Cardiac Resynchronization Therapy Using Left-bundle-branch Area Pacing and Coronary Sinus Pacing

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Research Article

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Abstract

Background:

Cardiac resynchronization therapy via biventricular pacing (BVP) is an established therapy for patients with heart failure. Recently, it has been shown that left bundle branch area pacing (LBBAP) is feasible and may also improve clinical outcomes. In this article, we describe a new technique (sequential LBBAP followed by coronary sinus pacing, designated LOT-CRT) and assess the feasibility of LOT-CRT.

Methods:

The database of all patients from single centre was reviewed retrospectively. The eligible patients were divided into two groups randomly, LOT-CRT and BV-CRT. The LBBAP lead implanted using our methods. The QRS duration (QRSd) was measured at baseline and during LBBAP, BVP, and LOT-CRT.

Results:

The study enrolled 11 consecutive heart failure patients with LBBB. LBBAP failed in 1 patient, succeed in 5 patients, while CS leads were implanted successfully in all patients. At baseline, the two groups (5 LOT-CRT cases in group 1, 6 BV-CRT cases in group 2) were matched for QRSd and ischemic cardiomyopathy (ICM, 3 cases in group 1, 2 cases in group 2).

In group 1, BVP resulted in significant reduction of the QRSd from 158.0 ± 13.0 ms at baseline to 132.0 ± 4.5 ms (P=0.019). Compared with BVP, unipolar LBBAP resulted in further reduction of the QRSd to 123.0 ± 5.7 ms (P < 0.01). However, LOT-CRT resulted in a significantly greater reduction of the QRSd to 117.0 ± 6.7 ms (P < 0.01). In group 2, BVP resulted in significant reduction of the QRSd from 176.7 ±19.7 ms at baseline to 143.3 ±8.2 ms (P=0.011). However, compared with LBBAP, BVP resulted in increase of the QRSd (P >0.05).

As compared to the baseline after 3 months of LBBAP, patients in group 1 showed significant improvement in LVEF and NT-proBNP levels (P < 0.01), while patients in group 2 showed non-significant changes in these parameters (P >0.05).

Conclusions:

The study demonstrates that LOT-CRT is clinically feasible in patients with systolic HF and LBBB. LOT-CRT was associated with significant narrowing of the QRSd and improvement in LV function, especially in patients with ICM.

Background

Cardiac resynchronization therapy (CRT) via biventricular pacing (BVP) is known to improve clinical outcomes and decrease all-cause mortality, particularly in patients with left bundle branch block (LBBB)

and reduced left ventricular function[1, 2]. However, up to one-third of patients treated with BVP-CRT are still considered non-responders [3]. The reasons for BVP-CRT nonresponse are many but include LV scar burden and distribution, a suboptimal LV stimulation site, sex, and limited electrical or mechanical dyssynchrony[4]. There is evidence that CRT is not salutary in patients with posterolateral scarring [5].

Recently, several groups have shown the feasibility of left bundle branch area pacing (LBBAP) as an alternative choice to HBP in patients with LBBB by pacing the LBB region beyond the block site with a stable threshold and short QRS duration (QRSd) [6-8]. However, LBBAP achieved only partial reduction of the QRSd in those patients with a baseline surface ECG of atypical LBBB morphology[9].

We hypothesized that electrical resynchronization measured by narrowing of the QRS complex can be accomplished more effectively using LBBAP followed by sequential coronary sinus pacing (LBB-optimized coronary sinus pacing, LOT-CRT) than using existing techniques. The patients with atypical LBBB and a higher overall scar burden might be the desired candidates for LOT-CRT.

It is unknown whether the clinical efficacy of LBBAP with an appropriate AV delay would be the same as or better than that of LV epicardial pacing or cardiac resynchronization therapy. The aim of our study was to assess the feasibility and efficacy of LOT-CRT as a means to improve electrical resynchronization in patients qualifying for CRT and evaluate clinical and echocardiographic response rates.

Methods

This study was approved by the Ethics Committee of Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine (approval number: XHEC-D-2020-148) and performed in accordance with the Declaration of Helsinki.

Patient selection

Patients with chronic LBBB according to the Strauss criteria[10], optimal medical therapy–refractory New York Heart Association (NYHA) class III to IV heart failure (HF) symptoms and a baseline left ventricular ejection fraction (LVEF, calculated by the Simpson method) ≤ 35% were enrolled at Shanghai Xinhua Hospital from February 1, 2019, to July 1, 2020.

Patients were excluded if they had disagreement with LOT-CRT, end-stage renal disease, use of a left ventricular assist device, metastatic cancer, or they had a life expectancy of less than 1 year.

All patients submitted written informed consent and demonstrated an understanding of LOT-CRT as a nonstandard approach to achieve physiologic pacing, and their data were analysed prospectively.

Study design

The clinical database of all patients from single centre was reviewed retrospectively and the study design was showed in Figure 1. In the analysis of ICD type, the patients were divided into two groups: LOT-CRT

(Group 1), conventional CRT using biventricular pacing (BV-CRT, Group2). If primary LBBAP was unsuccessful in patients for LOT-CRT, BIV-CRT would be implanted and the patient was transferred into group 2. Correspondingly，if primary CS lead was unsuccessful in patients with indication for CRT, a LBBAP lead was implanted and the patient could be exited from the study.

Procedural Details

The RV defibrillator lead was first implanted in the RV to provide backup ventricular pacing should the patient develop transient complete atrioventricular block during LBBAP lead placement. Subsequently, the coronary sinus (CS) lead was implanted using routine implantation techniques, targeting sites with maximal LV delay [11, 12]. Then, LBBAP was performed using the Select Secure pacing lead. All defibrillator electrodes were implanted in the RV apical position. The fluoroscopy durations for the entire procedure, LBBAP lead implantation and LV lead implantation were separately recorded.

LBBAP lead implantation technique

As previously described [13-16], a Select Site C315 His sheath and a Select Secure 3830 pacing lead (Medtronic Inc, Minneapolis, MN, USA) were advanced to the implantation site. The right ventricular septal location for LBBAP was identified using the anatomical location and pacing localization the nine-grid system[17]. Once this site was identified, the pacing lead is advanced deep into the septum while the unipolar pacing impedance, electrogram characteristics and paced QRS morphology were monitored.

Additionally, the lead orientation can be displayed in various projections. During the initial LBBAP lead fixation, if the lead twists back, this indicates that the lead and sheath are not oriented orthogonal to the RV septum. Generally, the sheath and the lead are oriented such that the lead is pointing in the 12- to 1-o'clock direction from a right anterior oblique viewing angle of 30° and the 2- to 3-o'clock direction from a left anterior oblique viewing angle of 30°[18].

If an acceptable LBB capture could not be achieved after 5 attempts of lead positioning, it was considered a failure [19].

Optimal CS location

The details of the device and procedure have been described elsewhere [11, 12]. Optimal vein selection and lead implantation is greatly facilitated by high-quality occlusive venography. Traditionally, CS intubation is performed by advancing a 0.035-inch hydrophilic wire to the region of the CS ostium via a preformed guide catheter and probing to locate the CS ostium. Venograms are typically performed in the anteroposterior and left anterior oblique projections. Optimal CS location was limited to the distribution of the coronary veins [11, 12].

Device Connection and Programming

In group 1, the patients undergoing CRT-defibrillator treatment, the LBBAP lead was connected to the pace-sensing portion of the RV port, and a CS lead was connected to the LV port. The pace-sensing portion of the spliced implantable cardioverter -defibrillator (ICD) lead (DF-1) was capped. In patients undergoing CRT-pacemaker (P) treatment, the CS lead was connected to the LV port. Then the LBBAP lead was connected to the RV port.

In group 2, the patients undergoing CRT-defibrillator treatment, the CS lead was connected to the LV port. Then the RV defibrillator lead was connected to the RV port.

Implant Measurements

The pacing output required to maximally narrow the QRS (BBB correction threshold) and LBB capture threshold (without BBB correction) was assessed and recorded at a pulse width of 1.0 ms. The QRSd values at baseline and during LBBAP, BVP (over RV defibrillator lead and the CS lead during procedure period firstly, or via the lead at the LBBA when RV defibrillator lead unavailable) and LBB-optimized LV pacing were measured on the EP recording system at 100 mm/s. The stimulus to left ventricular activation time during LBBAP was documented.

Programming and follow up

Before hospital discharge, separate “zones” can be programmed for detection of ventricular fibrillation and ventricular tachycardia. All patients were seen for routine clinical follow-up at standard time intervals (every 3 months) and had a follow-up period of at least 3 months. Functional status was assessed by the NYHA classification system. Device thresholds were checked and adjusted as needed to maximize battery longevity. The pacing threshold, impedance and R wave amplitude were measured. All device-detected and treated VT/VF episodes were reviewed and adjudicated by an independent episode reviewer.

According to previous literature[20], a high pacing threshold was defined as a pacing threshold over 2.5 V/0.4 ms or an increase of more than 1.0 V compared with the baseline after the procedure and at follow-up. Echocardiographic indices, including LVEF, LV end-diastolic dimension (LVEDD), and pulmonary artery systolic pressure, were recorded before implantation and at follow-up.

Statistical analysis

Continuous variables are presented as the mean ± SD or median. Paired comparisons were made using Student’s t-test if the data were normally distributed; otherwise, the nonparametric Wilcoxon signed-rank test was used. Paired categorical data (NYHA functional class) were compared using the Wilcoxon test. $P \leqq 0.05$ was considered significant.

Results

Four out of the 16 eligible patients were excluded from the study according to the exclusion criteria. Consequently, 12 patients were eligible for CRT. During follow-up, one patient in group 2 lost to follow-up.

So out of the 12 eligible patients, only 11 patients enrolled the study (6 in group 1, 5 in group 2). Among 6 patients in group1, 1 patient failed to complete LBBAP and transferred into group 2. In the end, five patients (45.5%) were defined as group LOT-CRT; six patients (54.5%) were defined as group BIV-CRT.

All patients had had at least 1 HF hospitalization 3 months before LBBAP implantation. Entresto (sacubitril/valsartan), β-blockers, and loop diuretics were prescribed to all patients.

Baseline characteristics

Among the 11 patients, six (54.5%) were male. All patients had cardiomyopathy (6 non-ischemic and 5 ischemic), and 3 patients had paroxysmal atrial fibrillation. Hypertension was present in 4 patients. Frequent ventricular premature contraction (VPC) (> 1,000 per 24 hours[21]) were found in 3 patients. The mean age was 69.1 ± 6.4 years, and the baseline characteristics of the patients were provided in Table 1. At baseline, the two groups were matched for age, gender, hypertension, diabetes mellitus, ICM, atrial fibrillation as illustrated in Table I (all P >0.05).

The echocardiographic indices, including LVEF, LVEDD, and NYHA classification, NT-proBNP were shown in Table 3. Both groups did not show significant difference (all P >0.05). The baseline LVEF and the baseline QRSd with LBBB (Figure 2a) were 33.9 ± 3.9% and 168.2 ± 18.9 ms, respectively.

Procedural Outcomes

Biventricular ICDs (CRT-D) were implanted in 9 patients (Figure 3A, 3B), and CRT pacemaker was implanted in the remaining 2 patients (Table 2). One in every group, CRTP did not differ between two groups (P > 0.05). The operation duration was 135 ± 26 min. The duration of X-ray fluoroscopy was 29.2 ± 8.8 min. In group 1, LBBAP was successfully achieved in 5 patients. Another one failed and transferred into group 2. So the acute success rate was 83.3%.

In group 2, CS lead was successfully implanted in all 6 patients. The acute success rate was 100%. Compared with group 2, the operation duration and the duration of X-ray fluoroscopy in group 1 all increased, but the later was not significantly (P > 0.05)(Table 2).

Both the LBBAP and LV capture thresholds remained stable during procedure (1.3 ± 0.6 V at 0.4 ms vs. 1.6 ± 0.7 V at 0.4 ms). Bipolar LBBAP resulted in partial but significant narrowing of the QRSd (BBB correction) in 5 patients.

Both groups did not show difference in CS pacing lead, RV defibrillator lead parameters, such as R-wave amplitude, threshold, and impedance and so on (Table 2).

ECG characteristics and pacing parameters

Individual electrocardiographic responses to RV, LV, and LBBAP at the time of implantation were shown in Table 2. Among the 11 patients, the baseline QRSd was 168.1 ± 18.9 ms (Figure 2a). At baseline, the two groups were matched for QRSd (158.0 ±13.0, vs. 176.7 ±19.7, P >0.05) as illustrated in Table 3.

In group 1, after unipolar LBBAP, 5 patients demonstrated a right bundle branch block (RBBB) pattern with a paced QRSd of 123.0 ± 5.7 ms (P = 0.001 vs. baseline) (Figure 2b). LBB potential could be recorded in 3 patients from the LBB lead (60%). The LVAT for all LBBAP patients was 72.5 ± 9.4 ms, and the R wave amplitude, pacing impedance, and unipolar pacing capture threshold were 9.9 ± 7.2 V, 678 ± 102 Ω, and 0.84 ± 0.17 V/0.4 ms, respectively.

In group 1, BVP resulted in significant reduction of the QRSd from 158.0 ± 13.0 ms at baseline to 132.0 ± 4.5 ms (P=0.019) (Figure 2c). Compared with BVP, unipolar LBBAP resulted in further reduction of the QRSd to 123.0 ± 5.7 ms (P=0.006 versus baseline and P=0.021 versus BVP). However, LOT-CRT resulted in a significantly greater reduction of the QRSd to 117.0 ± 6.7 ms (P < 0.01 versus baseline, BVP, or bipolar LBBAP).

In group 2, BVP resulted in significant reduction of the QRSd from 176.7 ±19.7 ms at baseline to 143.3 ±8.2 ms (P=0.011). However, compared with LBBAP, BVP resulted in increase of the QRSd (P >0.05, Table 3).

Follow-up

The mean follow-up time was 300 ± 185 days. At baseline, the two groups were matched for follow-up time (296±201, 305±190, P >0.05). Among all 11 patients, CS lead parameters were stable during follow-up. In group 1, the LBBAP capture threshold, R-wave amplitude, and lead impedance were 0.74 ± 0.25 V, 13.36 ± 5.23 mV, and 533.73 ± 32.31 Ω during the 3-month follow-up (all P > 0.05, respectively, between the time of device implantation and the follow-up visit). In group 2, the RV lead parameters were also stable during follow-up. No patients showed signs of dislodgement, loss of capture, infections, embolism, or stroke associated with the implantation. The ventricular pacing rate was 95%. There were 8 VT/VF episodes treated with antitachycardia pacing and/or shock that had an electrogram available for adjudication (3 in group 1, 5 in group 2). However, the rate of VT/VF therapy was not statistically different (P =0 .175) between in 2 groups.

Transthoracic echocardiogram (Figure 3) evaluation data at baseline and at the 1-month and 3-month follow-ups were available in all 11 patients receiving successful CRT. As shown in Table 3, the symptoms and the median NYHA classification score improved significantly, with the latter decreasing from 3.36 ±0.50 to 2.45 ±0.52 (P=0.016). LVEF (33.9 ±3.9% vs. 45.4 ±8.7%, P=0.002) and NT-proBNP (2937 ±1646 vs. 1832 ±1541, P=0.014) were brought a corresponding improvement at the follow-up visit significantly. LVEDD (65.1 ±9.1 mm vs. 58.7 ±10.2 mm, P=0.319) was improved at the 3-month follow-up visit, but not significantly (P > 0.05).

As compared to the base line, patients in group 1 showed significant improvement in LVEF and NT-proBNP levels, while patients in group 2 showed non-significant changes in these parameters (Table 3).

Discussion

Major findings

The present study demonstrates the following merits. (1) LOT-CRT was feasible in a small nonrandomized, nonconsecutive series of patients with reduced LVEF and LBBB. At the time of device implantation, ECG changes during LOT-CRT were characterized by LBBB correction, a reduced QRSd, and a short LVAT. (2) Significant improvements in clinical and echocardiographic assessments were achieved during the follow-up period of 3 months. (3) There were no major implantation-related adverse events during the perioperative period or follow-up.

Anatomical definition

CRT using BVP is an integral part of therapy for patients with HF that involves reduced LVEF and BBB, particularly LBBB[22]. However, up to one-third of patients treated with BVP-CRT are still considered non-responders [3]. The reasons for BVP-CRT nonresponse are many but include LV scar burden and distribution, a suboptimal LV stimulation site, sex, and limited electrical or mechanical dyssynchrony[4]. Patients with ischaemic cardiomyopathy experience a similar BVP-CRT response rate to their nonischaemic counterparts [23]. However, a higher overall scar burden, a larger number of severely scarred segments, and greater scar density near the LV lead tip portend an unfavourable response to BVP-CRT in ICM patients[24]. There is evidence that CRT is not salutary in patients with posterolateral scarring [5].

Electrophysiological definition

Permanent LBBAP is an effective form of physiologic pacing with high success rates in patients with intact His-Purkinje conduction[8]. LBBAP can serve as a new CRT technique to correct LBBB, provide ventricular synchrony, and improve clinical symptoms with reverse remodelling of the LV [25].

There is evidence that LV activation time is only minimally increased in RBBB but significantly increased in LBBB [26]. During unipolar LBBAP, as the right ventricle is predominantly activated via myocardial conduction, RV dyssynchrony may be present compared to HBP. However, it does not cause LV dyssynchrony since LV activation occurs via the His-Purkinje system. Therefore, in patients undergoing permanent LBBAP, synchronization of delayed RV activation and normal LV activation is feasible.

LOT-CRT advantage

However, in patients with intraventricular block or higher overall scar burden, success rates are somewhat limited depending on the site of block and the scar burden and distribution of the interventricular septum[9]. Intra- or interventricular dyssynchrony cannot be reduced through LBBAP. LBBAP achieved only partial reduction of the QRSd in those patients with a baseline surface ECG of atypical LBBB morphology[9]. LOT-CRT offers the advantage of using the LV lead in addition to LBBAP in a potential scenario in which conduction disease progresses.

In patients with LBBB and cardiomyopathy, LOT-CRT resulted in significant electrical resynchronization. In group 1 of our study, 60% of whose subjects had severe ischaemic cardiomyopathy, LOT-CRT resulted in high clinical and echocardiographic response rates. Our results indicated that patients with LBBB and a higher overall scar burden might be the desired candidates for LOT-CRT.

Limitations

First, LOT-CRT is time consuming. The duration of the operation was 152 ± 31 min, and the duration of X-ray fluoroscopy was 26.2 ± 5.9 min; both were longer than stated in a previous report (117 ± 48 and 16.4 ± 12.3 min)[8] and control group. Second, this study included only a small sample at a single centre. Third, this study had a short follow-up interval, although we expect favourable long-term clinical benefits. Furthermore, this study enrolled only 5 ischaemic patients. Although this study does not provide sufficient data to support a general conclusion, we observed significant echocardiographic and clinical improvement in these HF patients treated with LOT-CRT.

Conclusions

The study demonstrates that LOT-CRT is clinically feasible in patients with systolic HF and LBBB. LOT-CRT was associated with significant reduction of QRS duration and improvement in LV function, especially in patients with ICM.

Abbreviations

CRT: cardiac resynchronization therapy; BVP: biventricular pacing; LBBAP: left bundle branch area pacing; QRSd: QRS duration; HBP: His bundle pacing; LOT-CRT: LBB-optimized LV pacing; HF: heart failure; LVEF: left ventricular ejection fraction; LV: left ventricle; RAO: right anterior oblique; LAO: left anterior oblique; UTP: unipolar tip pacing; LVAT: left ventricular activation time; ICD: implantable cardioverter-defibrillator

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Xinhua Hospital Affiliated with Shanghai Jiao Tong University School of Medicine (approval number: XHEC -D-2020-148) and performed in accordance with the Declaration of Helsinki. All participants signed an informed consent form.

Consent for publication

Not applicable.

Availability of data and materials

Data are available from the corresponding author upon reasonable request due to privacy or other restrictions.

Funding

none

Authors' contributions

XFF was the study advisor. XFF and RZ designed the study. RZ collected data and performed TTE. BL analysed the data. XFF, RZ, BL, YQH, and QFL performed the procedures. RZ was the main investigator and provided the first draft. YGL critically revised the manuscript. XFF provided the final draft. All authors read and approved the final manuscript.

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Competing interests

We do not have any potential financial or non-financial conflicts of interest.

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Tables

Table 1: Baseline Characteristics in 11 Patients with Procedure of CRT/D (n=11)

	Total(n = 11)	Group 1 (n = 5)	Group 2 (n =6)	P value
Age (years)	69.1 ±6.4	71.8 ±5.1	66.8 ± 6.9	0.217
Gender, Male, n (%)	6(54.5%)	3(60.0%)	3(50.0%)	1.000
Diabetes mellitus, n (%)	2(18.2%)	1(20.0%)	1(16.7%)	1.000
Hypertension, n (%)	4(36.4%)	2(40.0%)	2(33.3%)	1.000
Frequent VPC, n (%)	3(27.3%)	1(20.0%)	2(33.3%)	0.751
ICM, n(%)	5(45.5%)	3(60.0%)	2(33.4%)	0.567
PCI, n (%)	5(45.5%)	3(60.0%)	2(33.3%)	0.567
NT-ProBNP (pg/ml)	2937 ±1646	3240 ±2258	2684 ±1083	0.634
LVEF (%)	33.1 ±3.0	32.0 ±4.2	34.0 ±1.3	0.302
AF, n (%)	3(27.3%)	2(40%)	1 (16.7%)	0.545

Abbreviations: NT-proBNP, N terminal pro B type brain natriuretic peptide; LVEF, left ventricular ejection fraction; PCI, percutaneous transluminal coronary intervention; VPC, ventricular premature contraction; AF, atrial fibrillation; ICM, ischemic cardiomyopathy

Table 2: Procedural Characteristics in Patients with CRT/D Procedure (mean ± SD) (n = 11)

		Total (n = 11)	Group 1 (n = 5)	Group 2 (n =6)	P value
LBBAP	R-wave amplitude	-	9.9 ±7.2	-	-
	Threshold (unipolar) (V/0.4 ms)	-	0.84 ±0.17	-	-
	Impedance (unipolar) (Ω)	-	678 ±102	-	-
	LVAT (ms)	-	75.2 ±9.4	-	-
RV	R-wave amplitude	23.5 ±8.4	24.3 ±11.8	23.0 ±6.5	0.825
	Threshold (unipolar) (V/0.4 ms)	0.82 ±0.20	0.93 ±0.10	0.75 ±0.23	0.187
	Impedance (unipolar) (Ω)	578 ±147	626 ±77	546 ±180	0.434
LV	R-wave amplitude	18.3 ±9.4	13.8 ±2.6	22.1 ±11.6	0.145
	Threshold (unipolar) (V/0.4 ms)	1.0 ±0.24	0.96 ±0.27	1.12 ±0.20	0.301
	Impedance (unipolar) (Ω)	708 ±134	745 ±97	678 ±160	0.434
ICD (%)		9(81.8%)	4(80%)	5(83.3%)	0.727
Fluoroscopic Time (min)		18.8 ±12.2	19.3± 11.5	18.1± 13.8	-
Procedure time (min)		135 ± 26	152 ± 31	122 ± 10	0.04

LBBAP, left bundle branch area pacing; LV, left ventricle; RV, right ventricle

Table 3: Follow-Up Characteristics during a Follow-Up Period of 3 Months in Patients with CRT/D Procedure (mean ± SD) (n = 11)

		Total (n = 11)	Group 1 (n = 5)	Group 2 (n =6)	P value
NYHA classification score	Before procedure	3.36 ±0.50	3.4 ±0.55	3.3 ±0.52	0.840
	1 month after procedure	2.54 ±0.52	2.6 ±0.55	2.5 ±0.55	0.770
	3 month after procedure	2.45 ±0.52	2.4 ±0.55	2.5 ±0.55	0.770
	P value	0.000	0.032	0.024	-
LVEDD (mm)	Before procedure	65.1 ±9.1	68.2 ±12.3	62.6 ±5.3	0.336
	1 month after procedure	63.4 ±10.1	64.4 ±12.6	62.4 ±8.3	0.781
	3 month after procedure	58.7 ±10.2	62.2 ±11.3	55.2 ±8.7	0.303
	P value	0.319	0.735	0.229	-
LVEF (%)	Before procedure	33.1 ±3.0	32.0 ±4.2	34.0 ±1.3	0.302
	1 month after procedure	40.9 ±7.0	41.6 ±7.5	40.3 ±7.3	0.782
	3 month after procedure	45.4 ±8.7	45.0 ±5.1	45.8 ±12.0	0.894
	P value	0.002	0.011	0.143	-
QRSd	Before procedure	168.2 ±18.9	158.0 ±13.0	176.7 ±19.7	0.104
	1 month after procedure	131.4 ±15.5	117.0 ±6.7	143.3 ±8.2	0.001
	P value	0.001	0.005	0.011	-
NT-ProBNP (pg/ml)	Before	2937 ±1646	3240 ±2258	2684 ±1083	0.634

	procedure				
	1 month after procedure	1832 ±1541	1151 ±1774	2066 ±1444	0.607
	P value	0.014	0.04	0.219	-
VT/VF episodes		8	3	5	0.175
Follow-Up Period (d)		300±185	296±201	305±190	0.941

LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N terminal pro B type brain natriuretic peptide; NYHA, New York Heart Association.

Figures

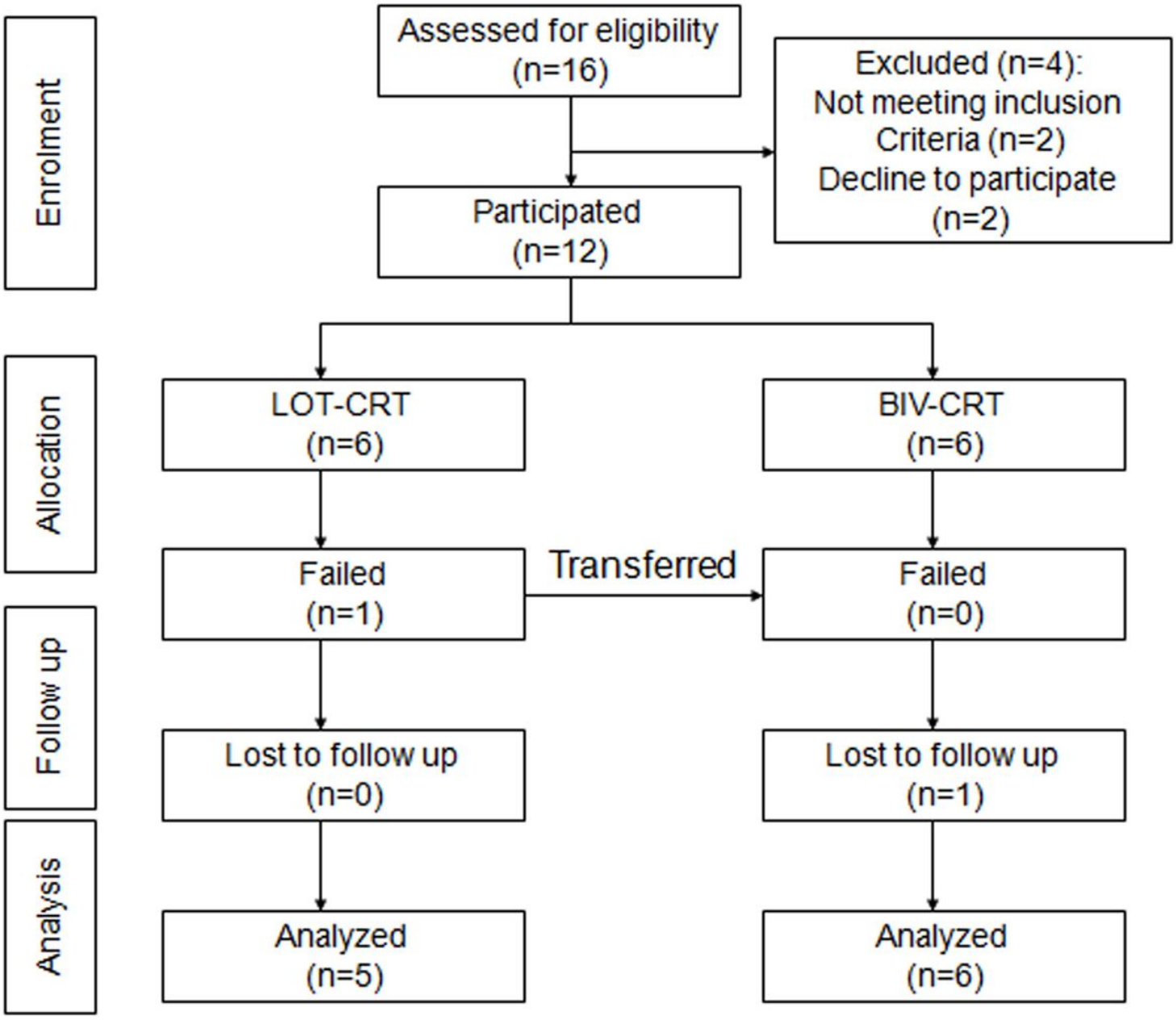

Figure 1

Flowchart showing study design

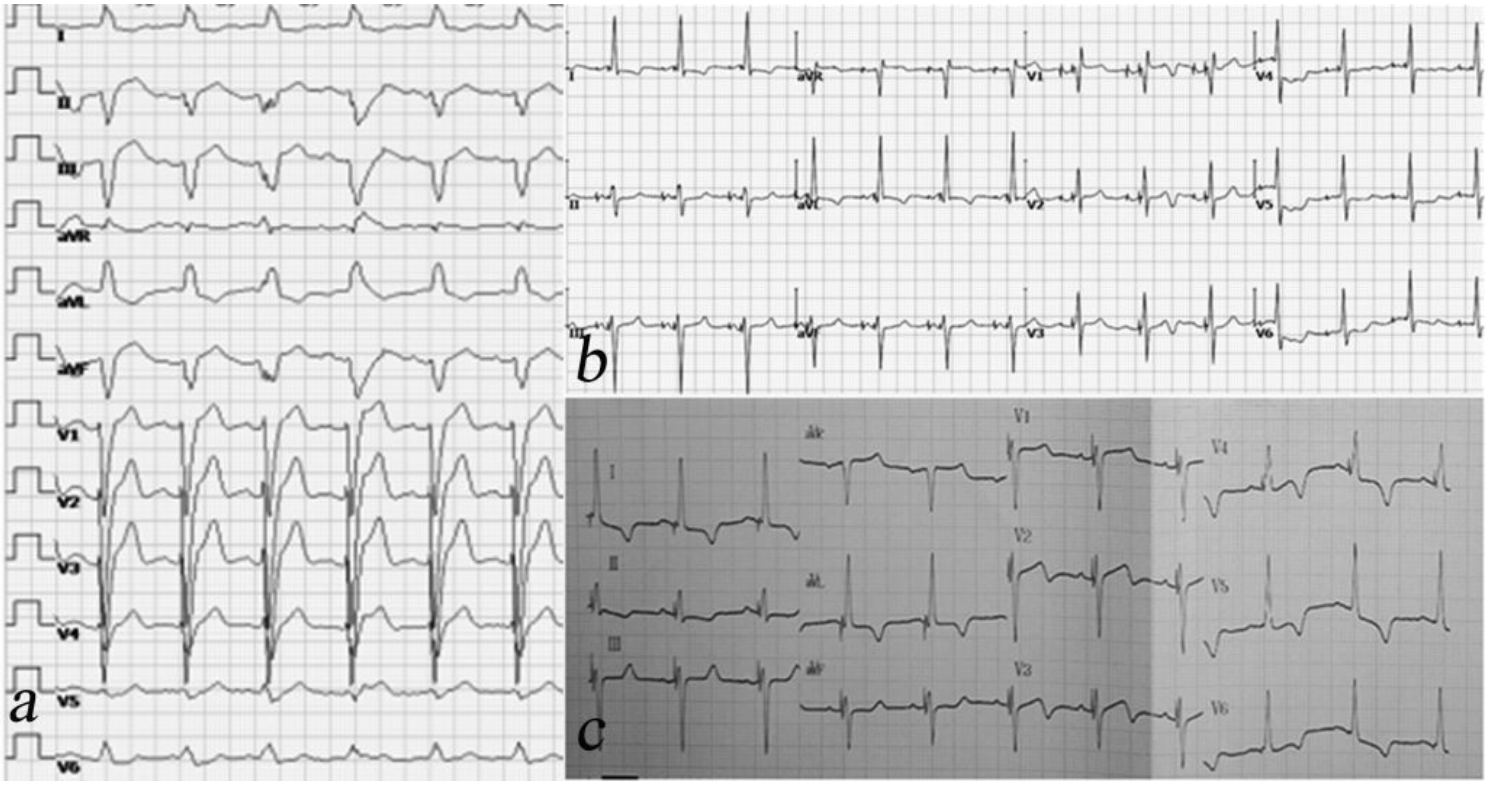

Figure 2

Left-bundle-branch-optimized cardiac resynchronization therapy in a patient with ischemic cardiomyopathy. A, Baseline ECG shows LBBB with a QRS duration of 160 ms. b, During unipolar LBBAP pacing, a right bundle branch block pattern with a QRS duration of 122 ms is visible. c, During pacing with LOT-CRT, a left bundle branch block correction pattern with a QRS duration of 120 ms is visible.

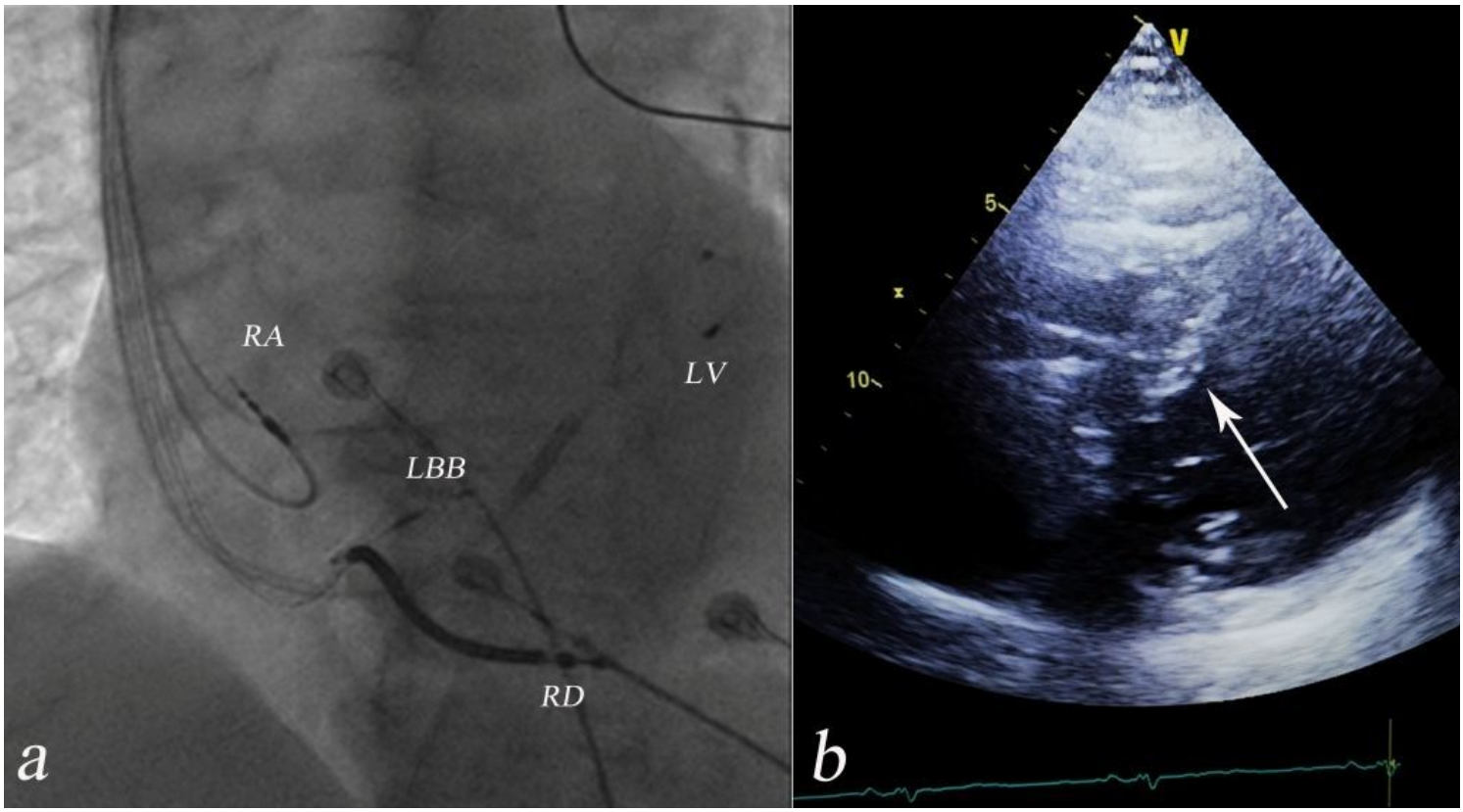

Figure 3

Fluoroscopic image and echo image of LOT-CRTD in a patient with ischemic cardiomyopathy. A Fluoroscopic image in the RAO 30° projections This image shows the final lead position in the IVS. RA, right atrial lead; LV, left ventricular lead; LBB, left bundle branch lead; RD, right defibrillator lead. B Intracardiac echocardiography image Parasternal short-axis view demonstrating the depth of the lead in the interventricular septum Arrow, left bundle branch lead