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Six months clinical outcome comparison between quadripolar and bipolar left ventricular leads in cardiac resynchronization therapy: A prospective, non-randomized, single-centre observational study

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ABSTRACT

Background and objectives: Quadripolar left ventricular (LV) leads in cardiac resynchronization therapy (CRT) offer multi-vector pacing with different pacing configurations and hence enabling LV pacing at most suitable site with better lead stability. We aim to compare the outcomes between quadripolar and bipolar LV lead in patients receiving CRT.

Methods: In this prospective, non-randomized, single-center observational study, we enrolled 93 patients receiving CRT with bipolar (BiP) (n = 31) and quadripolar (Quad) (n = 62) LV lead between August 2016 to August 2019. Patients were followed for six months, and outcomes were compared with respect to CRT response (defined as ≥5% absolute increase in left ventricle ejection fraction), electrocardiographic, echocardiographic parameters, NYHA functional class improvement, and incidence of LV lead-related complication.

Results: At the end of six months follow up, CRT with quadripolar lead was associated with better response rate as compared to bipolar pacing (85.48% vs 64.51%; p = 0.03), lesser heart failure (HF) hospitalization events (1.5 vs 2; p = 0.04) and better improvement in HF symptoms (patients with ≥1 NYHA improvement 87.09% vs 67.74%; p = 0.04). There were fewer deaths per 100 patient-year (6.45 vs 9.37; p = 0.04) and more narrowing of QRS duration (Δ12.56 ± 3.11 ms vs Δ7.29 ± 1.87 ms; p = 0.04) with quadripolar lead use. Lead related complications were significantly more with the use of bipolar lead (74.19% vs 41.94%; p = 0.02).

Conclusions: Our prospective, non-randomized, single-center observational study reveals that patients receiving CRT with quadripolar leads have a better response to therapy, lesser heart failure hospitalizations, lower all-cause mortality, and fewer lead-related complications, proving its superiority over the bipolar lead.

1. Introduction

Cardiac resynchronization therapy (CRT) is a novel non-pharmacological modality for heart failure (HF) patients remaining in NYHA functional classification II, III, and IV despite optimal medical therapy, with decreased left ventricular ejection fraction (LVEF) ≤ 35% and evidence of ventricular desynchrony seen as wide QRS complex of ≥150 ms on electrocardiogram (ECG) [1]. CRT is associated with improvement in morbidity and mortality in patients with severe left ventricular (LV) dysfunction by inducing reverse remodeling by synchronized biventricular pacing. Despite this, only two-thirds of patients receiving CRT respond to the therapy, while the one-third patient has suboptimal response [2]. Response to therapy is dependent on the selection of patients, placement of LV lead in the posterolateral branch of the coronary sinus, avoiding apical position, and proper biventricular pacing percentage [3].

Formerly, bipolar (BiP) leads with two poles distally were used for LV pacing, these poles were distally wedged in posterolateral vein for an appropriate response, their use was limited by the

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coronary sinus anatomy, instability of lead in large branches, and phrenic nerve stimulation leading to discontinuation of LV pacing or revision of lead to another branch. This led to the development of more stable, and with four distal poles quadripolar (Quad) lead with the property of multi-vectoral and multi configurational pacing of LV at most suitable site, and to change pacing vector in case of phrenic nerve stimulation of non-responder in subsequent periods [4]. This study is aimed to compare the outcomes between quadripolar (Quad) and bipolar LV lead in patients receiving CRT.

2. Methods

2.1. Study population

This study enrolled patients who received CRT with a defibrillator or pacemaker with quadripolar or bipolar LV leads at the Department of Cardiology, in a tertiary care center in North India between August 2016 to August 2019. The basic demographic characteristics of the study population in both groups are shown in Table 1. Indication for CRT was New York Heart Association (NYHA) functional class II-IV symptoms despite optimal medical therapy, LVEF ≤35%, and QRS duration ≥150 ms (ms) according to the ACA/AHA/HRS guidelines [5].

Patients who were upgraded to CRT from a pacemaker or implantable cardioverter-defibrillator were also included in the study. Patients who underwent CRT implant with bipolar LV leads during the same period were included in the control group.

Fig. 1 shows the study design, and the outcome were compared in five variables; the CRT response rate (defined as ≥5% absolute increase in LV ejection fraction from baseline) [6–9], NYHA functional class improvement, all-cause mortality, HF hospitalization events (defined as hospitalization for ≥24 h or any admission requiring intravenous administration of inotropes, diuretics or vasodilators) and LV lead-related complications. All patients admitted during the follow up of the study received guideline-directed medical therapy (GDMT).

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

2.2. Data collection

Baseline characteristics were recorded in standard proforma. Pre-implant NYHA functional class, etiologic characteristics of heart failure, concomitant diseases were assessed. Electrocardiography was used to evaluate the QRS duration and transthoracic echocardiography using Philips Model Sonos 5500 machine (Phillips Medical Systems, Andover, MA, USA) was done. Parameters in echocardiography evaluation were LVEF; LV end-diastolic dimension (LVEDD); LV end-systolic dimension (LVESD), LV end-diastolic volume (LVEDV), and LV end-systolic volume using standard guidelines (LVESV) [10].

CRT implantation was done using the standard procedure in the catheterization laboratory of the department. We have used the commercially available transvenous system of bipolar, quadripolar LV lead, and devices (Quartet™ quadripolar LV by St Jude® or Attain™ Performa™ Advanced Quadripolar Lead ® by Medtronic or SentusProMRI® quadripolar lead by BIOTRONIK) using over the wire technique. LV lead was selectively placed in the posterolateral or middle cardiac vein of coronary sinus aiming for activating lateral free wall of the left ventricle. The choice of the LV lead was decided by the operator firsthand. The LV lead pacing configuration was determined by pacing location using different poles (four poles of Quad lead LV 1,2,3,4 and two poles on BiP lead LV tip and ring; mid or basal ventricle is considered favorable), pacing threshold, impedance, and phrenic nerve stimulation (at 10 V output).

Table 1
Baseline characteristics of patients in two group.

BASELINE CHARACTERISTICS					
		Total (93)	Bipolar (31)	Quadripolar (62)	P-value
Age (years)		61.19 ± 7.89	60 ± 7.67	61.79 ± 8.00	0.30
Sex	Male	60	19 (61.29)	41 (66.13)	0.653
Etiology	NICM	49	17 (54.84)	32 (51.61)	0.828
Device Type	CRT-D	80	24 (77.42)	56 (90.32)	0.117
Diabetes		35	9 (29.03)	26 (41.94)	0.265
Hypertension		39	16 (51.61)	23 (37.1)	0.191
CKD Stage	2	17	6 (19.35)	11 (17.74)	0.638
	3	66	23 (74.19)	43 (69.35)	
	4	10	2 (6.45)	8 (12.9)	
PCI/CABG/Angina		45	14 (45.16)	31 (50)	0.826
ECG LBBB		82	28 (90.32)	54 (87.1)	0.746
NYHA Class	II	28	11 (35.48)	17 (27.42)	0.631
	III	60	19 (61.29)	41 (66.13)	
	IV	5	1 (3.23)	4 (6.45)	
Beta Blocker		88	29 (93.55)	59 (95.16)	0.71
ACEI/ARB		82	28 (90.32)	54 (87.1)	0.746
Loop Diuretics/Thiazides		93	31 (100)	62 (100)	
Potassium sparing drug		39	16 (51.61)	23 (37.1)	0.191
QRS duration (ms)		163.87 ± 10.33	163.87 ± 10.86	163.87 ± 10.14	0.875
LVEF %		31.82 ± 2.87	32.27 ± 1.27	31.59 ± 3.13	0.617
LVESD mm		53.48 ± 2.81	53.42 ± 2.96	53.51 ± 2.76	0.879
LVEDD mm		61.96 ± 2.89	62.03 ± 3.14	61.92 ± 2.79	0.866
LVEDV ml		202.01 ± 26.75	204.35 ± 28.37	200.84 ± 26.07	0.565
LVESV ml		138.61 ± 21.52	139.19 ± 23.55	138.32 ± 20.63	0.862

Values are presented as mean ± standard deviation and N (%).
ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; CABG = coronary artery bypass graft; CKD = chronic kidney disease; CRT D = cardiac resynchronization therapy with defibrillator; LBBB = left bundle branch block; 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; ml = milliliter; mm = millimeter; ms = millisecond; NYHA= New York heart association; NICM = non ischemic cardiomyopathy; PCI = percutaneous coronary intervention.

CRT= cardiac resynchronization therapy; LV= left ventricle; NYHA= New York Heart Association

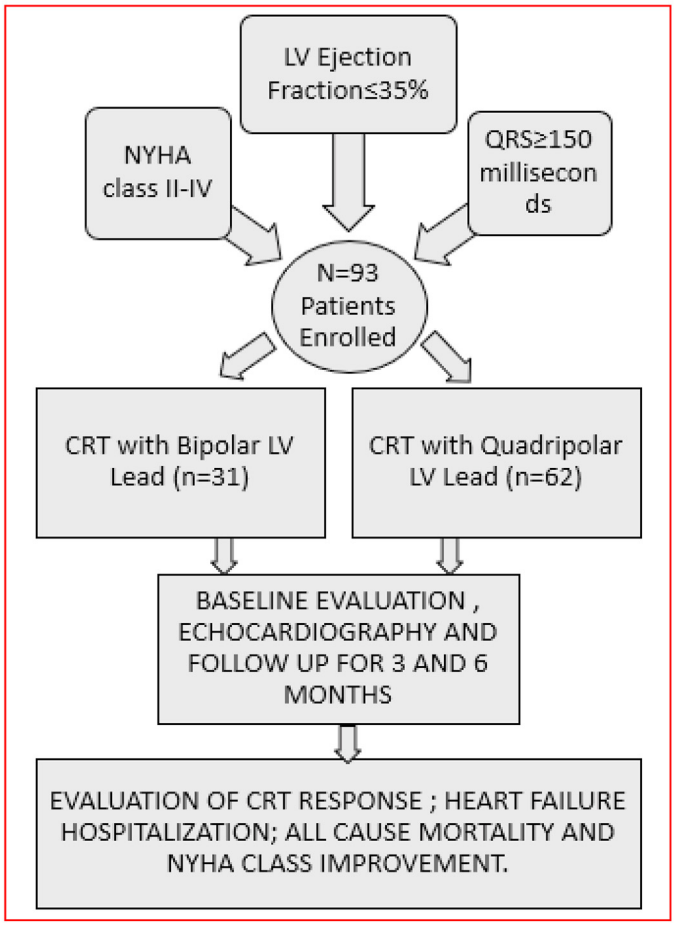

Fig. 1. Study Design. CRT = cardiac resynchronization therapy; LV = left ventricle; NYHA= New York Heart Association.

2.3. Follow up

Enrolled patients were followed up in the pacemaker clinic as per the departmental protocol. The follow-up visits were recorded at three months and six months of implantation. NYHA functional class, electrocardiography, and transthoracic echocardiography were reassessed at every visit, and device interrogation and optimization using intrinsic device algorithms was done at every visit.

2.4. Statistical analysis

Categorical variables were expressed as percentages, and continuous variables were expressed as mean ± standard deviation. The chi-square test with Fisher's exact test was used to compare categorical variables between the two groups. Continuous variables were compared using the student's t-test. The survival rate was evaluated using the Kaplan-Meier method. All the p values were two-sided, and a value < 0.05 was taken to be statistically significant. Logistic regression was done to analyze the predictors of CRT response at six months. Data were analyzed with SPSS version 23.0 (SPSS, Chicago, IL, USA).

3. Results

3.1. Baseline characteristics

Among the total 93 patients enrolled in the study, 33.34% (31) patients received bipolar LV lead, and 66.6% (62) patients received quadripolar LV lead. The mean age of the patients in the study was 61.19 ± 7.89 years, 60% were male, and 86.02% received CRT with a defibrillator. Baseline characteristics and echocardiographic parameters were similar between the two LV lead groups, as shown in Table 1.

3.2. Improvement in heart failure and survival

At the follow up of three and six months, there was a statistically significant improvement in the number of patients with ≥1 class improvement in NYHA class and LVEF in the quadripolar group. All the echocardiographic parameters were similar in both the groups except for the LV remodeling parameter of LVESV, where its reduction was more with quadripolar lead use (111.27 ± 16.93 ml vs 113.61 ± 18.94 ml in BiP; p 0.039). The response to CRT at three months was statistically more in the Quad group (40.32% vs 25.81%

Table 2
Follow up parameters between the two groups at three and six months.

	BIPOLAR			QUADRIPOLAR			P-value	
	Baseline	3 Months	6 Months	Baseline	3 Months	6 Months	3 Months	6 Months
LVEF %	32.27 ± 2.27	36.63 ± 2.69	37.89 ± 2.53	31.59 ± 3.13	36.24 ± 3.31	42.98 ± 3.15	**0.041**	**0.006**
LVEDD, mm	62.03 ± 3.14	60.48 ± 2.98	60.06 ± 3.03	61.92 ± 2.79	60.81 ± 3.19	60.53 ± 3.20	0.279	0.295
LVESD, mm	53.42 ± 2.96	49.71 ± 3.16	49.45 ± 3.15	53.52 ± 2.76	49.67 ± 2.85	49.38 ± 2.84	0.411	0.297
QRS duration, ms	163.87 ± 10.86	155.68 ± 11.02	155.19 ± 10.88	163.87 ± 10.14	153.24 ± 7.33	149.94 ± 7.44	0.272	**0.047**
LVEDV, ml	204.35 ± 28.37	179.39 ± 28.98	177.97 ± 27.53	200.84 ± 26.07	178.84 ± 25.97	174.55 ± 23.90	0.926	0.558
LVESV, ml	139.19 ± 23.55	116.65 ± 19.99	113.61 ± 18.94	138.32 ± 20.63	116.31 ± 18.57	111.27 ± 16.93	**0.036**	**0.039**
%≥1 NYHA Class improvement		48.3	67.74		61.29	87.09	**0.041**	**0.04**
Response rate%		25.81	64.51		40.32	85.48	**0.009**	**0.031**

Values are presented as mean±standard deviation.
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; ms = millisecond; mm = millimeter; NYHA= New York heart association.

in BiP; p 0.009), which further increased to 85.48% in the Quad group at six months to 64.51% in the BiP group (p 0.031) of follow-up as shown in Table 2.

Comparing the delta (Δ) changes from baseline and at six months follow up between the two groups, there was more narrowing of QRS (Δ12.56 ± 3.11 vs Δ7.29 ± 1.87 in BiP; p 0.041) and better LVEF improvement (Δ9.39 ± 1.48 vs Δ5.61 ± 1.05 in BiP; p 0.004) in the Quad group. A greater reduction in the LV remodeling parameter of LVESV (Δ19.42 ± 4.65 vs Δ18.20 ± 3.98 in BiP; p 0.009) and LVEDV (Δ13.13 ± 2.49 vs Δ13.08 ± 2.34; p 0.028) was seen in the Quad group when compared to the BiP group.

The mean HF hospitalization events were fewer in the Quad group (1.5 vs 2 episodes in BiP; p 0.04). Mortality per 100-person year was also less with the Quad group (6.45 vs 9.37 in BiP; p 0.04).

3.3. Predictors of CRT response

Patients with LBBB morphology and in NYHA class III and IV were more likely to respond to CRT at six months as per univariate analysis and this significance was lost in multivariate analysis. Female sex, use of quadripolar leads, and LV pacing site (basal/mid-ventricular) were the only factors associated with a better likelihood of response to CRT as per the multivariate analysis as shown in Table 3.

3.4. LV - lead related complications

A total of 74.19% of patients had LV lead-related complications in the BiP group, which was statistically more when compared to the Quad group (41.94%; p 0.02). The overall most common complication was device-related local site infections in both the groups, whereas LV lead-related complications like lead dislodgement/non-capture, implant failure, and phrenic nerve stimulation was more in the BiP group when compared to the Quad group as shown in Table 4.

3.5. LV lead position and configurations

The LV lead was placed in the lateral wall in 57 patients (91.93%) in the Quad group and 27 patients (87.09%) in the BiP group (p 0.47). The optimal pacing site (basal & mid-ventricular) was achieved in 52 patients (83.87%) and 20 patients (64.51%) in BiP group (p 0.063). The most common LV lead pacing configuration was between LV1-LV2 in the Quad group and LV tip-RV in the BiP group. The mean threshold of pacing was also similar between the two groups at implant (1.2 ± 0.7 V in Quad vs 1.3 ± 0.9 V in BiP; p 0.74) and six months (1.3 ± 0.8 V in Quad vs 1.5 ± 0.8 V in BiP; p 0.31). Bipolar leads had a significantly more impedance at implant (629.0 ± 280.2 Ω vs 691.4 ± 264.9 Ω in Quad; p 0.01) and six months (759.9 ± 296.9 Ω vs 866.9 ± 415.0 Ω Quad; p 0.02). The mean biventricular pacing was 98.38 ± 0.6% vs 96.87 ± 2.1% in bipolar (p 0.26 NS), respectively in BiP and Quad group at six months.

4. Discussion

In this study, we analyzed the outcomes of quadripolar and bipolar lead in patients receiving CRT. Outcomes were analyzed in terms of response to therapy, improvement in NYHA class, heart failure hospitalization events, and all-cause mortality. Along with the echocardiographic parameter, electrocardiography was used to determine the predictors of CRT response among the two groups. The mean age of the patients in this study was younger (61.19 ± 7.89 years) compared to Multicenter InSync Randomized Clinical Evaluation (MIRACLE) (63.9 ± 10.7 years) [11], Cardiac Resynchronization — Heart Failure (CARE HF) (67years) [12] and Resynchronization–Defibrillation for Ambulatory Heart Failure

Table 3
Univariate and multivariate analysis for predictors for CRT response.

	Univariate analysis			Multivariate analysis		
Variable	P-value	H. R	95% CI	P-value	H. R	95% CI
AGE	0.472	1.028	0.9529 to 1.1097			
NICM	0.675	0.7692	0.2254 to 2.6255			
Female Sex	**0.036**	1.338	1.0978 to 2.1655	**0.0392**	1.479	1.0287 to 2.7936
QRS Duration	0.445	1.035	0.9476 to 1.1305			
LBBB morphology	**0.039**	1.875	1.7612 to 2.1264	0.5813	1.67	0.9199 to 2.7764
NYHA Class III & IV	**0.03**	4	1.1453 to 13.9702	0.2871	1.506	0.6926 to 3.8310
Quadripolar leads	**0.014**	1.511	1.3378 to 5.2153	**0.0219**	1.663	1.1978 to 5.2153
Pacing site (basal/mid ventricular)	**0.006**	4.575	1.5340 to 13.6449	**0.0215**	3.816	2.1348 to 11.8215

CRT = cardiac resynchronization therapy; ECG = electrocardiogram; LBBB = left bundle branch block; NICM = non ischemic cardiomyopathy; NYHA= New York heart association.

Table 4
Left Ventricular (LV) lead related complications.

	LV Lead–Related Complications		P-value
	Bipolar (%) (N = 31)	Quadripolar (%) (N = 62)	
Device related local Site infection	5 (16.13)	7 (11.29)	0.773
Implant failure	2 (6.45)	3 (4.84)	**0.039**
Phrenic nerve stimulation	4 (12.90)	6 (9.68)	0.178
Eliminated by reprogramming	3 (75)	5 (83.33)	0.341
Eliminated by lead revision	0 (0)	0 (0)	
LV lead turned off	1 (25)	1 (16.67)	0.682
Minimal PNS	0 (0)	0 (0)	
LV lead dislodgement/non-capture	4 (12.90)	2 (3.23)	**0.045**
Solved by lead revision	3 (75)	2 (100)	0.199
LV lead turned off	1 (25)	0 (0)	0.291
Solved by reprogramming	0 (0)	0 (0)	
Total complications	23 (74.19)	26 (41.94)	**0.024**

Values are presented as N (%).
PNS = phrenic nerve stimulation.

Trial (RAFT) (66.1 ± 9.3 years) [13]. The most common etiology for heart failure was non-ischemic cardiomyopathy (NICM) (52.6%), which was similar when compared with NICM incidence in CARE HF (60%) [12] and MIRACLE (50%) [11] trials. 64.5% of the patients had advanced heart failure symptoms (NYHA class III) which were less when compared to 86% in Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (CHAMPION) (86%) [14] and 90% in MIRACLE trial [11]. Patients were having a higher mean LVEF (31.82 ± 2.87%) in comparison with mean LVEF in CARE HF (22%) [12], REsynchronizationreVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) (26.8 ± 7.05%) [15] and RAFT (22.6 ± 5.4%) [13] trials. The mean QRS duration was 163.87 ± 10.33 ms, which was suggestive of greater electromechanical desynchrony in our patients [16] and was wider when compared with the mean QRS duration in CHAMPION (160 ms) [14] and REVERSE (153 ms) [15] trials. 88.1% of patients were having LBBB morphology and none of the patients were in AF/Flutter, which was more than the previous trials patients, as in the RAFT trial LBBB was present in 72.9% and 12.8% patients had AF/Flutter [13] and Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT CRT) trial [17] (LBBB in 69% & 11.1% with AF/Flutter).

The improvement in LVEF was significantly more in the Quad group at six months (42.98 ± 3.15 vs 37.89 ± 2.53% in BiP group; p 0.006) which was more than the study done by Bencardino et al. (2016) [7] 35 ± 13% for Quad and 31 ± 4% for BiP (p 0.001). This higher gain in LVEF in our study can be explained with longer follow up in our study (6 months) and a better baseline echocardiographic parameters of LV remodeling, LVESV (138 ± 21.52 ml) and LVEDV (202 ± 26.75 ml) in comparison to (LVESV 197 ± 74; LVEDV 268 ± 89 ml) in the REVERSE trial [15], which has been linked to a greater magnitude of response to CRT, which also suggests earlier intervention in heart failure with CRT [18]. Another contributing factor to this observation can be the wider QRS duration in this study, which is an independent predictor of better LV remodeling [19].

4.1. CRT response

In this study, response to CRT was significantly more in patients with quadripolar lead at both three months (40.32% vs 25.81% in bipolar lead; p 0.009) and six months (85.48% vs 64.51% in BiP; p 0.03) which was consistent with the finding of previous studies by Bencardino et al. (2016) [7] (65.2% Quad vs 35% BiP; P 0.047) and Earth et al. (2019) [19] (77% Quad vs. 63% BiP; $p < 0.001$).

NYHA class improvement was more with quadripolar lead at six months, and this was in concordance with previous studies by Yang et al. (2018) [6] (62.9 Quad vs 51.4 BiP; p 0.04) and Earth et al. (2019) [20] (QP LV leads (OR = 2.30; 95% CI 1.37–3.85; p 0.002). Taking ≥1 NHYA class improvement as a criterion of response [6,7,12,20] CRT responder at six months were more in the quadripolar group (87.09% vs 67.74% in BiP; p 0.04). Greater NYHA improvement can be attributed to better LVEF improvement at six months (Δ9.39 ± 1.48% in Quad vs Δ 5.61 ± 1.05% in BiP; p 0.004) and extensive use of diuretics (100% in both the study groups) which was higher when compared to diuretic use in MIRACLE (91%) [11], RAFT (84.7%) [13] and MADIT CRT (75.7%) [17] trials. QRS shortening was also more in the Quad group (Δ 12.56 ± 3.11 vs Δ 7.29 ± 1.87 ms in BiP; p 0.04) which was in line with the study done by Earth et al. (2019) [20] (Δ-21 ms in Quad vs Δ-8 in BiP; $p < 0.001$).

This better CRT response with quadripolar lead can be attributed to greater narrowing of QRS duration which is a predictor of better CRT response as shown in metanalysis by Korantzopouloset al [21]. Another contributory factor is a numerically greater percentage of biventricular pacing in the quadripolar group (98.38 ± 0.6% vs 96.87 ± 2.1% in bipolar; p 0.26) which has been shown in the previous study that the greatest benefit of CRT is obtained at an excess of 98% of biventricular pacing [22]. Previously it has been shown that the LV lead pacing position is associated with CRT response [23]. In this study, we found a lesser rate of pacing from the distal pole and achieved more pacing at the basal or mid ventricular part of LV with quadripolar lead (83.87% vs 64.51% in BiP; p 0.06). This has an advantage of additional stability in quadripolar leads as the distal part can be pushed deep in vein and more probability for pacing at the most optimum position of basal/mid-ventricular part of LV which is considered the gold standard for pacing and is associated with better survival [24,25]. This technical superiority of quadripolar lead may be the key contributor for better CRT response when compared to bipolar lead.

Predictors for the response to CRT was the use of quadripolar lead with basal/mid-ventricular pacing [24,25] in females [26] with LBBB type of morphology on ECG [13,27] and with advanced heart failure symptoms (NYHA class III/IV) [11,12,14].

4.2. Lead related outcomes

Consistent with the available data, in this study also LV lead-related complications were significantly more with bipolar lead (74.9% vs 41.94% in Quad; p 0.024). The most common LV lead complication was phrenic nerve stimulation (PNS) (12.9% BiP vs 9.68% Quad; p 0.039). Previously it has been demonstrated in a

metanalysis by Turagam et al. (2016) [28] that quadripolar lead is associated with a 76% reduction in PNS. In a study done by Ziacchi et al. (2018) [29], quadripolar lead was associated with fewer PNS (8% vs 17% in BiP; p 0.014) and LV lead dislodgement (5%vs 15% BiP; p 0.005) which was also observed in this study where the rates of dislodgement was (3.23% in Quad vs 12.9% in BiP; p 0.045). These findings can be attributed to the design of quadripolar LV lead as it is more flexible and available in preformed curves providing the upper hand to the operator for selection as per the anatomy of coronary sinus tributaries. As quadripolar lead offers multi-vector pacing, the tip of lead can be wedged in more distally while other electrodes are placed at optimum pacing sites providing better stability and more vectors for effective biventricular pacing [30]. PNS was managed with reprogramming in both the groups (83.3% in Quad vs 75% in BiP) consistent with previous studies [29,31–33]. Electronic repositioning due to multiple poles in the quadripolar lead is an easy answer to high thresholds and PNS in the Quad group. The bipolar lead had a significantly higher impedance at implant and 6 months in our study, which has been shown in independent studies, that increased LV lead impedance and the threshold are contributory to chances of LV lead deactivation or revision procedures in follow up [20,34].

The overall device-related local site infection (DRI) was 13.9% in our study, however, none led to device explant and all were managed conservatively with appropriate antibiotics. This increased infection can be attributed to the patient characteristics as most of them had renal insufficiency in form of CKD stage 3/4 (81.72%) and diabetes mellitus (37.63%) making them frailer and more vulnerable to infection as already shown in previous studies [35,36]. In our study, maximum number of the patients received CRT-D (86.02%) which is associated with increased chances of infection [36]. Another factor for increased infection can be the re-intervention done in 5 (5.37%) patients, which also pre-disposes for DRI [35]. Prevention of DRI is challenging and can be reduced with proper preparation of patient and lab before CRT implantation, using quadripolar lead to avoid chances of re-intervention. Newer modalities like the use of antibiotic envelope during pacemaker implantation have shown to be effective for the prevention of DRI and is a subject of further evaluation [37].

4.3. Clinical outcomes

The mean hospitalization events were significantly less in the Quad group (1.5 vs 2.0 in BiP; p 0.043) which has been shown in MORE CRT study [31] where the composite endpoint of HF hospitalization was 83.0% in Quad vs. 74.4% in BiP, (p 0.0002). In a review by Earth et al. (2019) [32] relative risk for HF hospitalization was lower in patients implanted with Quad compared to patients with BiP LV leads (OR = 0.67, 95% CI 0.55–0.83; $p < 0.01$). This significant difference is attributed to the increased LVEF, better improvement in NYHA class, and narrower QRS post-implantation [21] in the quadripolar LV lead group.

The number of mortalities per 100 patient-year was significantly less in the Quad group (6.45 vs 9.37 in BiP; p 0.04) in this study, similar results favoring quadripolar lead was obtained in the study done by Turakhia et al. (2016) (5.04 Quad vs 6.45 BiP lead; $p < 0.001$) [33]. Similar results were obtained by Behar et al. (2015) [34] where they showed that quadripolar leads were associated with a decrease in all-cause mortality (13.2% vs. 22.5% in BiP; $p < 0.001$). A large metanalysis showed a 44% reduction in all-cause mortality when quadripolar lead was used in CRT [28]. In all the three studies, this benefit was directly mediated by the observed lower risk of LV lead deactivation, thereby preserving a longer duration of CRT pacing and a reduced risk of LV lead replacement, reducing the exposure for potential complications of lead or device revisions. An additional property of vector reprogramming to attain maximum biventricular pacing and avoidance of PNS with quadripolar lead may also mediate the effect seen in our study.

5. Limitation

This prospective, observational study lacks randomization and was done at a single center with a small sample size, hence for its result to be applied to the general population large study is required. All the patients in this current study had Class Ia indications of the CRT, and all of them were in sinus rhythm; hence outcomes cannot be applied to patients outside this specified group, and a larger study is required to confirm the findings.

6. Conclusion

In this prospective, non-randomized, single-center observational study, CRT with quadripolar lead was found to be superior to bipolar lead in terms of better CRT response, lesser heart failure hospitalization, and all-cause mortality benefit. The quadripolar lead was associated with less lead-related complications providing a technical superiority over the bipolar lead.

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CRediT authorship contribution statement

Ajay Raj: Conceptualization, Visualization. **Ajay Pratap Singh:** Conceptualization, Writing – original draft, Visualization. **Ranjit Kumar Nath:** Writing – review & editing, Project administration. **Neeraj Pandit:** Formal analysis, Supervision. **Puneet Aggarwal:** Writing – review & editing. **Ashok Kumar Thakur:** Investigation, Software. **Rajeev Bharadwaj:** Formal analysis. **Vinod Kumar:** Investigation, Software.

Declaration of competing interest

None.

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