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Lead one ratio: A new electrocardiogram marker for cardiac resynchronization therapy response

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Original Article

Abstract

BACKGROUND: Wider QRS duration and presence of left bundle branch block (LBBB) predict better cardiac resynchronization therapy (CRT) response. Despite strict patient selection, one-third of patients have a sub-optimal response. We aim to evaluate the impact of lead one ratio (LOR) on CRT response.

METHODS: We enrolled 93 patients receiving CRT from August 2016 to August 2019. Pre-implant 12-lead electrocardiogram (ECG) was recorded, and LOR was derived by dividing the maximum positive deflection of QRS complex in ECG lead I by the maximum negative deflection in lead I; cut-off value of 12 was used to divide the cohort into two groups. Patients were followed for 6 months, and outcomes were compared for CRT response, New York Heart Association (NYHA) class improvement, all-cause mortality, and heart failure (HF) hospitalization events.

RESULTS: At the end of 6-month follow-up, LOR ≥ 12 was associated with significantly better CRT response (75.76% vs. 51.85% in LOR < 12, P = 0.02), lower mortality per 100 patient-years (9.09 vs. 14.81 in LOR < 12, P = 0.012), and more improvement in HF symptoms (NYHA improvement) (78.79% vs. 55.56% in LOR < 12, P = 0.02). Patients with LOR < 12 had more HF hospitalization events (2.04 vs. 1.81 episodes in LOR ≥ 12, P = 0.029) and less QRS narrowing (Δ5.74 ± 2.09 vs. Δ7.10 ± 3.97 ms in LOR ≥ 12, P = 0.01). QRS duration and LBBB morphology were predictors of response in both groups of patients.

CONCLUSION: LOR ≥ 12 was associated with better response to CRT, less HF hospitalization, and more relief in HF symptoms. This ratio helps to identify possible sub-optimal response among patients with an indication for CRT.

Keywords: Electrocardiography; Left Bundle Branch Block; Cardiac Resynchronization Therapy; Heart Failure

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Introduction

Cardiac resynchronization therapy (CRT) as a treatment modality for patients with heart failure with reduced ejection fraction (HFrEF) has been proved to be of great benefit, but this is limited to a selected group of patients with QRS duration ≥ 130 milliseconds (ms) and with left bundle branch block (LBBB) who continue to be in New York Heart Association (NYHA) class II-IV.[1] Despite such strict selection criteria for CRT implantation, only two-thirds of patients respond, while one-third have a sub-optimal response.[2]

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Multiple risk scores and electrocardiographic (ECG) predictors have been proposed and validated to date for a better selection of patients before CRT implantation to increase the probability of optimal response. Scores like ScREEN, VALID-CRT, EAARN,[3] L2ANDS2,[4] and ECG markers like QRS duration,[5] QRS area,[6] pre-implant interlead heterogeneity,[7] prolonged PR interval,[8] S wave in V1 lead,[9] RS-V1 interval,[10] and T wave area[11] have been studied to predict CRT response. Recently, a new ECG predictor for the late rightward ECG forces called as lead one ratio (LOR) has been proposed to predict left ventricular (LV) dysfunction [ejection fraction (EF) ≤ 35%] in patients with LBBB.[12] LOR is derived by dividing the maximum positive deflection of QRS complex in the lead I by the maximum negative deflection. This ECG marker identifies a more dyssynchronous LV conduction pattern like asymmetric "U-shaped" pattern of LV conduction, which is considered to be a better predictor of CRT response in previous studies.[13,14] Recent work by Loring et al. has demonstrated that a lower value of LOR is associated with worse outcomes in patients receiving CRT.[15] In this prospective study, we aim at studying LOR for prediction of CRT response in patients with HFrEF receiving CRT.

Materials and Methods

Study population: In this prospective study, we enrolled patients who received CRT with or without a defibrillator in the cardiology department at a tertiary care center in North India between August 2016 to August 2019. Indication for CRT was NYHA functional class II-IV symptoms despite optimal medical therapy, LVEF ≤ 35%, and QRS duration ≥ 150 ms according to the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) guideline.[16]

The study population was divided into two groups (group A with LOR < 12 and group B with LOR ≥ 12) based on the pre-implant LOR ratio using a cut-off value of 12 as per the previous study by Loring et al.[15] The study design was as shown in figure 1. The outcome was compared using 4 variables:

1) CRT response is defined as a combined ≥ 5% absolute increase in LVEF from baseline and greater than 1 class improvement in NYHA functional class[17,18]
2) All-cause mortality

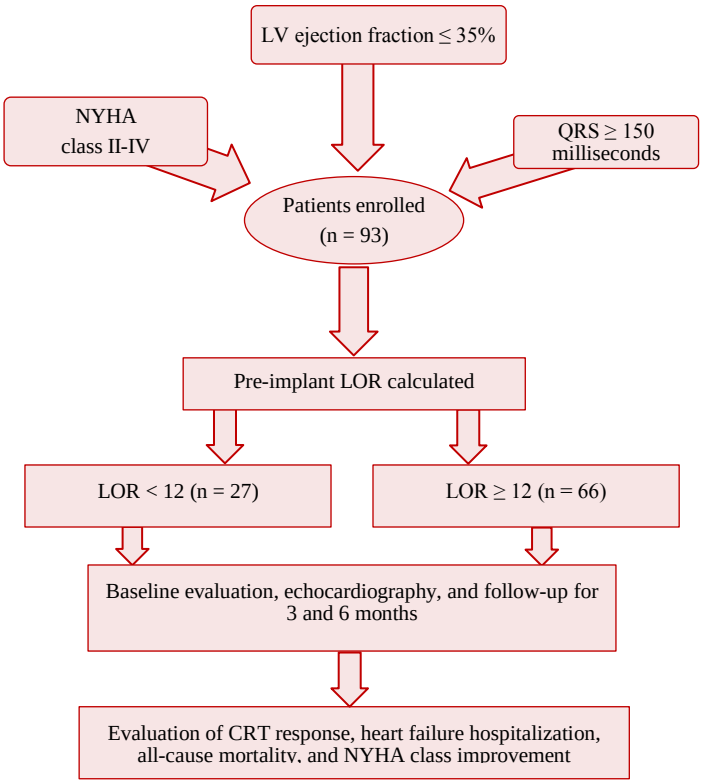

Figure 1. Study design (LV: Left ventricle; NYHA: New York Heart Association; LOR: Lead one ratio; CRT: Cardiac resynchronization therapy)

3) Heart failure (HF) hospitalization rate [defined as hospitalization for ≥ 24 hours or any admission requiring intravenous (IV) administration of inotropes, diuretics, or vasodilators]
4) HF improvement (improvement in NYHA functional class of dyspnea)

All patients during the follow-up of the study received guideline-directed medical therapy (GDMT).

Written informed consent was taken from the participants and patients who did not consent for research were excluded from this study. The study protocol was cleared by the Institutional Ethical Committee.

Data collection: Baseline characteristics were recorded in standard proforma. Pre-implant NYHA functional class, etiologic characteristics of HF, and concomitant diseases were assessed. Transthoracic echocardiography (TTE) was performed using Philips Model Sonos 5500 machine (Phillips Medical Systems, Andover, MA, USA). All the chamber quantification (LV diastolic and systolic dimensions including volume evaluation) was done as per the 2015 guidelines for chamber quantification in adults.

Volumetric measurements were usually based on tracings of the interface between the compacted myocardium and the LV cavity. At the mitral valve level, the contour is closed by connecting the two opposite sections of the mitral ring with a straight line. LV length is defined as the distance between the bisector of this line and the apical point of the LV contour, which is most distant to it. LVEF was calculated using the biplane method of disks (modified Simpson's rule) using the manual tracing on apical two and apical four-chamber views. All the echocardiographic parameters were measured as per the standard guidelines.[19]

Standard supine 12-lead ECGs (filter range: 0.15 to 100 Hz; AC filter: 60 Hz, 25 mm/s, 10 mm/mV) were obtained at baseline pre-CRT implantation using Edan USA SE-1200 Express. ECGs were analyzed blinded to echocardiographic results, and all measurements were made with the use of digital calipers at 200% magnification calibrated for paper speed of 25 mm/s for calculation of LOR and QRS duration. LOR was derived by dividing the maximum positive deflection of QRS complex in ECG lead I by the maximum negative deflection as shown in figure 2.

CRT implantation was done using the standard procedure in the catheterization laboratory. Commercially available transvenous system of bipolar or quadripolar LV lead with devices was implanted, and LV lead was selectively placed in the posterolateral/middle cardiac branch of coronary sinus aiming for activating the lateral free wall of the LV. The choice of the LV lead was decided by the operator firsthand.

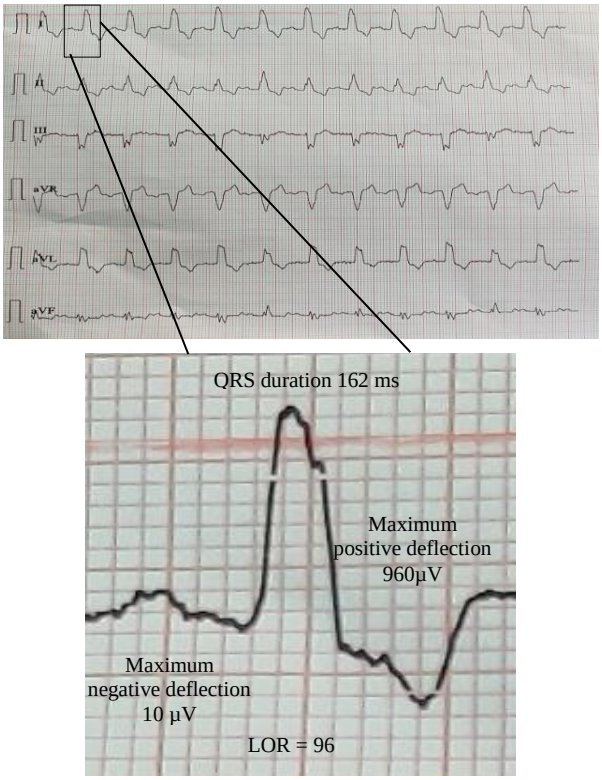

Figure 2. Lead one ratio (LOR) calculation, 12-lead electrocardiograms (ECGs) with zoomed inset displaying median beat of lead I. The full 12-lead ECG is displayed with standard scale of 10 mm/mV with a paper speed of 25 mm/s. The zoomed inset depicts the median beat for lead I displayed at a magnification of 200%, brackets not to scale. A patient with bundle branch block (LBB) QRS duration of 162 ms, a maximum positive amplitude of 960 µV, and a maximum negative amplitude of 10 µV corresponding to a LOR of 96

Follow-up: Enrolled patients were followed up in the pacemaker clinic as per the departmental protocol. The first visit was at 3 months of implantation and the second at 6 months. NYHA class, ECG, and TTE were reassessed at every visit. Device interrogation and optimization using intrinsic device algorithms were also done at every visit.

Statistical analysis: Categorical data were expressed in percentages, and continuous data were expressed in mean ± standard deviation (SD). Chi-square (χ^2) test with Fisher's exact test were used for comparison of categorical variables and Student's t-test was used for continuous variables between the two groups.

For survival rate evaluation, Kaplan-Meier

method was used. All the P-values were two-sided, and a P-value < 0.05 was taken to be statistically significant. Logistic regression was done to analyze the predictors of CRT response at 6 months. Data were analyzed with SPSS software (version 23, IBM Corporation, Armonk, NY, USA).

Results

Out of the total 93 patients enrolled in this study, the majority (86.02%) received CRT with a defibrillator. The mean age of patients was 61.19 ± 7.89 years, and 65.6% were men. Table 1 illustrates the baseline characteristics between the two groups, both the groups were identical except for the prevalence of stroke which was more in group A [7 (58.33%) in group A vs. 5 (41.66%) in group B, P = 0.014] and the use of potassium-sparing drugs which was more in group B when compared to group A (P = 0.003). The most common etiology of HF was non-ischemic cardiomyopathy (NICM) seen in 51.6% of patients. Most of the enrolled patients had advanced HF, with the majority having NYHA class III (66.7%) dyspnea. All the echocardiographic parameters were similar between the two groups, as shown in table 2.

Improvement in HF and survival: At the follow-up of 6 months, there was a statistically significant improvement in LVEF, QRS duration, and remodeling parameter of LV end-systolic volume (LVESV) in patients with LOR ≥ 12. All the echocardiographic parameters were comparable between the two groups at 6-month follow-up except for LVESV, where its reduction was more in group B (108.23 ± 15.77 ml vs. 118.81 ± 20.75 ml in group A, P = 0.009) as shown in table 3. The CRT response rate was statistically more in group B (LOR ≥ 12) when compared to group A (LOR ≤ 12) (75.76% vs. 51.85%, respectively, P = 0.02) as shown in table 4.

Table 1. Baseline characteristics of the study population

		Total population (n = 93)	LOR		P*
			< 12	≥ 12	
Age (year)		61.19 ± 7.89	59.26 ± 7.31	61.83 ± 7.97	0.145
Sex	Men	61 (65.60)	17 (27.80)	44 (72.13)	0.811
Etiology	NICM	48 (51.60)	9 (18.75)	39 (81.25)	0.072
	ICM	45 (48.40)	15 (33.33)	30 (66.66)	
Device type	CRT-D	80 (86.00)	23 (28.75)	57 (71.25)	0.781
	CRT-P	13 (14.00)	4 (30.76)	9 (69.23)	
LVEF (%)		31.82 ± 2.87	31.17 ± 2.95	32.08 ± 2.82	0.176
QRS duration (ms)		163.87 ± 10.32	163.70 ± 9.67	163.94 ± 10.65	0.918
NYHA class	II	26 (28.00)	8 (30.76)	18 (69.23)	0.339
	III	62 (66.70)	19 (30.64)	43 (69.35)	
	IV	5 (5.40)	0 (0)	5 (100)	
LBBB morphology	No	11 (11.80)	3 (27.27)	8 (72.72)	0.490
	Yes	82 (88.20)	24 (29.26)	58 (70.73)	
Diabetes	No	58 (62.40)	20 (34.48)	38 (65.51)	0.162
	Yes	35 (37.60)	7 (20.00)	28 (80.00)	
Stroke	No	81 (87.10)	20 (24.69)	61 (75.30)	0.014
	Yes	12 (12.90)	7 (58.33)	5 (41.66)	
HTN	No	54 (58.10)	14 (25.92)	40 (74.07)	0.492
	Yes	39 (41.90)	13 (33.33)	26 (66.66)	
CKD stage	2	17 (18.30)	4 (23.52)	13 (76.47)	0.272
	3	66 (71.00)	22 (33.33)	44 (66.66)	
	4	10 (10.80)	1 (10.00)	9 (90.00)	
PCI/CABG/angina	No	48 (51.60)	13 (27.08)	35 (72.91)	0.820
	Yes	45 (48.40)	14 (31.11)	31 (68.88)	
Beta blocker	No	5 (5.40)	0 (0)	5 (100)	0.317
	Yes	88 (94.60)	27 (30.68)	61 (69.31)	
ACE/ARB	No	11 (11.80)	1 (9.09)	10 (90.90)	0.167
	Yes	82 (88.20)	26 (31.70)	56 (68.29)	
Potassium sparing	No	54 (58.10)	9 (16.66)	45 (83.33)	0.003
	Yes	39 (41.90)	18 (46.15)	21 (53.84)	

Values are presented as mean ± standard deviation (SD) or number and percentage

*Independent t-test for age, left ventricular ejection fraction (LVEF), QRS duration, and Fisher's exact test for all categorical variables

NICM: Non-ischemic cardiomyopathy; ICM: Ischemic cardiomyopathy; LOR: Lead one ratio; LVEF: Left ventricular ejection fraction; ACE: Angiotensin converting enzyme; ARB: Angiotensin receptor blocker; CABG: Coronary artery bypass graft; HTN: Hypertension; CKD: Chronic kidney disease; CRT D/P: Cardiac resynchronization therapy with defibrillator/pacemaker; LBBB: Left bundle branch block; NYHA: New York Heart Association; PCI: Percutaneous coronary intervention

Table 2. Baseline echocardiographic parameters of the study population

Parameter	Total (n = 93)	LOR		P*
		< 12 (n = 27)	≥ 12 (n = 66)	
LVEF (%)	31.82 ± 2.87	31.17 ± 2.95	32.08 ± 2.82	0.176
LVESD (mm)	53.48 ± 2.81	53.96 ± 2.67	53.28 ± 2.86	0.283
LVEDD (mm)	61.96 ± 2.89	62.26 ± 2.77	61.83 ± 2.85	0.512
LVEDV (ml)	202.01 ± 26.75	203.33 ± 30.44	201.47 ± 25.32	0.780
LVESV (ml)	138.61 ± 21.52	137.26 ± 25.41	139.17 ± 19.91	0.729

Values are presented as mean ± standard deviation (SD), *Independent t-test
LOR: Lead one ratio; LVEF: Left ventricular ejection fraction; LVESD: Left ventricle end-systolic diameter; LVEDD: Left ventricle end-diastolic diameter; LVEDV: Left ventricle end-diastolic volume; LVESV: Left ventricle end-systolic volume

Table 5 shows the comparison between the two groups as per the delta (Δ) changes from the baseline echocardiographic parameters and QRS duration. There was more narrowing of QRS and better LVEF increment among patients with LOR ≥ 12 when compared to those with LOR ≤ 12.

The mean HF hospitalization events in the study was 0.74 episodes/patient; the number of HF hospitalization was less with group B (1.81 vs. 2.04 episodes in group A, P = 0.029). There was a total of 6 mortalities during the study period (4 in group A vs. 2 in group B, P = 0.38) and the meantime for mortality was 60.25 and 131.17 days, respectively, for group A and group B. Mortality per 100 person-years was statistically less in patients with LOR ≥ 12 (9.09 vs. 14.81 in LOR < 12, P = 0.012).

Predictors of CRT response: Using univariate analysis in both groups, QRS duration ≥ 150 ms in group A [Hazard ratio (HR)]: 1.32, 95% confidence interval (CI): 1.09-3.90] and group B (HR: 1.78, 95% CI: 1.40-3.90), the presence of LBBB morphology in group A (HR: 1.56, 95% CI: 1.14-3.32) and group B (HR: 2.58, 95% CI: 1.16-3.90), and NYHA grade III/IV only in group B (HR: 1.36, 95% CI: 1.14-3.81) were associated with better CRT response.

Subgroup analysis: Patients were divided into two groups, based on the etiology of HF, patients with ischemic cardiomyopathy (ICM) and those with NICM. All the four outcomes were compared within each subgroup. LOR ≥ 12 was associated with less HF hospitalization (1.53 ± 0.31 vs. 2.00 ± 0.51 in LOR < 12, P = 0.021) and better CRT response (79.1% vs. 58.2% in LOR < 12, P = 0.02) in NICM. Whereas in ICM, LOR ≥ 12 was associated with better NYHA improvement (80.56% vs. 66.67% in LOR < 12, P = 0.01).

Table 4. Comparing response to cardiac resynchronization therapy (CRT) in both groups at the end of six-month follow-up

Parameter	LOR < 12 (n = 27)	LOR > 12 (n = 66)	P*
Response rate (% with LVEF)	16 (59.26)	54 (81.80)	0.030
≥ 1 NYHA class improvement (%)	15 (55.56)	52 (78.79)	0.040
Composite response rate (%)	14 (51.85)	50 (75.76)	0.020

Values are represented as number and percentage
*Chi-square test
LVEF: Left ventricular ejection fraction; NYHA: New York Heart Association; LOR: Lead one ratio

Discussion

In this study, we analyzed ECG LOR < 12 to predict the outcome of CRT implantation in patients with HFrEF. The outcome was analyzed in terms of CRT response, all-cause mortality, HF hospitalization events, and improvement in HF symptoms measured as improvement in the NYHA class of dyspnea.

Table 3. Follow-up data of echocardiographic, and electrocardiographic (ECG) parameters between the two groups at six months along with the response rate to cardiac resynchronization therapy (CRT)

Parameter	LOR < 12		LOR ≥ 12		P*	
	Baseline	6 months	Baseline	6 months	Baseline	6 months
LVEF (%)	31.17 ± 2.95	37.25 ± 3.31	32.08 ± 2.82	41.24 ± 2.76	0.176	0.017
LVEDD (mm)	62.26 ± 2.77	60.36 ± 2.97	61.83 ± 2.85	60.38 ± 3.22	0.512	0.975
LVESD (mm)	53.96 ± 2.67	49.96 ± 2.80	53.28 ± 2.86	49.18 ± 2.98	0.283	0.240
QRS duration (ms)	163.70 ± 9.67	154.49 ± 10.06	163.94 ± 10.65	151.74 ± 3.43	0.918	0.016
LVEDV (ml)	203.33 ± 30.44	178.29 ± 29.31	201.47 ± 25.32	174.62 ± 23.28	0.780	0.565
LVESV (ml)	132.26 ± 20.41	118.81 ± 20.75	141.17 ± 15.91	108.23 ± 15.77	0.026	0.009

Values are presented as mean ± standard deviation (SD), *Independent t-test
LOR: Lead one ratio; LVEF: Left ventricular ejection fraction; LVESD: Left ventricle end-systolic diameter; LVEDD: Left ventricle end-diastolic diameter; LVEDV: Left ventricle end-diastolic volume; LVESV: Left ventricle end-systolic volume

Table 5. Clinical, echocardiographic, and electrocardiographic (ECG) parameters' delta change comparison between the two groups

Parameter	Delta (Δ) changes at 6 months with respect to baseline		
	LOR < 12	LOR ≥ 12	P*
LVEF (%)	6.08 ± 1.49	9.15 ± 1.36	0.019
LVESD (mm)	7.45 ± 0.93	7.74 ± 1.21	0.229
LVEDD (mm)	2.98 ± 4.14	2.31 ± 2.74	0.442
LVEDV (ml)	15.35 ± 4.84	20.27 ± 3.42	0.014
LVESV (ml)	18.20 ± 3.98	19.42 ± 4.65	0.009
QRS duration (ms)	5.74 ± 2.09	7.10 ± 3.97	0.010

Values are presented as mean ± standard deviation (SD), *Independent t-test
LOR: Lead one ratio; LVEF: Left ventricular ejection fraction; LVESD: Left ventricle end-systolic diameter; LVEDD: Left ventricle end-diastolic diameter; LVEDV: Left ventricle end-diastolic volume; LVESV: Left ventricle end-systolic volume

The mean age of the patients enrolled in this study was 61.19 ± 7.89 years, and the majority of patients were men (65.6%). The most common etiology was NICM present in 51.6% of patients, with the majority of patients in advanced HF as assessed by NYHA class (66.7% in class III); these findings were in concordance with previous studies where the mean incidence of NICM was 53% and 58.5%.[12,15] ECG LOR ≥ 12 was associated with better CRT response, less hospitalization events for HF, and better improvement in symptoms of HF when compared to patients with LOR < 12. These findings are suggestive that LOR ≥ 12 identifies patients who are more likely to benefit from CRT implantation including patients with LBBB and QRS duration > 150 ms who have class I indication for CRT according to recent guidelines.[16]

In a study by Loring et al., CRT response was 66% in patients with LOR ≥ 12 and 47% in patients with LOR < 12.[15] The mean QRS duration of patients in this study was 163.87 ± 10.32 ms which was wider with respect to 152 ms and 156 ms in two previous studies.[12,15] We found a better response as all the patients enrolled in the current study were in sinus rhythm, whereas in the study by Loring et al., atrial fibrillation (AF)/flutter was present in 30.1% and 23.8%, respectively, in LOR < 12 and LOR ≥ 12 groups and the mean QRS duration was narrower (156.00 ± 22.00 ms), compared to that in our study group (163.87 ± 10.32 ms).[15]

Patients with LOR < 12 experienced more mortality per 100 person-years during the follow-up period (9.09 vs. 14.81 in LOR < 12, P = 0.012), comparing the HF hospitalization; it was also statistically more in this group of patients. CRT response was also seen only in 51.85% of patients, which was significantly less than the response rate of patients with LOR ≥ 12 (75.76%, P = 0.02). Symptomatic HF was also less improved in patients with LOR < 12 (≥ 1 NYHA class improvement) (55.56% vs. 78.79% in LOR ≥ 12, P = 0.04). All these variables point towards the predictive power of LOR < 12 for adverse clinical and low CRT response rate in patients with HFrEF even after adjustment of previously known predictors of poor outcome like sex,[20] non-LBBB morphology,[21] QRS duration,[6] baseline LVEF,[22] and AF.[23] Subgroup analysis showed that LOR ≥ 12 was associated with better CRT response, which was numerically more in patients with ICM (68.00% vs. 52.40% in LOR < 12) and statistically more in patients with NICM (79.10% vs. 58.20% in LOR < 12, P = 0.04). In patients with ICM, LOR < 12 was associated with less improvement in HF symptoms (≥ 1 NYHA class improvement) when compared to LOR ≥ 12 (66.67% vs. 80.56%, respectively).

Patients with LOR ≥ 12 had a more reduction in LV end-diastolic volume (LVEDV) at 6 months (Δ19.42 ± 4.65 ml vs. Δ18.20 ± 3.98 ml in LOR < 12, P = 0.01); similarly marked reduction in LVEDV was also seen (Δ20.27 ± 3.42 ml vs. Δ15.35 ± 4.84 ml in LOR < 12, P = 0.014). LVEF was also increased more in patients with LOR ≥ 12 (Δ9.15 ± 1.36% vs. Δ6.08 ± 1.49% in LOR < 12, P = 0.019). These findings were in concordance with the previous study done by Loring et al., where they showed a 4% more reduction in LVEDV and 9% more reduction in LVESV in patients with LOR ≥ 12.[15]

This observation of LOR < 12 association with CRT response can be explained by two factors. First, in previous independent studies done, it has been shown that LOR < 12 was associated with the presence of a myocardial scar, and hence, CRT with LV lead placement in such patients may lead to sub-optimal response.[24] The association of LOR < 12 with myocardial scar can also be implied indirectly by the subgroup analysis of this study, where LOR < 12 in the ICM group had less CRT

response, which may be attributed to previous scar injury in these patients.

Secondly, LOR can be a marker of marked desynchrony; it has been shown that LBBB leads to delayed depolarization and contraction of the lateral LV free wall, but the inter-ventricular septum shows normal early contraction resulting in paradoxical septum motion. This activation has been demonstrated to be a "U-shaped" activation sequence that turns around the apex and inferior wall of the LV. This activation pattern is generated by a functional line of the block that is oriented from the base toward the apex of the LV. This functional line of the block is very variable and differs from patient to patient.[25] Using ECG mapping and cardiac magnetic resonance imaging (MRI), it has been proved in previous studies that patients with U-shaped LV activation patterns are better responders to CRT.[13,14] Asymmetric "U-shaped" activation of the LV results in a late, rightward shift of the ECG vector, which manifests in lead one as a terminal negative deflection and a low LOR.[12] Hence, in such patients, individual patient ECG mapping and placing of LV lead according to the position of the functional line of block will provide the optimal response to CRT. Previous studies of ECG mapping and cardiac MRI have shown a better response to CRT in patients with asymmetric activation.[13,14] This response can be attributed to the fact that they identified the patients in earlier stages of HF leading to a better response, whereas patients with LOR < 12 have an advanced HF that can be seen with the increased echocardiographic parameters [LV end-systolic diameter (LVESD) and LV end-diastolic diameter (LVEDD)], suggesting a more advanced structural remodeling pattern which implies that LOR < 12 is a marker of the advanced disease process which is difficult to amend fully by CRT implantation.

This new ECG marker can be used in helping us reinforce the benefits of CRT for patients who are likely to have a high response rate as per the LOR value and it will also help us identify a group of likely non-responder patients with all the guideline-directed indications for CRT. We can individualize our approach to patients who are likely to have a sub-optimal response in form of regular algorithm optimization, medical therapy optimization with novel drugs, use of novel endocardial pacing modality, or early referral for heart transplant clinic.

Limitations: This was a single-center study with small sample size and all the patients enrolled were in sinus rhythm, with class I indication[16] for CRT; hence, the result cannot be extrapolated on every subset of the population and requires larger studies.

Conclusion

To our knowledge, this is the first prospective study evaluating the value of this new ECG marker, LOR, in patients with HFrEF and LBBB receiving CRT. LOR ≥ 12 was associated with less HF hospitalization, better response to CRT, and more relief in HF symptoms. In patients with LOR < 12, further studies are required for assessing the benefits of an individualized approach for CRT implantation.

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Conflict of Interests

Authors have no conflict of interests.

Authors' Contribution

Conceptualization: ARj and APS; Writing, original draft: APS; Writing, review and editing: RKN and PA; Formal analysis: NP; Investigation: APS, RKN, and AR; Supervision: RKN and BNP.

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