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Original Article

The Clinical, Electrocardiographic, and Echocardiographic Outcomes of Posterolateral vs Anterolateral Lead Position in Patients With Nonischemic Cardiomyopathy Receiving Cardiac Resynchronization Therapy

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) is a safe and effective method to treat heart failure (HF) in selected patients after failed medical therapy. We aimed to compare the effects of left ventricular (LV) lead position on the clinical, electrocardiographic (ECG), and echocardiographic parameters in patients with nonischemic cardiomyopathy (NICM) considering the absence of a large regional scar.

Methods: Thirty consecutive patients with NICM referred to the Imam Khomeini Hospital Complex for CRT implantation were enrolled in this study. Clinical, ECG, and echocardiographic parameters at baseline and 6 months of follow-up in patients whose left ventricular lead (LV) was implanted in the anterolateral (AL) vs posterolateral (PL) branch of the coronary sinus were compared.

Results: The majority of the patients were women (16, 53%). In both groups, functional class improved significantly after CRT implantation, but this decrease was not related to the position of the LV lead. The QRS width in ECG was significantly reduced in the AL group after CRT implantation (from 157.7: 95% CI, 156.13 to 158.27 to 137.3: 95% CI, 133.37 to 141.24; *P* =0.000). This decrease was also seen in the PL group (from 157.6: 95% CI, 154.26 to 160.01 to 137.6: 95% CI, 133.46 to 141.84; *P* =0.000), but the decrease was not related to the LV lead position.

Conclusions: Our data showed no significant differences in clinical, ECG, or echocardiographic outcomes between PL and AL lead positions in patients receiving CRT. ***(Iranian Heart Journal 2023; 24(3): 70-76)***

KEYWORDS: Cardiac resynchronization therapy, Heart failure, Cardiomyopathies, Nonischemic cardiomyopathy, Coronary sinus lead

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Heart Failure (HF) has been recognized as a significant cause of morbidity and mortality in all communities. [1] Cardiac resynchronization therapy (CRT) is an efficient treatment for patients with drug-refractory, chronic HF. [2] Multiple single-center and multicenter studies have shown considerable reductions in left ventricular (LV) volumes and an increase in LV systolic function following CRT implantation. [3] More importantly, CRT reduces mortality and morbidity during long-term follow-ups. [4] Current guidelines consider CRT a Class I indication for HF patients in New York Heart Association (NYHA) functional class (FC) II or III or ambulatory IV despite guideline-directed medical therapy with depressed left ventricular ejection fraction (LVEF, <35%) and left bundle branch block (LBBB) morphology on electrocardiography (ECG). [5] The principal therapeutic goal of CRT is the restoration of coordinated myocardial contraction (the resolution of interventricular dyssynchrony). The current preferred method to achieve this goal is to position the LV lead at a lateral or posterolateral (PL) branch of the coronary sinus (CS) based on the results of early hemodynamic studies. [6,7] Later reports have challenged this view and suggested that there is great individual variation in the optimal LV pacing site and that the effects of resynchronization may be optimally facilitated when the LV is paced at the most delayed site, avoiding myocardial scars. [8,9] Newer techniques, such as speckle-tracking and targeted LV lead placement, have been used to shortcut the scar and place the LV lead as far away from the regional scar as possible. [10] Pacing the most delayed LV region appears to result in better clinical response, greater LV reverse remodeling, reduced mortality, and curtailed HF-related hospitalization. [11] Similarly, LV lead placement in areas of the scar is associated with attenuated clinical and echocardiographic response. [12] However, this problem is less challenging in nonischemic cardiomyopathy (NICM) since the large regional scar caused by an ischemic accident is less prominent in these patients, and the fibrosis pattern has a more diffuse distribution than in ischemic cardiomyopathy (ICM). In this study, we aimed to investigate the clinical and echocardiographic outcomes of the LV lead position in patients with NICM who received CRT.

METHODS

Study Population

Thirty consecutive patients with NICM identified by a variety of methods, including noninvasive diagnostic methods and coronary angiography, eligible for CRT at the Imam Khomeini Hospital Complex were included. The patients were initially evaluated and prospectively enrolled in this study. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences. All the patients received CRT according to the guidelines of the American College of Cardiology (patients with NYHA FC II or III or ambulatory IV HF, LVEF <35%, and QRS duration >150 ms). No patients with complete heart block, atrial fibrillation, and non-LBBB morphology were included in this study.

Measurements

The selected patients who entered this cross-sectional study received CRT according to the conventional protocol with multimodal anesthesia. [13] The patients underwent baseline clinical assessments before CRT implantation, including the Minnesota LIVING WITH HEART FAILURE Questionnaire, the QRS width in baseline ECG, and echocardiographic evaluations, including LVEF, LV end-systolic dimension (ESD), LV (end-diastolic volume (EDV), and the severity of mitral regurgitation (MR). After 6 months of CRT implantation, all clinical, ECG, and echocardiographic parameters were reassessed.

Statistical Analysis

The results were summarized as mean values and 95% confidence intervals (CIs). Categorical data were expressed as percentages. Continuous variables were compared using the paired and unpaired Student *t* and Fisher exact tests for proportions. The paired Student *t* test was used to compare continuous data within the subgroups. For all the tests, a *P* value of less than 0.05 was considered statistically significant.

RESULTS

In the current study, we enrolled 30 patients with NICM, the majority of whom were women (16, 53.33%). In these patients, the positions of anterolateral (the AL group) and posterolateral (the PL group) leads were evaluated separately by gender and age (minimum: 41 y and maximum 77 y). The mean age was 58.15 (95% CI, 53.41 to 62.90) years in the AL group and 59.88 (54.49 to 65.27) years in the PL group. The baseline characteristics of the patients are detailed in Table 1.

Table 1: Baseline characteristics of the study population

Sex (male)	14
Age, y	59.13 (55.65-62.61)
NYHA Functional Class, n III IV	 26 4
QRS duration, ms	157.67 (155.29-160.04)
LVEF, %	18.83 (16.21-21.46)
LVESV, mL	160.57 (147.56-173.58)
LVEDV, mL	205.17 (192.85-217.49)
LVEDD	65.07 (63.02-67.11)
LVESD	54.53 (52.56-56.51)
MR severity (moderate/severe)	18/12

LV, Left ventricle; LVEDD, Left ventricular end-diastolic dimension; LVEDV, Left ventricular end-diastolic volume; LVEF, Left ventricular ejection fraction; LVESD, Left ventricular end-systolic dimension; LVESV, Left ventricular end-systolic volume; NYHA, New York Heart Association; MR, Mitral regurgitation

Data are presented as mean + 95% CI (in parentheses) for quantitative variables.

As is addressed in Table 2, in both groups, FC improved significantly following CRT implantation, but this decrease was not related to the position of the LV lead (*P* =0.79). One of the clinical evaluations in this study was the number of days without hospitalization after CRT implantation during the first 6 months, which varied from 0 to 180 days. This clinical parameter has an important impact on the physician and the patient. None of the patients in each group was rehospitalized after CRT implantation.

The QRS width was significantly reduced in the AL group after CRT implantation (from 157.7: 156.13 to 158.27 to 137.3: 133.37 to 141.24; *P* =0.00). This decrease was also observed in the PL group (from 157.6: 154.26 to 160.01 to 137.6: 133.46 to 141.84; *P* =0.00); nonetheless, the decrease in the QRS width was not significantly related to the LV lead position (*P* =0.89).

In the patients who received CRT, there was a significant improvement in LVEF (from 18.8: 95% CI, 16.21 to 21.46 to 25.3: 95% CI, 23.14 to 27.52; *P* =0.00). Nevertheless, in neither of the groups did the LV lead position exert any significant effect on the degree of LVEF increase (*P* =0.15). Different degrees of improvement in LVEDD and LVESD were observed in both groups of patients, which can be attributed to the severity of underlying cardiomyopathy. Still, the position of the LV lead at the AL or PL sites had no significant effects on these parameters following CRT implantation. MR severity was classified as severe, moderate, and mild. Although MR intensity decreased after CRT implantation in both groups, this decrease was not significantly related to the LV position. A more detailed clinical, ECG, and echocardiographic report of the patients before and after CRT implantation is presented in Table 3.

Table 2: Clinical, electrocardiographic, and echocardiographic findings of the studied patients with AL and PL LV lead positions in follow-up

Variable	AL Group (N=13)	PL Group (N=17)	*P* value
NYHA Functional Class II III	 12 1	 15 2	 0.79
QRS width(m)	137.31 (133.37-141.24)	137.64 (133.46-141.84)	0.89
LVEF (%)	24.61 (21.25-27.98)	25.88 (22.70-29.06)	0.15
LVEDD (mm)	61.46 (58.39-64.53)	60.18 (57.72-62.64)	0.93
LVESD (mm)	49.00 (45.76-52.24)	49.53 (46.96-52.09)	0.16
LVEDV (mL)	175.00 (153.11-196.89)	169.41 (154.87-183.95)	0.48
MR severity (Moderate / Severe)	8/5	9/8	0.63

AL, Anterolateral; PL, Posterolateral; LV, Left ventricle; LVEDD, Left ventricular end-diastolic dimension; LVEDV, Left ventricular end-diastolic volume; LVEF, Left ventricular ejection fraction; LVESD, Left ventricular end-systolic dimension; LVESV, Left ventricular end-systolic volume; NYHA, New York Heart Association; MR, Mitral regurgitation

Data are presented as mean + 95% CI (in parentheses) for quantitative variables.

Table 3: Clinical, electrocardiographic, and echocardiographic findings of patients before and after CRT implantation

	LV Lead Position	Sex	Age	EF 1	EF 2	LVDD 1	LVDD 2	LVSD 1	LVSD 2	LVEDV 1	LVEDV 2	QRS1	QRS 2	NYHA 1	NYHA 2	Days of Hospitalization	LVESV 1	LVESV 2	MR1	MR2
1	PL	F	69	20	25	65	60	54	49	200	175	160	145	3	2	140	160	132	3	2
2	PL	M	63	15	20	70	65	60	55	245	205	165	140	3	2	150	160	132	3	2
3	AL	M	62	15	20	59	58	48	45	185	145	155	140	3	1	100	155	115	3	1
4	PL	M	53	15	15	67	64	59	55	240	210	150	145	2	2	40	195	180	2	2
5	AL	F	70	10	20	70	62	60	55	240	200	160	130	3	2	120	215	160	2	1
6	PL	F	47	30	35	57	55	48	45	170	140	150	130	3	1	0	115	95	2	1
7	AL	M	57	10	15	73	69	60	54	250	220	155	135	3	2	0	220	185	3	2
8	PL	F	69	15	20	69	65	58	50	215	190	153	135	3	2	150	175	150	3	1
9	PL	F	56	20	20	60	61	48	45	175	175	157	140	3	3	50	135	135	2	2
10	PL	M	74	30	35	60	53	55	50	155	130	154	135	3	1	0	110	82	2	1
11	AL	F	49	20	30	59	56	47	42	150	110	155	135	3	2	0	120	75	3	1
12	PL	M	59	30	30	57	56	48	45	135	140	153	153	3	3	60	90	95	2	2
13	PL	M	53	10	20	75	65	63	58	235	190	185	130	4	3	110	210	150	2	1
14	AL	M	47	15	20	72	68	61	58	245	210	155	135	3	2	130	200	165	2	2
15	PL	F	71	20	30	58	57	47	43	150	110	155	132	3	1	150	115	75	3	1
16	AL	F	58	30	35	57	54	46	41	160	120	159	140	3	1	0	110	77	2	1
17	AL	F	70	25	25	70	65	59	52	220	220	155	155	3	2	75	160	160	2	2
18	PL	F	71	30	35	69	63	59	50	235	170	154	131	3	1	110	160	110	2	2
19	PL	F	57	30	30	61	62	49	49	200	200	155	145	2	2	80	135	135	2	2
20	PL	F	41	15	25	73	70	62	60	230	190	160	154	4	4	30	190	145	2	2
21	AL	F	65	10	20	71	64	60	54	240	190	165	140	4	3	95	210	150	3	2
22	PL	F	58	10	20	68	59	58	50	220	180	155	132	3	2	165	190	140	3	1
23	PL	M	49	15	25	65	59	53	48	215	160	160	130	3	2	170	180	117	2	1
24	AL	F	61	20	30	63	61	52	48	215	180	160	135	3	2	80	172	125	2	2
25	PL	M	77	25	30	62	55	52	47	210	170	160	134	3	2	170	155	120	3	1
26	PL	F	51	15	25	60	54	49	43	185	145	153	129	3	2	100	155	105	3	1
27	AL	M	60	20	25	69	68	56	51	235	200	157	137	3	2	120	180	145	2	2
28	AL	M	51	20	30	65	59	55	46	200	165	160	140	3	1	0	155	120	2	1
29	AL	M	47	15	25	65	60	54	46	205	165	155	128	3	1	0	160	125	3	1
30	AL	M	59	10	25	63	55	56	45	195	150	160	135	3	2	0	130	75	2	1

CRT, Cardiac resynchronization therapy; PL, Posterolateral; AL, Anterolateral; M, Male; F, Female, 1, Before device implantation; 2, After device implantation; LV, Left ventricle; LVEDD, Left ventricular end-diastolic dimension; LVEDV, Left ventricular end-diastolic volume; EF, Ejection fraction; LVESD, Left ventricular end-systolic dimension; LVESV, Left ventricular end-systolic volume; NYHA, New York Heart Association; MR, Mitral regurgitation

DISCUSSION

In the current study, we found that both PL and AL LV lead locations in NICM patients with CRT were associated with a significant reduction in the QRS width and an improvement in LVEF, LVEDD, and LVESD; however, these improvements were not related to the position of the LV lead.

One of the limitations in providing resynchronization to CRT candidates is the implantation of the CS lead in the appropriate site, which is strongly related to the presence of a suitable branch and the absence of regional scars. Previous research indicates that targeting the lateral or PL wall with a suitable CS branch is an important factor in clinical results. [6,14] This technique is predicated on the premise that the majority of patients eligible for CRT implantation have LBBB in baseline ECG; consequently, the latest activation of the LV is along the lateral or posterolateral wall. [15] In a study by Kutyifa et al, [16] a reduction in the long-term mortality rate was observed in patients who received CRT with a lateral or posterior LV lead compared with patients with the anterior position of the LV lead. Our study showed that the implantation of the LV lead in AL and PL positions both led to similar clinical, ECG, and echocardiographic improvements. Our findings support the notion that the implantation of the CS lead whether anteriorly or posteriorly, when it is in the lateral vicinity of the LV, is optimal, and clinical, ECG, and echocardiographic improvements are anticipated.

Earlier research suggests that effective resynchronization can be achieved by appropriately implanting the LV lead in the region of the maximal mechanical LV delay. [17] The Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy (TARGET) [18] trial reported promising improvements in both echocardiographic and clinical outcomes by speckle-tracking imaging leads in a study on 220 patients. Later on, the Speckle-Tracking-Assisted Resynchronization Therapy for Electrode Region (STARTER) [19] trial showed improvements in survival rates (HR, 0.40; 95% CI, 0.22 to 0.71; *P* =0.002) by using radial strain values for lead positioning. Our study is based just on fluoroscopy guidance and coronary anatomy rather than high-technology imaging tools (speckle-tracking echocardiography, computed tomography angiography, or magnetic resonance imaging for guiding the LV lead implantation).

Despite clinical and echocardiographic improvements in the current study, our data indicated no differences in patients with AL vs PL LV lead implantation, which chimes with a prior study by Dong et al, [20] who showed comparable improvements in NYHA FC and LVEF in both AL and PL groups. Additionally, their study revealed that survival was reduced if the LV lead was implanted in the anterior wall of the LV, and survival was improved if the LV lead was positioned in the AL wall. It is noteworthy that the assumption that patients with NICM do not always have a regional scar is a form of simplification, and one should not neglect the diverse pathophysiology of NICM.

Patients with cardiomyopathy have a higher risk of complications during and after the procedure, and curtailing the procedure time would reduce complications, such as device infection and bleeding complications. Since we witnessed no significant differences in the endpoints between our 2 groups, it may be reasonable not to prolong the procedure for the cannulation of a particular vein in the complex anatomy of the CS.

CONCLUSIONS

The findings of the present study showed no significant differences in clinical, ECG, and echocardiographic outcomes of patients with the AL or PL LV lead position. Further

studies, including large-scale randomized clinical trials, are needed to reach a more comprehensive and accurate recommendation.

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Authors' Contributions
ME collected the initial data. SMM collected the data. ES and AB conducted the literature review and wrote the initial draft of the manuscript. RM and RP helped with the initial draft. RM implanted the CRT for the patients, corrected and improved the draft, and submitted the manuscript. All the authors read and approved the final manuscript.

Conflict of Interest
The authors declare that they have no conflicts of interest regarding this manuscript.

REFERENCES

1. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. *Nature reviews Cardiology* 2016; **13**(6): 368-78.

2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal* 2016; **37**(27): 2129-200.

3. Dokuni K, Matsumoto K, Tatsumi K, et al. Cardiac resynchronization therapy improves left atrial reservoir function through resynchronization of the left atrium in patients with heart failure with reduced ejection fraction. *The international journal of cardiovascular imaging* 2020: 1-10.

4. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *The New England journal of medicine* 2002; **346**(24): 1845-53.

5. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology* 2022; **79**(17): e263-e421.

6. Butter C, Auricchio A, Stellbrink C, et al. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001; **104**(25): 3026-9.

7. Bleeker GB, Kaandorp TA, Lamb HJ, et al. Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. *Circulation* 2006; **113**(7): 969-76.

8. Sassone B, Nucifora G, Mele D, Valzania C, Bisignani G, Boriani G. Role of cardiovascular imaging in cardiac resynchronization therapy: a literature review. *J Cardiovasc Med (Hagerstown)* 2018; **19**(5): 211-22.

9. Satish P, Narasimhan B, Hagendorff A, Tayal B. Evolving concept of dyssynchrony and its utility. *J Geriatr Cardiol* 2022; **19**(1): 44-51.

10. Khan FZ, Virdee MS, Palmer CR, et al. Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy: The TARGET Study: A Randomized, Controlled Trial. *Journal of the American College of Cardiology* 2012; **59**(17): 1509-18.

11. Ansalone G, Giannantoni P, Ricci R, Trambaiolo P, Fedele F, Santini M. Doppler myocardial imaging to evaluate the effectiveness of pacing sites in patients receiving biventricular pacing. *Journal of the American College of Cardiology* 2002; **39**(3): 489-99.

12. Wong JA, Yee R, Stirrat J, et al. Influence of pacing site characteristics on response to cardiac resynchronization therapy. *Circ Cardiovasc Imaging* 2013; **6**(4): 542-50.

13. Mollazadeh R, Eftekhari MR, Eslami M. Efficacy of Intravenous Acetaminophen in

Periimplantation Pain of Cardiac Electronic Devices: A Randomized Double-Blinded Study. *Journal of PeriAnesthesia Nursing* 2017; **32**(3): 215-8.

14. Dekker A, Phelps B, Dijkman B, et al. Epicardial left ventricular lead placement for cardiac resynchronization therapy: optimal pace site selection with pressure-volume loops. *The Journal of thoracic and cardiovascular surgery* 2004; **127**(6): 1641-7.

15. Auricchio A, Fantoni C, Regoli F, et al. Characterization of left ventricular activation in patients with heart failure and left bundle-branch block. *Circulation* 2004; **109**(9): 1133-9.

16. Kutyifa V, Kosztin A, Klein HU, et al. Left Ventricular Lead Location and Long-Term Outcomes in Cardiac Resynchronization Therapy Patients. *JACC: Clinical Electrophysiology* 2018; **4**(11): 1410-20.

17. Ypenburg C, van Bommel RJ, Delgado V, et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. *Journal of the American College of Cardiology* 2008; **52**(17): 1402-9.

18. Khan FZ, Virdee MS, Palmer CR, et al. Targeted left ventricular lead placement to guide cardiac resynchronization therapy: the TARGET study: a randomized, controlled trial. *J Am Coll Cardiol* 2012; **59**(17): 1509-18.

19. Saba S, Marek J, Schwartzman D, et al. Echocardiography-guided left ventricular lead placement for cardiac resynchronization therapy: results of the Speckle Tracking Assisted Resynchronization Therapy for Electrode Region trial. *Circ Heart Fail* 2013; **6**(3): 427-34.

20. Dong Y-X, Powell BD, Asirvatham SJ, et al. Left ventricular lead position for cardiac resynchronization: a comprehensive cinegraphic, echocardiographic, clinical, and survival analysis. *EP Europace* 2012; **14**(8): 1139-47.