Effects of Adaptive Cardiac Resynchronization Therapy With Left-Bundle-Branch Area Pacing and Coronary Sinus Pacing

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Research Article

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Abstract

Adaptive cardiac resynchronization therapy (aCRT) is associated with improved clinical outcomes. Left bundle branch area pacing (LBBAP) has shown encouraging results as an alternative option for CRT. In this study, we observed the clinical and echocardiographic outcome of LBB-optimized aCRT in combination with synchronized LV pacing (LOT-aCRT) in heart failure patients with reduced ejection fraction and LBBB. Heart failure patients with preserved AV conduction and LBBB morphology, who underwent aCRT from February 1, 2019, to September 30, 2020 were included. The eligible patients with or without LBBAP were divided into LOT-aCRT group or BV-CRT group. In LOT-aCRT group, the CS lead was connected to the pace-sensing portion of the RV port, and the LBBAP lead was connected to the LV port. Seventeen patients were enrolled in this study (8 cases in LOT-aCRT group, 9 cases in BV-CRT group). Patients were matched for ischemic cardiomyopathy (ICM) at baseline (5 cases vs. 4 cases). QRS duration (QRSd) via BVP was narrowed from 158.0 ± 13.0 ms at baseline to 132.0 ± 4.5 ms in LOT-aCRT group (P=0.019), and further narrowed to 123.0 ± 5.7 ms (P < 0.01) via LBBAP. However, LOT-aCRT resulted in further reduction of the QRSd (121.0 ± 3.8 ms), but no statistical significance (P > 0.05). In BV-CRT group, 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 LOT-aCRT, BVP has no any advantage in reducing QRSd (P > 0.05). During follow-up, patients in LOT-aCRT group showed significant improvement in LVEF and NT-proBNP levels (P < 0.01), while patients in BV-CRT group showed non-significant changes in these parameters (P >0.05). The study demonstrates that LOT-aCRT is clinically feasible in patients with systolic HF and LBBB. LOT-aCRT was associated with significant narrowing of the QRSd and improvement in LV function, especially in patients with ICM.

Introduction

Cardiac resynchronization therapy (CRT) with biventricular pacing (BVP) is an established therapy for symptomatic heart failure (HF) patients with left ventricular systolic dysfunction and a wide QRS, particularly left bundle branch block (LBBB).[1, 2] However, up to one-third of patients treated with BVP-CRT are non-responders.[3] The reasons for non-response are multiple, including left ventricular (LV) scar burden and distribution, 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]

His bundle pacing (HBP) has the potential to restore physiological activation by engaging the intrinsic His-Purkinje system.[6] It has been shown to correct LBBB, and is currently considered as a viable alternative to BVP-CRT in patients requiring CRT. [7] However, HBP may be associated with high pacing thresholds to capture the distal His bundle and/or correct LBBB.[8]

Recently, several groups have reported exciting results 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 and this procedure is related to a stable threshold and short QRS duration (QRSd).[9, 10] However, LBBAP could

only achieve partial reduction of the QRSd in those patients with a baseline surface ECG of atypical LBBB morphology.[11]

A novel adaptive CRT (aCRT) algorithm, which provides ambulatory adjustment of pacing configuration (LV pacing only or BVP) and AV and VV delays based on periodic automatic evaluation of electrical conduction, demonstrated the non-inferiority of the aCRT algorithm compared to echo-guided BVP.[12]

In this study, we developed a technique, in that LBB-optimized aCRT was applied in combination with synchronized LV pacing (LOT-aCRT) to achieve optimal CRT effects in heart failure patients with reduced left ventricular ejection fraction (LVEF) and LBBB. The patients with atypical LBBB and a higher overall scar burden might be the desired candidates for this procedure. Present study summarized the initial experience in patients undergoing LOT-aCRT in our centre.

Methods

This single-centre retrospective study enrolled all consecutive patients with aCRT between February 1, 2019 and September 30, 2020. Patients with or without LBBAP were divided into two groups: LOT-aCRT (group 1), conventional CRT using biventricular pacing (BV-CRT, group 2). The choice of LBBAP was based on the patient's consent. To reduce the selection bias, we only included patients with currently available models from Medtronic Inc, USA (DTBA2D1, DTBA2D4, and C5TR01).

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 drug-refractory New York Heart Association classes II to IV HF symptoms, LVEF ≤ 35%, LBBB, or QRSd ≥ 150 ms were eligible for BV-CRT.[13] According to the Strauss criteria,[14] patients with preserved AV conduction and LBBB morphology were selected firstly for LOT-aCRT. Intrinsic preserved AV conduction was defined as PR interval ≤ 200ms as documented on an at-rest 12-lead-ECG.[15]

Patients were excluded if they had disagreement with CRT, right bundle branch block (RBBB), chronic atrial fibrillation, use of a left ventricular assist device, metastatic cancer, or the life expectancy was less than 1 year. Written informed consent was obtained from each patient.

Procedural Details

The right ventricular (RV) defibrillator lead was first implanted in the RV to provide backup ventricular pacing if the patient developed transient complete atrioventricular block during LBBAP lead placement. Subsequently, the coronary sinus (CS) lead was implanted using routine implantation techniques, targeting sites were determined by the value of maximal LV delay.[16, 17] 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,[18–21] 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.[22] Once the implantation site was identified, the pacing lead was advanced deep into the septum while the unipolar pacing impedance, electrogram characteristics and paced QRS morphology were monitored.

Additionally, the lead orientation was displayed in various projections. Generally, the sheath and the lead were oriented gently and the lead should point to 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°.[23]

If an acceptable LBB capture could not be achieved after 5 attempts of lead positioning, it was considered as procedure failure.[8]

Optimal CS location

The details of the device and procedure have been described elsewhere.[16, 17] 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.[16, 17]

Intra-operative measurements

Intra-operative lead testing included R waves, impedance, pace threshold at o.4 ms. Whether group 1 or group 2, the morphology and duration of QRS wave at baseline and during LBBAP, CS pacing, and BVP (RV defibrillator lead and CS lead) were measured on the EP recording system at 100 mm/s. The stimulus to left ventricular activation time during LBBAP was documented.

Device Connection

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

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

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.

LBBAP was set as bipolar pacing with 0.4 ms pulse width in all patients. According to previous literature, [24] 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.

The aCRT algorithm

The details of the aCRT algorithm have been published previously.[12] If the conduction interval from the right atrium to the right ventricle is normal (intrinsic AV ≤ 200 ms, if in sinus rhythm, or AV ≤ 250 ms, if receiving atrial pacing) and the heart rate does not exceed 100 beats/min, the algorithm provides synchronized LV pacing.[15] Conversely, if the intrinsic AV conduction interval is prolonged, the algorithm provides BV pacing. The QRSd values via LBB-optimized LV pacing were measured.

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 ≦ 0.05 was considered significant.

Results

Seventeen patients enrolled the study (8 cases were in group 1, 9 cases in group 2). All patients had preserved AV conduction and had at least 1 HF hospitalization within 3 months before CRT/D implantation. Entresto (sacubitril/valsartan), β-blockers, and loop diuretics were prescribed to all patients.

Baseline characteristics

Among the 17 patients, nine (52.9%) were male. All patients had cardiomyopathy (8 non-ischemic and 9 ischemic), and 6 patients had paroxysmal atrial fibrillation. Hypertension was present in 8 patients. Frequent ventricular premature contraction (VPC) (> 1,000 per 24 hours [25]) were found in 5 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, paroxysmal atrial fibrillation as illustrated in Table 1 (all P >0.05).

The echocardiographic indices, including LVEF, LVEDD, and NYHA classification, NT-proBNP were shown in Table 2. Baseline parameters were similar between the two groups (all P >0.05). The baseline LVEF and the baseline QRSd (Figure 1a) were 33.9 ± 3.9% and 168.2 ± 18.9 ms, respectively. At baseline, the two groups were matched for QRSd (158.0 ±13.0, vs. 176.7 ±19.7, P >0.05).

Procedural Outcomes

CRTDs were implanted in 15 patients (Figure 2a, 2b), and CRTPs were implanted in the remaining 2 patients (Table 3), one in each group. The operation duration was 135 ± 26 min. The duration of X-ray fluoroscopy was 25.2 ± 7.1 min.

In group 1, LBBA lead, RV lead and CS lead were successfully achieved in all 8 patients. In group 2, CS lead and RV lead was successfully implanted in all 9 patients. Compared with group 2, the operation duration was significantly prolonged and the duration of X-ray fluoroscopy tended to be longer in group 1 (Table 3).

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 3). Both the LBBAP and CS 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).

During the procedure, temporary RBBB and acute perforation of the ventricular septum were documented in 1 patient respectively in group 1. The lead was successfully repositioned and no pericardial effusion or cerebral ischemia was observed. In group 2, no complications were documented.

ECG characteristics and pacing parameters

Individual electrocardiographic responses to RV, CS, and LBBAP at the time of implantation were shown in Table 3. Among the 17 patients, the baseline QRSd was 168.1 ± 18.9 ms (Figure 1a).

In group 1, after unipolar LBBAP, 8 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 1b). LBB potential could be recorded in 5 patients from the LBB lead (62.5%). 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, intra-operative 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 1c). Compared with BVP, unipolar LBBAP resulted in further reduction of the QRSd to 123.0 ± 5.7 ms (P=0.006 vs. baseline and P=0.021 vs. BVP).

Post-operative LOT-aCRT resulted in a further reduction of the QRSd (121.0 ± 3.8 ms), but no statistical significance (P > 0.05).

In group 2, intra-operative 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 LOT-aCRT in group 1, BVP in group 2 has no any advantage in reducing QRSd (P > 0.05, Table 2).

As the aCRT algorithm provides mostly LV only pacing (Which means LBBAP in group1, CS pacing in group2) in patients with preserved AV conduction, the percentage of LV only pacing in the aCRT arm was high; 75.5% in the group 1 and 73.8% in group 2.

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 days, P > 0.05). Among all 17 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 that had an electrogram available for adjudication (3 episodes in group 1, 5 episodes in group 2). However, the rate of VT/VF therapy was not statistically different (P = 0.175) between two groups.

Transthoracic echocardiogram (Figure 2) evaluation data at baseline and at the 1-month and 3-month follow-ups were available in all 17 patients receiving successful aCRT. 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.

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-aCRT was feasible in a small nonrandomized, non-consecutive series of patients with reduced LVEF and LBBB. At the time of device implantation, ECG changes during LOT-aCRT 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.[26] 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 ischemic cardiomyopathy experience a similar BV-CRT response rate to their nonischemic counterparts.[27] 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 BV-CRT in ICM patients.[28] There is evidence that CRT is not salutary in patients with posterolateral scarring.[5]

A sub-study of the aCRT trial revealed that patients with a high percentage of adaptive LV pacing showed better clinical improvement and PQ-interval compared to patients within the normal range.[29] The mechanism of benefit in this patient cohort was speculated to be “fusion” of the excitation from LV pacing with intrinsic conduction propagating through the still preserved His-Purkinje system.[30]

Electrophysiological definition

Permanent LBBAP is an effective form of physiologic pacing with high success rates in patients with intact His-Purkinje conduction.[9] LBBAP can serve as a new CRT technique to correct LBBB, provide ventricular synchrony, and improve clinical symptoms with reverse remodelling of the LV.[31]

There is evidence that LV activation time is only minimally increased in RBBB but significantly increased in LBBB.[32] During unipolar LBBAP, as RV 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.

The advantage of LOT-aCRT

The aCRT algorithm is a novel algorithm that periodically measures intrinsic conduction and dynamically adjusts CRT pacing parameters as needed.[12] It provides RV-synchronized LV pacing when AV conduction is normal and BiV pacing when AV conduction is prolonged.[15] In group 1, the CS lead was connected to the pace-sensing portion of the RV port, and the LBBAP lead was connected to the LV port. So, LV pacing means LBBAP pacing, while RV pacing means CS pacing. When PR interval is normal, aCRT provides LBBAP only, while long PR interval, it provides BV pacing.

LBBAP achieved only partial reduction of the QRSd in those patients with a baseline surface ECG of atypical LBBB morphology.[11] Intra- or interventricular dyssynchrony cannot be reduced through LBBAP. LOT-aCRT offers the advantage of using the LV lead in addition to LBBAP in a potential scenario in which

conduction disease progresses. A previous study demonstrated the efficacy of aCRT in patients with preserved AV conduction.[29]

Group 2 had only an 18.8% reduction in QRSd, but previous study described a 25% reduction with CRT in LBBB and synchrony AV conduction.[33] These patients were insufficiently optimized and LOT-aCRT may have been better suited to the purposes.

In patients with LBBB and cardiomyopathy, LOT-aCRT resulted in significant electrical resynchronization. In group 1 of our study, 62.5% of whose subjects had severe ischemic cardiomyopathy, LOT-aCRT resulted in a significantly greater reduction of the QRSd to 121.0 ± 3.8 ms from 158.0 ± 13.0 ms and 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-aCRT.

Limitations

First, LOT-aCRT is time consuming. The duration of the operation was 152 ± 31 min, and the duration of X-ray fluoroscopy was 29.2 ± 8.8 min; both were longer than stated in a previous report (117 ± 48 and 16.4 ± 12.3 min)[9] 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 9 ischemic 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-aCRT.

Conclusions

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

Declarations

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Conflicts of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national).

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Tables

Table 1: Baseline Characteristics in 17 Patients with Procedure of aCRT/D (n=17)

	Total(n = 17)	Group 1 (n = 8)	Group 2 (n = 9)	P value
Age (years)	69.1 ±6.4	71.8 ±5.1	66.8 ± 6.9	0.217
Gender, Male, n (%)	9(54.5%)	4(50.0%)	5(55.6%)	1.000
Diabetes mellitus, n (%)	4(23.5%)	2(25.0%)	2(22.2%)	1.000
Hypertension, n (%)	8(47.0%)	4(50.0%)	4(44.4%)	1.000
Frequent VPC, n (%)	5(29.4%)	2(25.0%)	3(33.3%)	0.751
ICM, n(%)	9(52.9%)	5(62.5%)	4(44.4%)	0.567
PCI, n (%)	9(52.9%)	5(62.5%)	4(44.4%)	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 (%)	6(35.3%)	4(50.0%)	2 (22.2%)	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 = 17)

		Total (n = 17)	Group 1 (n = 8)	Group 2 (n =9)	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 (%)		15(88.2%)	7(87.5%)	8(88.9%)	0.727
Fluoroscopic Time (min)		25.2 ±7.1	29.2± 8.8	21.8± 3.1	0.086
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 = 17)

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

		Total (n = 17)	Group 1 (n = 8)	Group 2 (n =9)	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 procedure	2937 ±1646	3240 ±2258	2684 ±1083	0.634

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

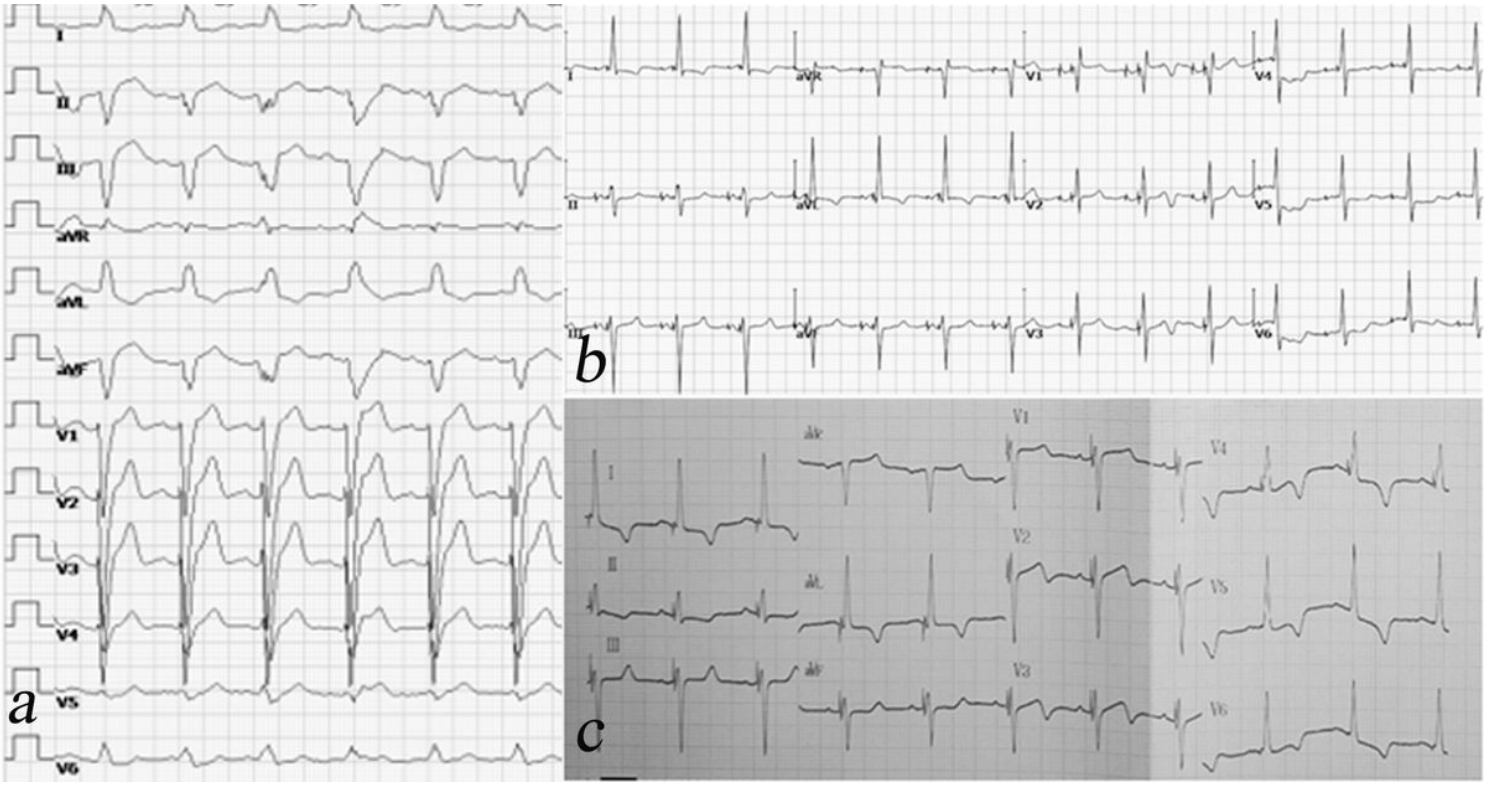

Figure 1

LOT-aCRT in a patient with ischemic cardiomyopathy and normal PR interval (a) Baseline ECG shows LBBB with QRS duration of 160 ms. (b) During unipolar LBBAP pacing, a right bundle branch block pattern with QRS duration of 122 ms is visible. (c) During pacing with LOT-aCRT, a left bundle branch block correction pattern with QRS duration of 120 ms is visible.

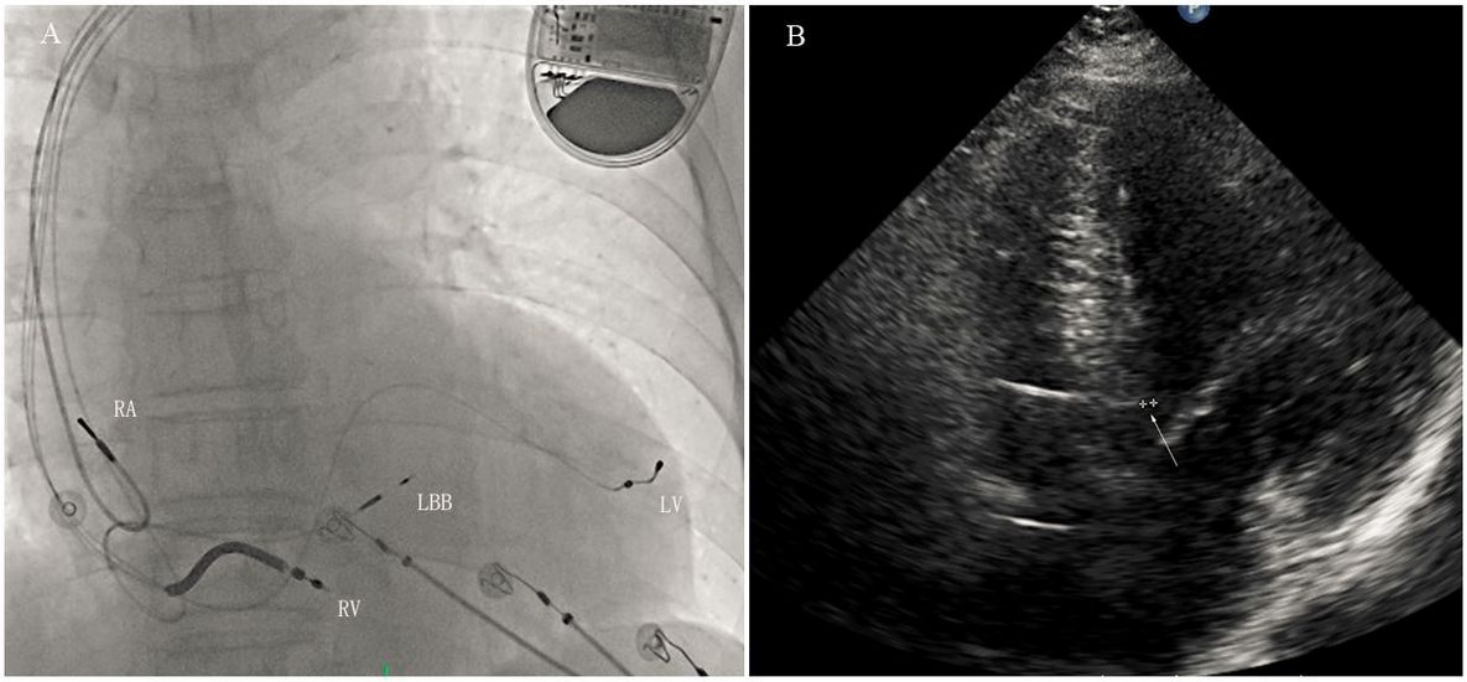

Figure 2

Fluoroscopic image and echo image of LOT-aCRTD in a patient with ischemic cardiomyopathy and normal PR interval (a) Fluoroscopic image in the RAO 30° projections This image shows the final lead position in the IVS. RA, right atrial lead; LV, coronary sinus lead; LBB, left bundle branch lead; RV, right ventricular defibrillator lead. (b) Transthoracic echocardiogram image The apical four-chamber view demonstrates the depth of the lead in the interventricular septum (arrow).