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ORIGINAL ARTICLE

Predictors of implantation failure in left bundle branch area pacing using a lumenless lead in patients with bradycardia

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Abstract

Background: Left bundle branch area pacing (LBBAP) is a novel conduction system pacing technique. In this multicenter study, we aimed to evaluate the procedural success, safety, and preoperative predictors of procedural failure of LBBAP.

Methods: LBBAP was attempted in 285 patients with pacemaker indications for bradyarrhythmia, which were mainly atrioventricular block (AVB) (68.1%) and sick sinus syndrome (26.7%). Procedural success and electrophysiological and echocardiographic parameters were evaluated.

Results: LBBAP was successful in 247 (86.7%) patients. Left bundle branch (LBB) capture was confirmed in 54.7% of the population. The primary reasons for procedural failure were the inability of the pacemaker lead to penetrate deep into the septum (76.3%) and failure to achieve shortening of stimulus to left ventricular (LV) activation time in lead V6 (18.4%). Thickened interventricular septum (odds ratio [OR], 2.48; 95% confidence interval [CI], 1.15–5.35), severe tricuspid regurgitation (OR, 8.84; 95% CI, 1.22–64.06), and intraventricular conduction delay (OR, 8.16; 95% CI, 2.32–28.75) were preoperative predictors of procedural failure. The capture threshold and ventricular amplitude remained stable, and no major complications occurred throughout the 2-year follow-up. In patients with ventricular pacing burden >40%, the LV ejection fraction remained high regardless of LBB capture.

Conclusions: Successful LBBAP was affected by abnormal cardiac anatomy and intraventricular conduction. LBBAP is feasible and safe as a primary strategy for patients with AVB, depending on ventricular pacing.

KEYWORDS
bradyarrhythmia, conduction system pacing, left bundle branch area pacing, left bundle branch pacing, left ventricular septal pacing

1 | INTRODUCTION

Left bundle branch area pacing (LBBAP) is an emerging technique for physiological pacing. This novel technique was first reported by Huang et al.[1] in which the left bundle branch (LBB) was captured by advancing lead deeply into the interventricular septum (IVS). Subsequent accumulation of clinical evidence for LBBAP demonstrated better clinical outcomes, including reduced mortality and heart failure hospitalization compared with conventional right ventricular (RV) pacing.[2] Furthermore, LBBAP was characterized by stable pacing parameters, including capture threshold and ventricular amplitude.[3–7] The success rate of LBBAP lead implantation was generally high,[8,9] although the criteria for successful LBBAP differed on previous studies. There are currently no standard criteria for successful LBBAP and LBB capture globally. The characteristics of unsuccessful LBBAP have been demonstrated by previous large-scale multicenter studies.[6,9] However, few studies evaluated the predictors of procedural success for LBBAP.[6] This multicenter observational study was conducted to explore the success rate and reasons for procedural failure in the LBBAP lead implantation. We aimed to evaluate the predictors of procedural failure, feasibility, and safety of LBBAP in patients with pacemaker indications for bradyarrhythmia.

2 | METHODS

2.1 | Study design and population

This retrospective, multicenter, observational study utilized the registry from five institutions in Japan. Consecutive patients with bradyarrhythmia and indication for pacemaker implantation in whom LBBAP was attempted between February 1, 2019, and April 30, 2021, in all participating hospitals were included. Detailed information about participating institutions is presented in Table S1. Patients with decreased cardiac function indicated for cardiac resynchronization therapy (CRT) defibrillator were not included in the study. The indications for pacemaker implantation complied with the recent guideline.[10] Informed consent for device implantation was obtained from all patients. The study protocol was approved by each institutional ethics committee. This study protocol complied with the principles of the Declaration of Helsinki.

2.2 | Implantation procedure

LBBAP lead implantation was performed in accordance with the transseptal approach as previously described.[11] Briefly, a lumenless, fixed helix SelectSecure lead (model 3830; Medtronic) was delivered to the RV septum using a specific sheath (model C315HIS; Medtronic). The lead tip electrode was used for unipolar pacing and mapping. Some patients underwent LBBAP using a dual-lead technique with two sets of 3830 leads and C315 sheaths to confirm LBB capture.[11] Twelve-lead electrocardiogram (ECG) waveforms and intracardiac ECGs were continuously recorded using electrophysiology recording systems during the procedure. The area, which was located 1.0–2.0 cm from the His bundle region toward the direction of the RV apex, was initially targeted for LBBAP lead deployment with the paced QRS morphology demonstrating a "W pattern" in lead V1. The pacing lead was rapidly rotated clockwise four to five times to penetrate the RV myocardial surface. While the pacemaker lead was advanced into the IVS, paced QRS morphology and pacing impedance were continuously monitored. The stimulus to peak left ventricular activation time in lead V6 (s-LVAT) was also measured during LBBAP lead deployment. When the paced morphology of late R-wave in lead V1 (qR, Qr, or rSR) was identified, the lead was no longer advanced or additional rotations were gradually provided to achieve LBB area capture in 0.5–1.0 turns at a time while measuring pacing parameters. If the pacing lead could not penetrate deep into the IVS or s-LVAT was not short enough despite the deep septal deployment, the lead was extracted and repositioned slightly apically. If an interventricular septal perforation had occurred during the procedure—diagnosed by unipolar lead impedance <450 ohms, sudden loss of pacing capture, and decrease in injury current amplitude on intracardiac electrograms recorded on the lead tip[12]—the lead was pulled out and repositioned away from the perforation site. Once the pacing parameters were acceptable, the sheath was withdrawn, leaving an appropriate lead slack. If a successful LBBAP was not achieved after several deep screw attempts, LBBAP was abandoned, and RV pacing was performed at the physician's discretion.

2.3 | Definition of successful LBBAP and the LBB capture

According to the latest guidelines, LBBAP includes selective left bundle branch pacing (LBBP), nonselective LBBAP, or left ventricular septal pacing (LVSP).[13,14] The criteria for successful LBBAP in this study were (1) unipolar paced QRS morphology of late R-wave in lead V1 and (2) s-LVAT <90 ms (Figure 1).[6,15]

LBB capture was confirmed based on the following criteria, as previously reported:[15,16] (1) transition from nonselective LBBAP to selective LBBP with constant s-LVAT at high and low output pacing, (2) transition from nonselective LBBAP to LVSP by an abrupt increase in s-LVAT of >10 ms with decreasing pacing output, (3) s-LVAT that was almost equal to the interval from LBB potential to peak R-wave in lead V6 during intrinsic conduction, and (4) identification of retrograde His bundle electrogram during LBBAP using dual-lead technique.

LVSP was defined as (1) late R-wave in V1, (2) s-LVAT <90 ms,[6,15] and (3) no evidence of LBB capture.

2.4 | Data collection and follow-up

Baseline patient characteristics, ECG data, and pacemaker indications were collected in all patients. Intraventricular conduction delay

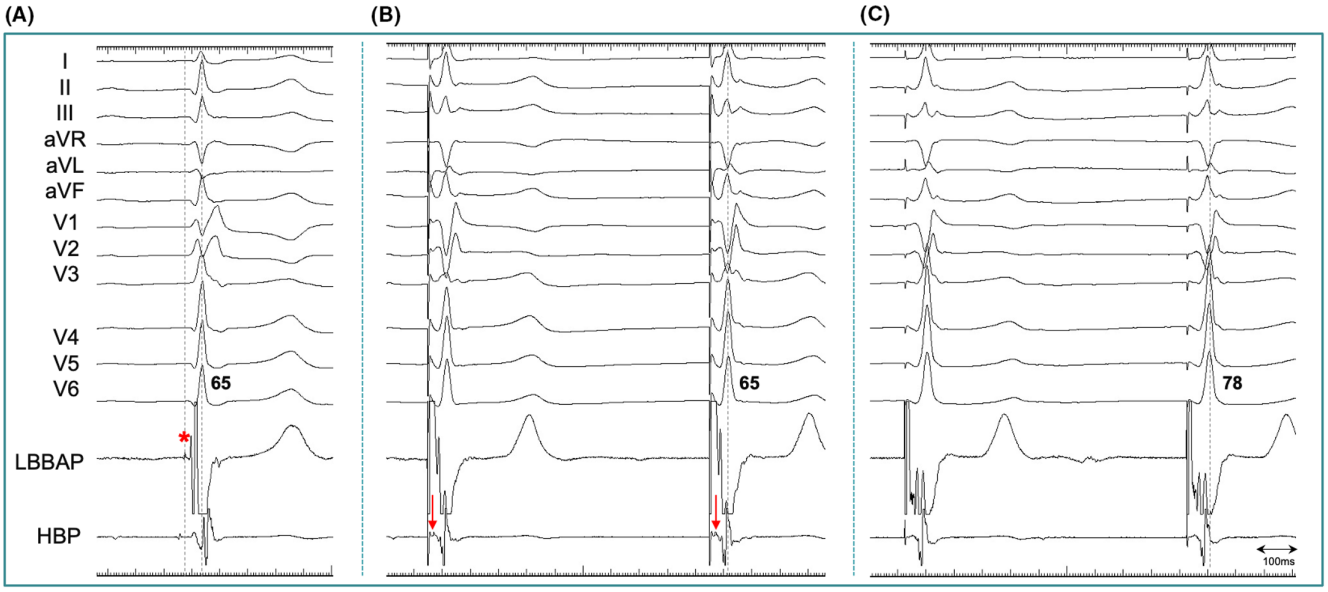

FIGURE 1 Electrocardiograms and intracardiac electrograms in a patient with atrioventricular block, who underwent LBBAP. (A) The LBB potential during intrinsic conduction (*red asterisk*). The interval from LBB potential to peak R-wave in lead V6 was 65 ms. (B) Pacing at 1.0 V at 0.4 ms demonstrates nonselective LBBAP. S-LVAT was 65 ms, consistent with the interval from LBB potential to peak R-wave in lead V6. Note the presence of retrograde His bundle potential during LBBP (*red arrows*). (C) Pacing at 0.9 V at 0.4 ms demonstrates LVSP without LBB capture. An abrupt increase in s-LVAT of >10 ms was confirmed with decreasing pacing output from 1.0 V to 0.9 V, which resulted in 78 ms. HBP, His bundle pacing; LBB, left bundle branch; LBBAP, left bundle branch area pacing; LBBP, left bundle branch pacing; LVSP, left ventricular septal pacing; s-LVAT, stimulus to peak left ventricular activation time in lead V6.

(IVCD) was defined as QRS duration ≥120 ms when both right and left bundle branch block (LBBB) were excluded. Echocardiographic parameters, including the left ventricular ejection fraction (LVEF), interventricular septal width in diastole, and degree of tricuspid regurgitation (TR), were evaluated. Thickened IVS was defined as interventricular septal width > 11 mm, which was measured at the presumed target site where LBBAP lead would advance on a parasternal short-axis view prior to the procedure. TR grade was categorized as 0 (none or trivial), 1 (mild), 2 (moderate), and 3 (severe). The capture thresholds, ventricular amplitudes, and pacing impedances were measured at implantation. In patients with unsuccessful LBBAP, the most probable reason for failure was assessed and reported in each institution. Patients were followed up in the device outpatient clinic at 1 month, 6 months, 1 year, and 2 years after implantation. The pacing parameters and paced ECG morphology were evaluated using the bipolar configuration. Follow-up echocardiography was also performed after 1 year to evaluate changes in LVEF and TR severity, if possible. LBBAP-related complications were recorded during the follow-up period.

2.5 | Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (first and third quartiles), and categorical variables are presented as numbers with percentages. Student's *t*-test and Mann–Whitney *U* test were performed to compare continuous variables. Pearson chi-square and Fisher's exact tests were performed to compare categorical variables, as appropriate. Differences between the baseline and follow-up parameters were compared using a paired *t*-test. An overall difference in outcomes among more than two different groups was analyzed using the chi-squared test. The predictive value of each factor was first evaluated using a univariable logistic regression analysis. Factors with values of $p < .05$ in the univariable analysis were included in the multivariable logistic regression model using a forward stepwise method to identify independent predictors. Linear regression analysis was performed to evaluate the correlation between the number of cases experienced by each participating institution and their corresponding success rates. Statistical significance was set at $p < .05$. All analyses were conducted using IBM SPSS Statistics for Windows, version 20 (IBM Corp.).

3 | RESULTS

3.1 | Baseline patient characteristics

A total of consecutive 285 patients undergoing LBBAP lead implantation were enrolled in the study. The mean number of enrolled cases was 57 ± 30 per participating institution. Baseline characteristics are summarized in Table 1. The mean age in the total population was 80.0 ± 8.3 years, and 46.7% were male. The pacemaker indications were atrioventricular block (AVB) in 68.1% of patients, sick sinus syndrome in 26.7%, atrial fibrillation (AF) with bradycardia in 4.2%, and refractory AF prior to AV node ablation in 1.1%. The mean LVEF was

TABLE 1 Baseline characteristics and comparisons between patients with LBBAP procedural success and failure.

Variable	All $n=285$	Successful LBBAP $n=247$	Unsuccessful LBBAP $n=38$	p-Value
Age, years	80.0 ± 8.3	79.6 ± 8.3	80.9 ± 8.3	0.452
Male	133 (46.7%)	105 (42.5%)	28 (73.7%)	<0.001
Body mass index, kg/m^2	22.6 ± 3.5	22.5 ± 3.6	22.8 ± 3.0	0.578
Indications				
AV block	194 (68.1%)	173 (70.0%)	21 (55.3%)	0.069
Sick sinus syndrome	76 (26.7%)	64 (25.9%)	12 (31.6%)	0.462
AF bradycardia	12 (4.2%)	8 (3.2%)	4 (10.5%)	0.060
AV nodal ablation	3 (1.1%)	2 (0.8%)	1 (2.6%)	0.350
Cardiomyopathy	38 (13.3%)	30 (12.1%)	8 (21.1%)	0.133
ICM	12 (4.2%)	10 (4.0%)	2 (5.2%)	0.492
HCM	7 (2.5%)	3 (1.2%)	4 (10.5%)	0.007
Others	19 (6.7%)	17 (6.9%)	2 (5.2%)	0.522
Baseline QRS duration, ms	118.0 ± 30.4	117.0 ± 29.6	124.7 ± 35.1	0.204
QRS morphology				
Narrow	143 (50.2%)	120 (48.6%)	22 (57.9%)	0.285
RBBB	86 (30.2%)	77 (31.2%)	9 (23.7%)	0.349
LBBB	22 (7.7%)	19 (7.7%)	3 (7.9%)	0.585
Paced rhythm	22 (7.7%)	18 (7.3%)	4 (10.5%)	0.334
IVCD	12 (4.2%)	6 (2.4%)	6 (15.8%)	0.002
Permanent AF	13 (4.6%)	8 (3.2%)	5 (13.2%)	0.019
Hypertension	193 (67.7%)	170 (68.8%)	23 (60.5%)	0.308
Diabetes mellitus	71 (24.9%)	64 (25.9%)	7 (18.4%)	0.320
Maintenance dialysis	10 (3.5%)	8 (3.2%)	2 (5.2%)	0.394
History of cardiac surgery	20 (7.0%)	16 (6.5%)	4 (10.5%)	0.269
TAVR	14 (4.9%)	10 (4.0%)	4 (10.5%)	0.100
LVEF, %	63.7 ± 10.1	64.0 ± 9.8	61.5 ± 11.7	0.160
IVS, mm	9.9 ± 1.5	9.8 ± 1.5	10.6 ± 1.8	0.005
Thickened IVS	64 (22.4%)	50 (20.2%)	14 (36.8%)	0.022
TR grade				
Mild	158 (61.2%)	138 (55.9%)	20 (52.6%)	0.708
Moderate	39 (15.1%)	34 (13.7%)	5 (13.2%)	0.919
Severe	5 (1.9%)	2 (0.8%)	3 (7.9%)	0.018
Right-sided implantation	19 (6.7%)	14 (5.7%)	5 (13.2%)	0.091

Note: Values are shown as mean ± SD or n (%). The p values are from the comparison between patients with LBBAP procedural success and failure. Thickened IVS was defined as interventricular septal width >11 mm.

Abbreviations: AF, atrial fibrillation; AV, atrioventricular; HCM, hypertrophic cardiomyopathy; ICM, ischemic cardiomyopathy; IVCD, intraventricular conduction delay; IVS, interventricular septum; LBBAP, left bundle branch area pacing; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; RBBB, right bundle branch block; SSS, sick sinus syndrome; TAVR, transcatheter aortic valve replacement; TR, tricuspid regurgitation.

63.7 ± 10.1%, whereas 29 (10.2%) patients had a reduced LVEF (≤50%). The mean IVS width was 9.9 ± 1.5 mm. Seven (2.5%) patients were previously diagnosed with hypertrophic cardiomyopathy (HCM).

3.2 | Procedural success rate

LBBAP was successfully achieved in 247 (86.7%) patients. LBBAP was successful in 89.5% and 86.4% of patients presenting with right bundle branch block and LBBB, respectively, but only in 50.0% of those with IVCD (Figure 2(A)). Patients with HCM had the lowest success rate (42.9%) compared with those with ischemic cardiomyopathy (83.3%) and other cardiomyopathies (89.5%) (Figure 2(B)). The primary reasons for unsuccessful LBBAP were the inability to advance the lead deep into the septum in 29 (76.3%) patients, failure to achieve s-LVAT <90 ms in seven (18.4%), and others in two (5.3%). The mean number of experienced cases per participating institution was 57 ± 30. There was no significant correlation between the

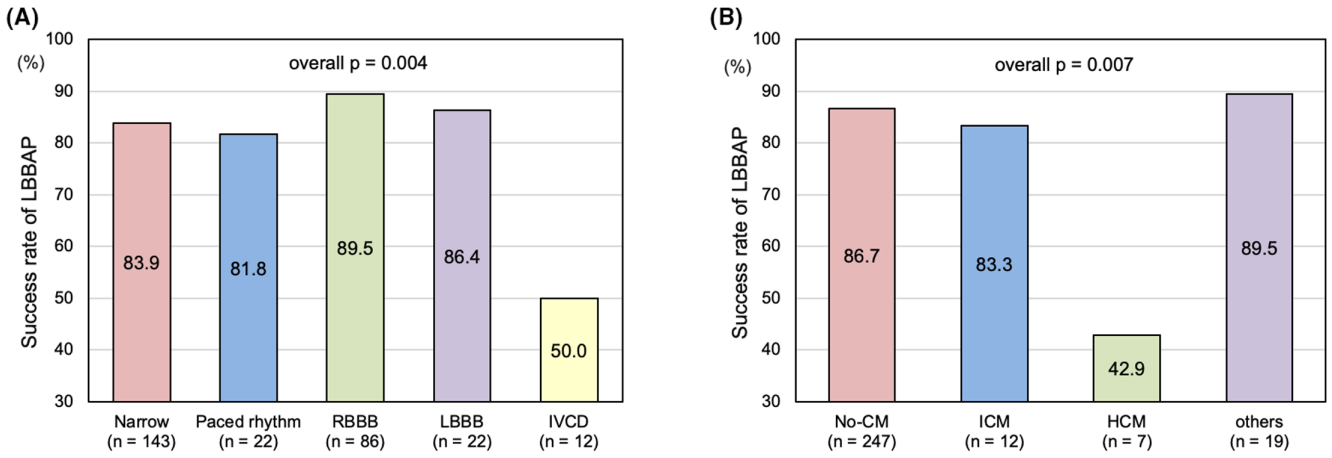

FIGURE 2 Success rates of LBBAP lead implantation. (A) Success rates depending on the baseline QRS morphology. (B) Success rates depending on the type of cardiomyopathy. CM, cardiomyopathy; HCM, hypertrophic cardiomyopathy; ICM, ischemic cardiomyopathy; IVCD, intraventricular conduction delay; LBBAP, left bundle branch area pacing; LBBB, left bundle branch block; RBBB, right bundle branch block.

TABLE 2 Univariable and multivariable analyses for the preoperative predictors of unsuccessful LBBAP lead implantation.

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-Value	OR (95% CI)	*p*-Value
Age, years	0.98 (0.94–1.03)	0.451		
Male gender	3.85 (1.79–8.27)	0.001		
AV block	0.53 (0.26–1.06)	0.072		
HCM	9.57 (2.05–44.60)	0.004		
Permanent AF	4.53 (1.40–14.66)	0.012		
TAVR	2.79 (0.83–9.39)	0.098		
IVCD	7.53 (2.29–24.76)	0.001	8.16 (2.32–28.75)	0.001
Thickened IVS	2.30 (1.11–4.76)	0.025	2.48 (1.15–5.35)	0.021
Severe TR	10.5 (1.70–65.06)	0.012	8.84 (1.22–64.06)	0.031
Right-sided implantation	2.5 (0.85–7.46)	0.095		

Note: Values are 95% confidence interval (CI). Thickened IVS was defined as interventricular septal width >11 mm.

Abbreviations: AF, atrial fibrillation; AV, atrioventricular; IVCD, intraventricular conduction delay; LBBAP, left bundle branch area pacing; OR, odds ratio; TAVR, transcatheter aortic valve replacement; TR, tricuspid regurgitation.

number of cases per institution and the success rate in this study ($p = .255$).

3.3 | Predictors for unsuccessful LBBAP lead implantation

The differences in baseline characteristics between patients with LBBAP procedural success ($n = 247$) and procedural failure ($n = 38$) are shown in Table 1. Univariable logistic regression analysis showed that males, HCM, permanent AF, IVCD, thickened IVS, and severe TR were significantly associated with procedural failure. In a multivariable logistic regression analysis, IVCD (odds ratio (OR), 8.16; 95% confidence interval (CI), 2.32–28.75; $p = .001$), thickened IVS (OR, 2.48; 95% CI, 1.15–5.35; $p = .021$), and severe TR (OR: 8.84; 95% CI, 1.22–64.06; $p = .031$) independently predicted procedural failure (Table 2). Inability of deep lead deployment was the primary reason for LBBAP procedural failure in 100% of severe TR, 79% of thickened IVS, and 50% of IVCD cases. The reason for LBBAP procedural failure in the remaining 50% of patients with IVCD was failure to achieve s-LVAT <90 ms.

3.4 | Procedural and electrophysiological characteristics

Procedural and electrophysiological characteristics in 247 patients with successful LBBAP are shown in Table 3. The mean procedural time for LBBAP lead implantation was 26.0 ± 17.2 min, which was significantly shorter compared to that of 38 patients with unsuccessful

TABLE 3 Procedural and electrophysiological characteristics in successful LBBAP cases.

Variable	*n* = 247
Number of attempts of deep lead deployment	2.4 ± 1.6
Procedure time for LBBAP lead implantation, min	26.0 ± 17.2
Right sided implantation	14 (5.7%)
Dual-lead technique performed	18 (7.3%)
LBB potential confirmed	148 (59.9%)
LBB capture confirmed	135 (54.7%)
S-LVAT, ms	72.0 ± 10.1
Paced QRS duration, ms	135.6 ± 13.0
LBBAP threshold, V at 0.4–0.5 ms	0.70 ± 0.33
Ventricular amplitude, mV	11.6 ± 5.2
Impedance, ohms	705.3 ± 142.5
Anodal capture	167 (67.6%)
Anodal capture threshold, V at 0.5 ms	3.8 ± 1.8

Note: Values are shown as mean ± SD or *n* (%). Procedure time denotes the time from the insertion of the delivery sheath into the right ventricle to the removal of the delivery sheath after successful LBBAP lead implantation.

Abbreviations: LBB, left bundle branch; LBBAP, left bundle branch area pacing; S-LVAT, stimulus to peak left ventricular activation time in lead V6.

LBBAP (38.4 ± 17.2 min, $p = .012$). The number of attempts for lead deployment was similar between cases with successful and unsuccessful lead implantation (2.4 ± 1.6 and 2.5 ± 2.2, respectively, $p = .702$). LBB potentials were observed in 148 (59.9%) patients during the procedure. LBB capture was recognized in 135 (54.7%) patients. Among the 19 patients in whom right-sided pacemaker implantation was attempted, 14 (73.7%) achieved successful LBBAP. The final bipolar-paced QRS duration and s-LVAT during the procedure were 136 ± 13 ms and 72 ± 10 ms, respectively. Bipolar LBBAP threshold at implantation was 0.70 ± 0.33 V at 0.4–0.5 ms. The ventricular amplitude and bipolar pacing impedance were 11.6 ± 5.2 mV and 705 ± 143 ohms, respectively. An anodal capture during bipolar pacing was documented in 167 (67.6%) patients with the mean anodal capture threshold at 3.8 ± 1.8 V.

3.5 | LBB capture versus LBB noncapture

LBB capture was confirmed in 135 (54.7%) patients (Table 3). The rationales for LBB capture were transition from nonselective LBBAP to selective LBBP in 70 (52%) patients, transition from nonselective LBBAP to LVSP in 40 (29.6%), s-LVAT identical with the time from LBB potential to peak R-wave in lead V6 in 32 (23.7%), and recognition of retrograde His bundle potential during LBBAP using a dual-lead technique in 18 (13.3%). The mean LBB capture threshold was 1.0 ± 1.0 V.

Differences in baseline and procedural characteristics between the LBBP group with LBB capture ($n = 135$) and LVSP group without LBB capture ($n = 112$) are shown in Table S2. The LBBP group had shorter IVS width (9.6 ± 1.5 mm vs. 10.0 ± 1.4 mm, $p = .031$) and narrower baseline QRS duration (112.6 ± 26.2 ms vs. 122.3 ± 32.6 ms, $p = .012$) than the LVSP group. In terms of procedural parameters, LBB potential was more often confirmed in the LBBP group (81.5% vs. 33.9%, $p < .001$). Furthermore, both s-LVAT and paced QRS duration were significantly shorter in the LBBP group than in the LVSP group (68.5 ± 9.2 ms vs. 76.3 ± 9.4 ms, $p < .001$; 133.1 ± 11.7 ms vs. 138.7 ± 13.9 ms, $p = .001$, respectively).

3.6 | Pacing parameters after implantation

Pacing parameters were measured during the 2-year follow-up (Figure 3). The mean follow-up period was 18 months. The bipolar capture thresholds remained stable with a slight increase during the follow-up. The ventricular amplitudes increased 1 month after implantation and remained stable thereafter. Bipolar lead impedance rapidly dropped 1 month after implantation and remained stable during the follow-up.

3.7 | Echocardiographic parameters of overall cases

Among the 247 patients who achieved successful LBBAP, 194 underwent follow-up echocardiography after 1 year. There was no significant change in LVEF before and after implantation in the LBBAP cases overall (63.5 ± 9.8% vs. 63.1 ± 8.4%, $p = .570$). One year after LBBAP, no significant differences in LVEF were observed between the LBBP and LVSP groups (63.1 ± 8.1% vs. 63.2 ± 8.8%, $p = .928$, respectively). Regarding tricuspid valve function, TR grade significantly improved after LBBAP (0.87 ± 0.70 vs. 0.73 ± 0.65, $p = .005$), whereas TR grade worsened by one level in 29 patients and by two levels in one.

3.8 | Echocardiographic parameters of patients dependent on ventricular pacing

As for 119 patients with ventricular pacing burden >40% (the mean burden of 94.9 ± 12.0%), no LVEF deterioration was observed after LBBAP lead implantation (62.6 ± 6.9%), compared with that at baseline (63.9 ± 9.2%, $p = .110$) (Figure 4(A)). In addition, LVEF remained high regardless of whether the LBB was captured or not (Figure 4(B)).

3.9 | Complications

No major complications, such as death, cardiac tamponade, acute coronary syndrome, or stroke, occurred during the procedure (Table 4). Interventricular septal perforation occurred in 10 (4.0%) patients during the procedure. The leads were successfully

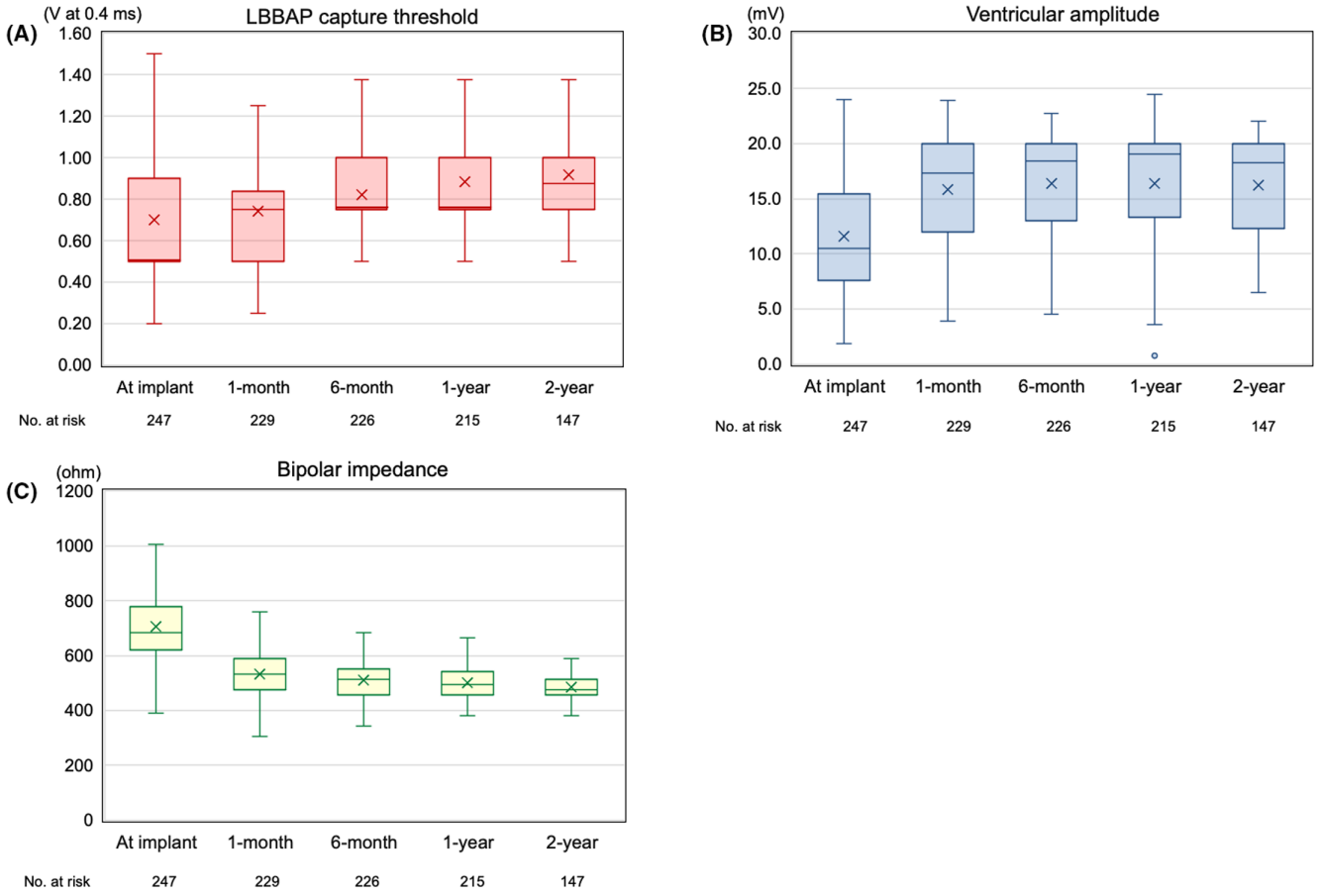

FIGURE 3 Pacing parameters after implantation. (A) LBBAP capture threshold. (B) Ventricular amplitude. (C) Bipolar impedance. Horizontal lines in the box plot indicate a median value, and cross mark indicate a mean value. LBBAP, left bundle branch area pacing.

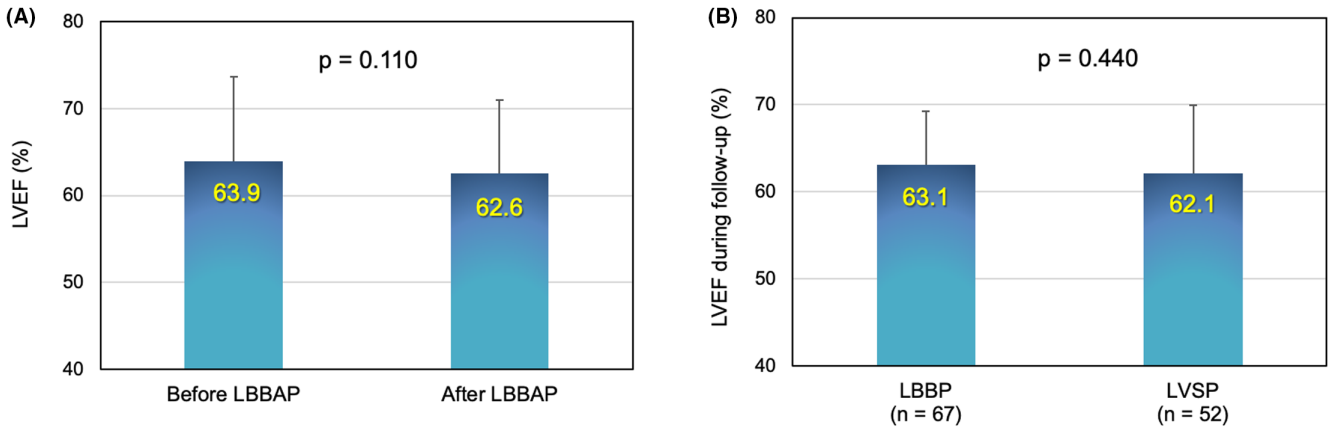

FIGURE 4 LVEF of the patients dependent on ventricular pacing. (A) Comparison of LVEF between before and 1 year after LBBAP in cases with ventricular pacing burden >40%. (B) Comparison of LVEF between the LBBP and LVSP of the patients dependent on ventricular pacing. LBBAP, left bundle branch area pacing; LBBP, left bundle branch pacing; LVEF, left ventricular ejection fraction; LVSP, left ventricular septal pacing.

repositioned slightly away from the perforation sites in all cases. No evidence of septal shunt flow was observed in the follow-up echocardiography. There were no late-onset interventricular septal perforations. Loss of LBB area capture was detected in eight (3.2%) patients after 1, 6, 12, and 24 months in four, one, one, and two patients, respectively, by assessing paced QRS morphology. Neither lead dislodgement from the IVS nor loss of ventricular myocardial capture occurred as complications in any patients. No cases had an increased threshold of >1.0 V from baseline, except for one patient with an increased threshold from 0.75 V at implantation to 2.25 V

TABLE 4 Complications in patients with successful LBBAP.

Intraprocedural septal perforation	10 (4.0%)
Late-onset septal perforation	0
Device infection	1 (0.4%)
Pocket hematoma	1 (0.4%)
LBBAP-related chest pain	0
Acute coronary syndrome	0
Loss of LBB area capture	8 (3.2%)
Lead complete dislodgement	0
Threshold rise >1.0 V from baseline	1 (0.4%)
Lead revision of LBBAP lead	1 (0.4%)
Lead helix or conductor fracture	0

Note: Values are shown as *n* (%).

Abbreviations: LBB, left bundle branch; LBBAP, left bundle branch area pacing.

after 1 year, though the threshold improved to 1.25 V thereafter. Lead fracture or LBBAP-related chest pain was not observed. No lead revision was performed except for one patient with a device infection.

4 | DISCUSSION

The primary findings in this study are as follows: (1) LBBAP using a lumenless lead was achieved in 86.7% of patients with pacemaker indications for bradyarrhythmia; (2) the presence of IVCD, thickened IVS, and severe TR were independent predictors for unsuccessful implantation of the LBBAP lead; (3) no major cardiac events occurred as complications, and capture thresholds and ventricular amplitudes remained stable during the 2-year follow-up; and (4) LVEF remained high 1 year after LBBAP in cases with ventricular pacing burden >40% regardless of whether the LBB was captured or not.

The success rate of LBBAP lead implantation was 86.7% in this study, which may be acceptable for the initial experience of LBBAP implantation. Wang et al.[17] reported that the success rate gradually improved as the number of experienced cases increased (1–50 cases, success rate of 88.0%; 51–150 cases, 90.0%; 151–406 cases, 94.5%). No significant correlation was observed between the number of experienced cases per participating institution and the success rate in this study. The mean number of cases per institution (57 ± 30) may not have been sufficient for institutions to attain mastery in LBBAP lead implantation skills. Thus, we expect that the success rate will improve as more cases will be reported in the future.

LBB capture was recognized in 54.7% of patients. The remaining cases of LVSP with s-LVAT <90 ms were regarded as successful LBBAP. In several studies,[2,9] LVSP was included in successful LBBAP, although s-LVAT was significantly shorter in the LBBP group than in the LVSP group. The European large-scale multicenter study also described that LVSP was an acceptable procedural outcome of successful LBBAP.[9] Shimeno et al.[18] demonstrated that most of LBBAP might be LVSP based on the strict criteria of output-dependent QRS transition and that the lead deployment should be deep enough to achieve LBB capture. Deep penetration might increase the risk of interventricular septal perforation because a left bundle fascicle lies on the left ventricular (LV) endocardium.[12,19] Notably, in our patients dependent on ventricular pacing, LVEF remained high through both LBBP and LVSP, with no significant difference. LVSP preserved LV pump function by maintaining the peak first derivative of the LV pressure, although RV pacing reduced it compared with that at baseline.[20] Thus, LVSP seems to be acceptable as a good procedural end point of LBBAP lead implantation in patients with bradycardia.[9]

Predictors of procedural failure were IVCD, thickened IVS, and severe TR. Possible reasons are as follows: (1) failure to advance the lead deep enough into the septum probably due to thickened and/or fibrous septum; (2) failure to bring the delivery sheath and lead sufficiently close to the septal target site likely due to the enlargement of cardiac chambers (e.g., dilated atrium and ventricle caused by severe TR); and (3) failure to obtain s-LVAT <90 ms probably due to a disturbance in the electrical connection of the ventricular myocardium, such as the presence of IVCD. The success rate in patients with IVCD was lower than that in patients with bundle branch block. This difference could potentially be attributed to the failure of deep lead deployment due to progressive fibrosis in the IVS or the inability to achieve sufficient shortening of the s-LVAT due to conduction disturbances between ventricular myocytes. In our study, the success rate was low (42.9%) in seven patients with HCM, which was similar to the results of Zhu et al.[21] They suggested that thickened septal myocardium and myocardial fibrosis might contribute to the inability of the lead to penetrate the septum deeply or reach the LBB area. Imaging modalities, such as echocardiography and cardiac magnetic resonance imaging, may be useful in assessing septal thickness and abnormal myocardial substrate preoperatively,[22] and patient selection via these modalities would be important to facilitate successful LBBAP. By contrast, an adequate reach and strong support from the guiding sheath for the septal target site is a key factor for the successful deep septal deployment of the lead. Lower success rates in patients with severe TR were probably due to dilated cardiac chambers, resulting in the poor backup force of the guiding sheath and failure of lead advancement into the deep septum. Padala et al.[6] demonstrated the efficacy of using a deflectable sheath for successful LBBAP when the fixed curve sheath could not reach the target location. However, the deflectable sheath is currently unavailable in Japan. In the future, when this sheath and new tools become available, success rates may expectedly improve in the Japanese population.

Lead-related complications occurred only in 8.9% of LBBAP lead implantations, and no major complications were observed in this study. Although the previous study reported acute coronary syndrome, acute ST-segment elevation, and chest pain as LBBAP-lead-related complications,[9] these complications were not confirmed as well in this study. Septal perforation is a major concern in performing LBBAP, with a reported incidence of 0.3–4.9%.[6,8,9,23] Intraprocedural

septal perforation was noted in 4.0% of the patients. In these patients, the lead was completely extracted and successfully repositioned at a different site. No late-onset septal perforations occurred during the follow-up period. Loss of LBB area capture based on ECG assessment was relatively common in eight cases (4.0%) probably due to the micro-dislodgement of the lead based on our experience. This complication was observed not only in the early phase but also in the chronic phase after implantation, while the lead parameters including capture threshold were stable in all cases. Although no lead dislodgements with pacing failure were noted, lead-related complications must be monitored carefully by continuously assessing the lead parameters, ECG, and imaging modalities after LBBAP lead implantation.

In this study, LBBAP was performed mainly for AVB patients with preserved LV function. Our results showed that LBBAP for AVB cases depending on ventricular pacing did not lead to the deterioration of LVEF after implantation. Furthermore, this efficacy was observed whether the LBB was captured or not, which is a novel finding. The latest guideline on cardiac physiologic pacing stated that LBBAP might be reasonable for patients with normal LVEF who require substantial ventricular pacing (class of recommendation IIb).[14] We believe that our results support the validity of LBBAP implantation for AVB depending on ventricular pacing. Further investigations are needed to validate the efficacy and safety of LBBAP as a first-line pacing therapy for AVB patients.

4.1 | Study limitations

This was a retrospective, nonrandomized, and observational study in Japan. Multiple institutions and operators were involved; therefore, there may have been no consistency in implantation techniques, procedure end points, and measurement methods of each parameter. Due to the lack of an independent central adjudication committee, the success rate may have been overestimated and echocardiographic measurements may have been subtly different depending on the institution. The insufficient number of patients may limit the power to assess predictors in the univariable and multivariable analyses. The LBBAP parameters and echocardiographic data were not obtained from all patients during the follow-up, which may have affected the outcomes. Further investigation is needed to determine the durability of the LBBAP lead and prognosis of patients with LBBAP during longer follow-up periods. We defined late R-wave in lead V1 as a prerequisite for the success criteria of this study. Although most previous reports have adopted this late R-wave in lead V1 for successful LBBAP, a recent paper showed that this finding was not observed in 5.6% of the successful LBBAP cases.[24] Based on this, the success rate may possibly be underestimated in this study.

LBBAP has been attempted as an alternative to conventional biventricular pacing with stable pacing parameters and improvements in clinical and echocardiographic outcomes.[23] This study involved only patients with pacemaker indications for bradyarrhythmia and not with CRT indication for heart failure. Jastrzebski et al.[25] denoted that clinical and echocardiographic improvements in the LBB capture group were superior to those in the LVSP group in patients with heart failure. Hence, the applied criteria in this study would not be suitable for LBBAP for CRT. Thus, further investigation is warranted to clarify how the presence or absence of LBB capture affects clinical outcomes and which patients should be targeted for LBB capture.[26]

5 | CONCLUSIONS

LBBAP could be achieved with a sufficiently high success rate and stable lead parameters and LVEF during the follow-up period with few complications. Preoperative factors, including IVCD, thickened IVS, and severe TR, were independent predictors of LBBAP procedural failure. LBBAP is feasible and safe as a primary strategy for patients with AVB depending on ventricular pacing in a Japanese population.

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CONFLICT OF INTEREST STATEMENT

T. Sato is affiliated with Endowed Department, Biotronik, Inc. The other authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

The de-identified participant data for this study will not be shared.

ETHICS STATEMENT

The study protocol was approved by the institutional ethics committee of Kyorin University (approval no. R01-078-02) and all institutions that participated in the study.

PATIENT CONSENT

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent. We applied the opt-out method to obtain consent for this study.

PERMISSION TO REPRODUCE MATERIAL

No requirement.

APPROVAL OF THE RESEARCH PROTOCOL

The study protocol was approved by the institutional ethics committee of Kyorin University (approval no. R01-078-02) and all institutions that participated in the study.

INFORMED CONSENT

Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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