 ± 12.06	0.840
SBP (mmHg)	146.71 ± 22.03	149.15 ± 22.51	144.30 ± 21.35	0.800
DBP (mmHg)	92.52 ± 16.00	95.36 ± 18.34	89.73 ± 12.35	0.005*
Weight (kg)	81.13 ± 15.70	86.85 ± 14.43	75.50 ± 14.89	< 0.001*
Height (m)	1.65 ± 0.06	1.69 ± 0.05	1.62 ± 0.06	< 0.001*
BMI (kg/m^2)	29.67 ± 5.45	30.6 ± 5.25	28.75 ± 5.50	0.006*
BSA (m^2)	1.88 ± 0.18	1.97 ± 0.15	1.80 ± 0.17	< 0.001*
Serum Sodium (mmol/L)	138.30 ± 5.83	139.23 ± 5.44	137.38 ± 6.07	0.011*
Serum Potassium (mmol/L)	4.05 ± 0.88	4.04 ± 0.62	4.06 ± 1.08	0.881
Serum Urea (mmol/L)	5.12 ± 3.31	6.02 ± 3.83	4.25 ± 2.41	< 0.001*
Serum Creatinine (µmol/L)	97.05 ± 37.39	106.04 ± 38.87	88.20 ± 33.74	< 0.001*
eGFR	88.77 ± 29.87	92.17 ± 32.59	85.42 ± 26.62	0.073
Total Cholesterol (mmol/L)	4.45 ± 1.13	4.64 ± 1.08	4.26 ± 1.15	0.007*
Triglycerides (mmol/L)	1.22 ± 0.61	1.40 ± 0.48	1.05 ± 0.67	< 0.001*
HDL-C (mmol/L)	0.86 ± 0.31	0.72 ± 0.22	0.99 ± 0.33	< 0.001*
LDL-C ((mmol/L)	3.29 ± 2.32	3.43 ± 0.98	3.15 ± 3.11	0.335

***= statistically significant; SBP = systolic Blood Pressure; DBP = Diastolic Blood Pressure; eGFR = estimated Glomerular Filtration Rate; HDL-C = High Density Lipoprotein Cholesterol; LDL-C = Low Density Lipoprotein Cholesterol.**

Table 2 – Echocardiographic Characteristics of the study population by gender

Characteristic	All subjects (n=252)	Males (n=125)	Females (n=127)	p-value
LA(cm)	3.57 ± 0.67	3.69 ± 0.67	3.46 ± 0.64	0.006*
IVSd(cm)	1.38 ± 0.40	1.40 ± 0.44	1.34 ± 0.35	0.280
LVIDd (cm)	4.62 ± 0.98	5.02 ± 1.01	4.21 ± 0.77	<0.001*
PWTd (cm)	1.20 ± 0.75	1.25 ± 0.97	1.16 ± 0.44	0.362
LVM (g)	181.52 ± 36.19	192.39 ± 41.97	170.82 ± 25.35	< 0.001*
LVMI (g/m^2)	97.12 ± 20.52	98.67 ± 24.59	95.59 ± 15.47	0.234
EF (%)	59.15 ± 15.21	54.92 ± 15.02	63.30 ± 14.27	< 0.001*
E/A ratio	1.08 ± 0.54	0.99 ± 0.52	1.16 ± 0.55	0.010*

*** =statistically significant; LA = left atrial diameter; IVSD = interventricular septal diameter in diastole; LVIDd; left ventricular internal diameter in diastole; PWTd = posterior wall thickness in diastole; LVM = left ventricular mass; LVMI = left ventricular mass index; E = early left ventricular filling phase; A = late left ventricular filling phase.**

Table 3 – Sensitivity, Specificity, Positive and Negative Predictive values of the various electrocardiographic criteria

Electrocardiographic criteria	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Sokolow-Lyon voltage	15.0	89.2	12.0	92.4
Cornell voltage	15.0	93.5	20.0	92.7
Wolff voltage	15.0	83.6	7.3	91.9
Araoye voltage	15.0	89.2	12.0	92.4
Sokolow-Lyon voltage-duration product	15.0	89.2	12.0	92.4
Cornell voltage-duration	15.0	89.2	12.0	92.4

product				
Strain pattern	30.0	78.4	10.7	92.7
Combined Cornell voltage and Strain Pattern	22.5	87.8	14.0	92.7

Table 4 – Correlation between the various electrocardiographic voltage criteria, clinical and biochemical indices with left ventricular mass index.

Parameter	**R**	**p-value**
Sokolow-Lyon voltage	0.335	< 0.001*
Cornell voltage	0.360	< 0.001*
Wolff voltage	0.364	< 0.001*
Araoye voltage	0.337	< 0.001*
Sokolow-Lyon voltage-duration product	0.318	< 0.001*
Cornell voltage-duration product	0.340	< 0.001*
SBP	0.208	0.001*
DBP	0.236	<0.001*
BMI	-0.279	<0.001*
Serum Sodium (mmol/L)	-0.107	0.091
Serum Potassium (mmol/L)	0.051	0.416
Serum Urea (mmol/L)	0.101	0.111
Serum Creatinine (µmol/L)	0.052	0.409
eGFR	-0.069	0.278
Total Cholesterol (mmol/L)	-0.120	0.058
Triglycerides	-0.046	0.471
HDL-C	0.083	0.187
LDL-C	-0.082	0.195

***=statistically significant; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; eGFR = estimated glomerular filtration rate; HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol.**

Figure 1 – Left ventricular geometric pattern of the study population