e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 1297-1302

Original Research Article

Study to Evaluate ECG Markers for Detection of Left Ventricular Systolic Dysfunction.

Amit Kumar[1], Dhananjay Singh Shekhawat[2] ,Chandra Bhan Meena[3]

[1]Senior Resident, Department of Cardiology, S.M.S. Medical College. Jaipur

[2]Assistant Professor, Department of Cardiology, SMS Medical College, Jaipur

[3]Senior Professor, Department of Cardiology, S.M.S. Medical College. Jaipur

Received: 12-11-2023 / Revised: 18-12-2023 / Accepted: 22-01-2024

Corresponding Author: Dhananjay Singh Shekhawat

Conflict of interest: Nil

Abstract:

Background: Early diagnosis of severe LV dysfunction with echocardiography improves outcome. But in developing country like India echocardiography and other advance imaging are not available in peripheral centre. We selected a combination of electrocardiogram (ECG) markers for screening of individuals with severely reduced LVEF.

Methods: A single centre crossectional observational study was conducted including 160 cases with LVEF <35% and 160 control with LVEF >35% . Subjects were evaluated for prevalence of conventional ECG markers and association of nine additional ECG markers with LV dysfunction.

Results: Conventional ECG abnormalities LBBB observed in 20% case and 5% control with significance(p=0.001) , atrial fibrillation observed in 11.8% case and 9.3% control (p=0.47) with no significance. At least one major ECG abnormality was observed in 46(28.75%) of cases with LVEF ≤35% and 22(13.75%) control with LVEF >35% ($p < 0.002$). Abnormal > 4 ECG parameter was observed in 15(9.37%) cases with LVEF ≤35% and 4(2.5%) control with LVEF >35% ($p < 0.016$). The presence of any one of these abnormalities for predicting LVEF ≤35% produced a sensitivity of 83%, specificity of 55%. Except delayed QRS transition and delayed intrinsicoid deflection rest other parameter were significantly associated with LVEF ≤35 ($p < 0.05$)

Conclusions: An expanded panel of nine obtained ECG markers correlated strongly with severely reduced LVEF. This electrical surrogate score could facilitate screening of severely reduced LVEF, and warrants further evaluation.

Keywords: echocardiography, electrocardiography, left ventricular ejection fraction, left ventricular systolic dysfunction.

Introduction

The heart is an electric generator and electromechanical pump. [1] Electric excitation initiates mechanical contraction, orchestrates excitation– contraction coupling, and coordinates myocardial pumping. Changes in the frequency, regularity, and order4 of cardiac electric excitation can cause electric heterogeneity, dyssynchrony, ventricular dysfunction, and ultimately clinical pump failure. [2–4] While inherited long QT syndrome (LQTS) has historically been considered a purely electrical disease, echocardiographic studies over the past two decades have demonstrated a crude but replicable relationship between a prolonged QT interval and abnormal mechanical function. [5] Observational data paired with animal studies suggest that electrical transmural dispersion of repolarization, manifest on the surface electrocardiogram (ECG), can be associated with mechanical dispersion of left ventricular relaxation observed using comprehensive echocardiography. [6]. Several studies have shown a positive association between LV size (diameter, volumes, and length) and QRS duration. [7,8,9] Agreement between ECG-LVH and LV mass has been extensively studied. [10] ECG-LVH predicts cardiovascular outcomes independent of LV mass. [11,12,13] There are no specific ECG features unique to LV dysfunction, however the ECG is usually NOT normal.

The most common ECG abnormalities are those associated with atrial and ventricular hypertrophy — typically, left sided changes are seen but there may be signs of biatrial or biventricular hypertrophy. Interventricular conduction delays (eg. LBBB) occur due to cardiac dilatation. Diffuse myocardial fibrosis may lead to *reduced* voltage QRS complexes, particularly in the limb leads. There may be a discrepancy of QRS voltages with signs of

hypertrophy in V4-6 and relatively low voltages in the limb leads. Abnormal Q waves are most often seen in leads V1 to V4 and may mimic the appearance of a myocardial infarction ("pseudoinfarction" pattern). Left atrial enlargement -> may progress to atrial fibrillation, Biatrial enlargement **,**Left ventricular hypertrophy or biventricular enlargement**,**Left bundle branch block (RBBB can also occur), Poor R-wave progression with QS complexes in V1-4 ("pseudo-infarction" pattern),Frequent ventricular ectopics and ventricular bigeminy (seen with severe DCM), Ventricular dysrhythmias (VT / VF).

Heart failure (HF) with severely reduced left ventricular ejection fraction LVEF ≤35% remains a major public health problem in the India, with an average 5-year mortality of 50% due to pump failure or sudden cardiac death [14]. Severely reduced LVEF is detected by cardiac imaging, mostly echocardiography, but due to practical and cost-effectiveness considerations, broad deployment of imaging tools for screening of asymptomatic patients in the community is not viable. Myocardial electrical remodeling is a consistent feature of the HF syndrome and manifests as abnormalities in the 12-lead electrocardiogram (ECG), reported in a variety of patient populations. However, published studies of the association between electrical remodeling with left ventricular (LV) dysfunction are relatively small and have focused mainly on a limited number of individual ECG variables, largely atrial fibrillation, left bundle branch block (LBBB), and ventricular pacing.

Material and Methods

This study is a single centre crossectional observational study with study period of 18 months and was conducted in department of cardiology, SMS Medical college Jaipur(Rajasthan). Patients were selected randomly for sample size of 160 case. Aim of the study is to identify combination of electrocardiogram(ECG) markers for severely reduced LVEF.

Patients with LVEF ≤35% identified from the echocardiography were included in the study. ECGs with evidence of acute ST-elevation MI and ventricular paced rhythms were excluded. Patient were evaluated for major ECG abnormalities (AF and LBBB) and expanded panel of all nine of abnormal ECG markers associated with reduced ejection fraction.

The nine parameters of the expanded ECG panel are the following:

1. heart rate >85 bpm
2. P-wave duration >110 ms
3. PR interval >200 ms
4. QRS duration >110 ms
5. QTc interval(Bazett's correction ≥460 ms for men and and ≥470 ms for women).
6. frontal QRS-T angle >90°; (calculated as the absolute difference between the frontal QRS axis and T-wave axis with values 0°−180°)
7. delayed QRS transition zone (R-wave amplitude less than S-wave amplitude in lead V4)
8. delayed intrinsicoid deflection (defined as R-peak time ≥50 ms in lead V5 or V6)
9. left ventricular hypertrophy (LVH; by Cornell voltage).

In addition 160 age and sex matched healthy control with normal ejection (EF> 50%)fraction were looked for major and expanded panel of ECG marker.

Statistical analyses were performed with SPSS 2021 version. Chi-square tests were used for univariate associations, and automated stepwise logistic regression to test the multivariable-adjusted association of each ECG marker, with LVEF ≤35% as the outcome and the nine individual ECG markers as predictors as the independent variables. Logistic regression models were calculated, one with ECG variables as continuous predictors if appropriate, and the second model with all ECG variables dichotomized. Continuous ECG variables will be dichotomized at clinically accepted cut-points: heart rate >85 bpm; QRS duration >110 ms; QTc interval ≥460 ms for men and ≥470 ms for women; QRS-T angle >90°; PR interval >200 ms; and P-wave duration >110 ms.

Observation

We enrolled 160 patients with LVEF <35% and 160 healthy age and sex matched control in this crossectional observational study .

Table 1: Demographics and electrocardiogram parameters based on left ventricular ejection fraction.

Demographics	**LVEF ≤ 35% n= 160**	**LVEF ≥ 35% n= 160**	**p -value**
Age	44.2±13.8	44.8±12.9	0.65
Female sex n(%)	26(16.25%)	22(13.75%)	0.44
BMI	22.7±2.7	23±2.7	0.42
Conventional abnormal ECG finding.			
Left bundle branch block (LBBB) (n,%)	20%	5%	0.001
Atrial fibrillation(n,%)	11.87	9.3%	0.47

Table 2: Univariate analysis of expanded panel of electrocardiographic variables in subset without conventional ECG abnormalities .

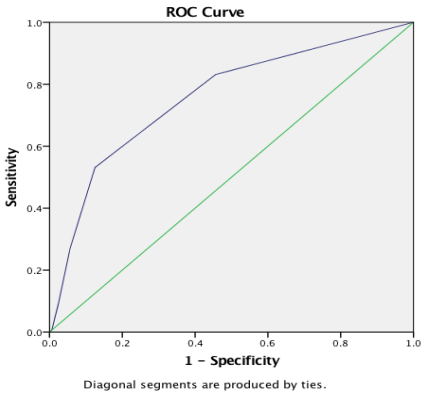
variables	LVEF ≤ 35% n= 160	LVEF ≥ 35% n= 160	p- value
Heart rate >85 bpm	42.5%	24.37%	0.009
QRS >110 ms	35%	7.5%	0.001
Prolonged QTc ≥460 ms men and ≥470 ms women	46.25%	10%	0.001
QRS-T angle >90°	20%	7.5%	0.002
Delayed QRS transition	18.75%	11.8%	0.06
Delayed intrinsicoid deflection	10%	3.75%	0.19
Left ventricular hypertrophy (Cornell voltage)	21.87%	12.5%	0.04
PR >200 ms	10%	1.87%	0.05
P-wave >110 ms	35%	6.8%	0.001

Table 3: Multivariate logistic regression analysis of expanded panel of electrocardiographic variables.

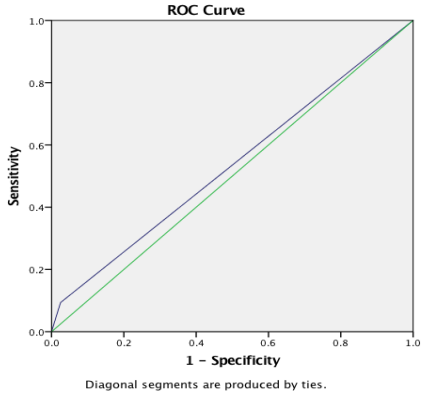
variables	Odds ratio	95% confidence interval for odds ratio	p- value
Heart rate >85 bpm	1.996	1.108-3.594	0.021
QRS >110 ms	6.491	3.059-13.776	0.001
Prolonged QTc ≥460 ms men and ≥470 ms women	8.335	3.993-17.397	0.001
PR >200 ms	3.243	0.546-19.252	0.195
P-wave >110 ms	7.732	3.456-17.298	0.001
Delayed QRS transition	0.388	0.149-1.005	0.051
QRS-T angle >90°	2.549	0.987-6.581	0.053

Table 4: Comparison of abnormal >1 ECG parameter and >4 ECG parameter with ROC curve analysis.

	Case N=160	Control N=160	p-value	ROC curve area	Asymptotic 95% confidence interval (ROC curve)
Abnormal > 1 ECG parameter	**46(28.75%)**	**22(13.75%)**	**0.002**	**0.758**	**0.704-0.811**
Abnormal > 4 ECG parameter	**15(9.37%)**	**4(2.5%)**	**0.016**	**0.534**	**0.471-0.598**



Abnormal > 1 ECG parameter



Abnormal > 4 ECG parameter

Observation:

We enrolled 160 cases with LVEF < 35% and 160 age and sex matched control with LVEF >35% control in this single centered cross-sectional observational study. Anthropomorphic and clinical characteristics of the study group are presented in Table 1. No significant differences were noted in age, sex and BMI between the case and control. Conventional ECG abnormalities LBBB observed in 20% case and 5% control with significance (p=0.001), atrial fibrillation observed in 11.8% case and 9.3% control (p=0.47) with no significance. So the presence of LBBB was significantly associated with LVEF ≤35% while AF was not associated with lower ejection fractions . At least one major ECG

abnormality was observed in **46(28.75%)** of cases with LVEF ≤35% and **22(13.75%)** control with LVEF >35% ($p < 0.002$) (Table 4). The presence of any one of these abnormalities for predicting LVEF ≤35% produced a sensitivity of 83%, specificity of 55%. In univariate comparisons of all nine of the expanded ECG parameters except delayed QRS transition and delayed intrinsicoid deflection rest other parameter were significantly associated with LVEF ≤35 ($p < 0.05$) (Table 2). In the multivariable model, heart rate, QTc interval, QRS duration, prolonged P wave and LVH remained independently associated with LVEF ≤35%, while prolonged PR, QRS-T angle delayed QRS transition zone and delayed intrinsicoid deflection interval were not significant (Table 3).

Based on the five statistically significant ECG markers, an unweighted expanded ECG panel sum was constructed ranging from ≥4 abnormal markers. Abnormal > 4 ECG parameter was observed in **15(9.37%)** of cases with LVEF ≤35% and **4(2.5%)** control with LVEF >35% ($p < 0.016$). There was no significant interaction by sex with the ECG panel sum ($p = 0.44$). The expanded ECG panel was significantly associated ($p < 0.001$) with decreasing LVEF in the validation population. Among patient with expanded panel of ECG parameter those with QTc prolongation had more LV dysfunction (OR-8.335 95% CI(3.993-17.397)) followed by p wave duration(OR-7.732 95% CI(3.456-17.298)) and QRS duration(OR-6.491 95% CI(3.059-13.776)).

Discussion

This study evaluated association of different sets of ECG marker apart from conventional ECG markers in identifying LV dysfunction. Among patients with major ECG abnormalities that are conventionally associated with LVEF, such as 11.87% atrial arrhythmias and 20% LBBB had LVEF ≤35%. In the remaining patients without conventional ECG abnormalities, five specific ECG parameters (heart rate, QTc interval, QRS duration, prolonged P wave and LVH) remained independently associated with LVEF ≤35%. Case with ≥4 abnormal ECG markers correlated strongly with LVEF ≤35% and in individuals with one or no abnormal ECG markers, severely reduced LVEF was not a common finding. Published studies have reported a correlation between abnormal ECG diagnoses such as atrial fibrillation, LBBB, ventricular paced rhythms and reduced LVEF; and in clinical practice, these findings generally prompt clinicians to evaluate the LVEF. [15]

However, a large subgroup of patients will have reduced LVEF in the absence of these conventionally accepted ECG markers. There is need of improvement for identification of patients with severely reduced LVEF.

The association between several individual ECG markers and LVSD has been previously reported. For example, increased resting heart rate has been associated with reduced LVEF even in asymptomatic individuals in the general population. [16] Several studies among HF patients and other populations

have linked QRS prolongation with decreased LV systolic function. [17] However, early attempts to directly estimate LV function using measures of QRS morphology from the ECG had limited success. [18] The more-specific depolarization measures included in the expanded panel, that is, delayed intrinsicoid deflection and QRS transition zone, were individually associated with low LVEF .[19,20]. Prolonged QTc-interval and wide QRS-T angle have been associated with LV dysfunction. [21,22]. There are very few study in which combination of all ECG parameter of LV dysfunction has been analyzed.

In this study, after excluding patients with major ECG abnormalities conventionally associated with LV dysfunction, 9.37% of patients had ≥4 abnormal ECG findings. This study, in accordance with previous reports (Nielsen et al.), suggests that a normal ECG virtually excludes severe LV dysfunction. [23]. All these findings imply that a markedly abnormal electrical profile, even in the absence of other conventionally used major ECG abnormalities, is strongly correlated

with LV systolic function. There are factors that can explain the relationship between increasing number of ECG abnormalities and decrease in LVEF. Pathologic LV remodeling in ischemic or non-ischemic cardiomyopathy has electrical components that are reflected as abnormalities in cardiac conduction and myocardial depolarization/ repolarization markers.[17,21]. Structural and electrical remodeling contribute independently to risk of morbidity and mortality. [24] Manifestation of the HF syndrome is abnormal autonomic remodeling, reflected by increased resting heart rate. [25]

Conclusions

Apart from conventional ECG marker of LV dysfunction i.e atrial fibrillation and LBBB, an expanded panel of nine obtained ECG markers correlated strongly with severely reduced LVEF. This electrical surrogate score could facilitate screening of severely reduced LVEF, and warrants further evaluation.

References

1. Bers DM. Cardiac excitation-contraction coupling. Nature. 2002; 415:198– 205.
2. Spinale FG, Fulbright BM, Mukherjee R, Tanaka R, Hu J, Crawford FA, Zile MR. Relation between ventricular and myocyte function

with tachycardiainduced cardiomyopathy. Circ Res. 1992; 71:174–187.
3. Huizar JF, Kaszala K, Potfay J, Minisi AJ, Lesnefsky EJ, Abbate A, Mezzaroma E, Chen Q, Kukreja RC, Hoke NN, Thacker LR II, Ellenbogen KA, Wood MA. Left ventricular systolic dysfunction induced by ventricular ectopy: a novel model for premature ventricular contraction-induced cardiomyopathy. Circ Arrhythm Electrophysiol. 2011; 4:543–549.
4. Sweeney MO, Prinzen FW. Ventricular pump function and pacing: physiological and clinical integration. Circ Arrhythm Electrophysiol. 2008; 1:127–139.
5. Nador F, Beria G, De Ferrari GM, Stramba-Badiale M, Locati A, Lotto A, et al. Unsuspected echocardiographic abnormality in the long QT syndrome. Diagnostic, prognostic, and pathogenetic implications. Circulation 1991 Oct; 84(4):1530–42.
6. Belardinelli L, Dhalla A, Shryock J. Abnormal left ventricular relaxation in patients with long QT syndrome. Eur Heart J 2009 Nov;30(22): 2813–4.
7. Dhingra R, Ho Nam B, Benjamin EJ, Wang TJ, Larson MG, D'Agostino RB Sr, Levy D, Vasan RS. Cross-sectional relations of electrocardiographic QRS duration to left ventricular dimensions: the Framingham Heart Study. J Am Coll Cardiol. 2005; 45:685–689.
8. Chan DD, Wu KC, Loring Z, Galeotti L, Gerstenblith G, Tomaselli G, Weiss RG, Wagner GS, Strauss DG. Comparison of the relation between left ventricular anatomy and QRS duration in patients with cardiomyopathy with versus without left bundle branch block. Am J Cardiol. 2014; 113:1717–1722.
9. Stewart RA, Young AA, Anderson C, Teo KK, Jennings G, Cowan BR. Relationship between QRS duration and left ventricular mass and volume in patients at high cardiovascular risk. Heart. 2011; 97:1766–1770.
10. Jain A, Tandri H, Dalal D, Chahal H, Soliman EZ, Prineas RJ, Folsom AR, Lima JA, Bluemke DA. Diagnostic and prognostic utility of electrocardiography for left ventricular hypertrophy defined by magnetic resonance imaging in relationship to ethnicity: the Multi-Ethnic Study of Atherosclerosis (MESA). Am Heart J. 2010; 159:652–658.
11. Patel N, O'Neal WT, Whalen SP, Soliman EZ. Electrocardiographic left ventricular hypertrophy predicts atrial fibrillation independent of left ventricular mass. Ann Noninvasive Electrocardiol. 2017; 22:1–5.
12. Almahmoud MF, O'Neal WT, Qureshi W, Soliman EZ. Electrocardiographic versus echocardiographic left ventricular hypertrophy in prediction of congestive heart failure in the elderly. Clin Cardiol. 2015; 38:365–370.
13. Bacharova L, Chen H, Estes EH, Mateasik A, Bluemke DA, Lima JA, Burke GL, Soliman EZ. Determinants of discrepancies in detection and comparison of the prognostic significance of left ventricular hypertrophy by electrocardiogram and cardiac magnetic resonance imaging. Am J Cardiol. 2015; 115:515–522.
14. Roger, V. L., Weston, S. A., Redfield, M. M., Hellermann-Homan, J. P., Killian, J., Yawn, B. P., & Jacobsen, S. J. Trends in heart failure incidence and survival in a community-based population. JAMA, 2004; 292: 344–350.
15. Baker, D. W., Bahler, R. C., Finkelhor, R. S., & Lauer, M. S. Screening for left ventricular systolic dysfunction among patients with risk factors for heart failure. American Heart Journal, 2003; 146: 736–740.
16. Opdahl, A., Ambale Venkatesh, B., Fernandes, V. R., Wu, C. O., Nasir, K., Choi, E. Y., … Lima, J. A. Resting heart rate as predictor for left ventricular dysfunction and heart failure: Mesa (multi-ethnic study of atherosclerosis). Journal of the American College of Cardiology, 2014;63: 1182–1189.
17. Ilkhanoff, L., Liu, K., Ning, H., Nazarian, S., Bluemke, D. A., Soliman, E. Z., & Lloydjones, D. M. Association of qrs duration with left ventricular structure and function and risk of heart failure in middle-aged and older adults: The multi-ethnic study of atherosclerosis(mesa). European Journal of Heart Failure, 2012; 14: 1285–1292.
18. Young, S. G., Abouantoun, S., Savvides, M., Madsen, E. B., & Froelicher, V. Limitations of electrocardiographic scoring systems for estimation of left ventricular function. Journal of the American College of Cardiology, 1983; 1:1479–1488.
19. Darouian, N., Narayanan, K., Aro, A. L., Reinier, K., Uy-Evanado, A., Teodorescu, C., Chugh, S. S. Delayed intrinsicoid deflection of the qrs complex is associated with sudden cardiac arrest. Heart Rhythm: the Official Journal of the Heart Rhythm Society, 2016; 13: 927–932.
20. Aro, A. L., Phan, D., Teodorescu, C., Uy-Evanado, A., Reinier, K., Gunson, K. Chugh, S. S. Cardiac structural and functional profile of patients with delayed qrs transition zone and sudden cardiac death. Europace, 2017;19: 629–635.
21. Davey, P. Qt interval lengthening in cardiac disease relates more to left ventricular systolic dysfunction than to autonomic function. European Journal of Heart Failure, 2000;2: 265–271.
22. Pavri, B. B., Hillis, M. B., Subacius, H., Brumberg, G. E., Schaechter, A., Levine, J. H., & Kadish, A. Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation I. Prognostic value and temporal behavior of the planar

qrs-t angle in patients with nonischemic cardiomyopathy. Circulation, 2008;117, 3181–3186.
23. Nielsen, O. W., Hansen, J. F., Hilden, J., Larsen, C. T., & Svanegaard, J. Risk assessment of left ventricular systolic dysfunction in primary care: Cross sectional study evaluating a range of diagnostic tests. BMJ (Clinical Research ed.), 2000;320: 220–224.
24. Aro, A. L., & Chugh, S. S. Clinical diagnosis of electrical versus anatomic left ventricular hypertrophy: Prognostic and therapeutic implications. Circulation: Arrhythmia and Electrophysiology, 2016;9: e003629.
25. Floras, J. S. Sympathetic nervous system activation in human heart failure: Clinical implications of an updated model. Journal of the American College of Cardiology, 2009;54, 375–385.