Original Article

Comparison of the left ventricular dyssynchrony between stylet-driven and lumen-less lead technique in left bundle branch area pacing using myocardial perfusion scintigraphy

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Background: Left bundle branch area pacing (LBBAP) has emerged as a novel physiological pacing method to reduce left ventricular (LV) dyssynchrony due to ventricular pacing. Only lumen-less pacing leads (LLLs) with fixed helixes could achieve LBBAP previously, but recently, LBBAP has been performed using stylet-driven leads (SDLs). This study aimed to evaluate the LV dyssynchrony between SDLs and LLLs techniques in LBBAP.

Methods: We retrospectively evaluated patients who underwent LBBAP with either SDLs or LLLs. We compared both groups' electrocardiogram (ECG) findings and LV dyssynchrony parameters derived from myocardial perfusion scintigraphy. LV dyssynchrony parameters consisted of phase analysis and regional wall motion analysis. We evaluated bandwidth, phase standard deviation (PSD), and entropy in the phase analysis. The time to the end-systolic frame (TES) was calculated in regional wall motion analysis using single-photon emission computed tomography (SPECT). We also evaluated the maximum differences between segmental TES (MDTES), the standard deviation of TES (SDTES), and the difference in the TES between the lateral wall and septum (DTES-LS).

Results: In total, 97 patients were enrolled. The success rate of LBBAP did not differ between the groups [SDLs: 47/48 patients (98%) *vs.* LLLs: 47/51 patients (92%), P=0.36]. The paced QRS duration and the stimulus to the peak LV activation time (stim-LVAT) also did not differ between SDL and LLL groups (122±10 *vs.* 119±12 ms, P=0.206; 69±12 *vs.* 66±13 ms, P=0.31, respectively). There were no differences in bandwidth, PSD, and entropy between SDL and LLL groups (73°±37° *vs.* 86°±47°, P=0.18; 19°±8.5° *vs.* 21°±9.7°, P=0.19; 0.57±0.08 *vs.* 0.59±0.08, P=0.17, respectively). The regional wall motion analysis parameters MDTES, SDTES, and DTES-LS also did not differ between SDL and LLL groups (19%±10% *vs.* 20%±10%, P=0.885; 5.0%±2.5% *vs.* 5.0%±2.5%, P=0.995; 5.0%±3.7% *vs.* 4.8%±4.2%, P=0.78, respectively).

Conclusions: LBBAP using SDLs was comparable to LV electrical and mechanical synchrony with LLLs.

Keywords: Left bundle branch area pacing (LBBAP); lumen-less pacing leads (LLLs); stylet-driven pacing leads; mechanical dyssynchrony

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Introduction

The effectiveness of right ventricular pacing (RVP) has been established for bradycardia. However, some problems associated with RVP have also been reported, such as decreased left ventricular (LV) synchrony, depressed left ventricular ejection fraction (LVEF), and the development of pacemaker-induced cardiomyopathy due to non-physiological pacing (1,2).

Recently, direct His bundle pacing (HBP) and left bundle branch area pacing (LBBAP) have been established as useful physiological alternative pacing methods to RVP (3,4). HBP can maintain the LV physiological activation and LV synchrony and can thereby reduce the risk of LVEF depression, heart failure hospitalization, and cardiovascular death compared to RVP (3). HBP has limitations such as threshold elevation in the chronic phase and low success rate of the procedure; however, LBBAP has fewer problems and provides a shorter QRS duration comparable to HBP (5). Several reports have demonstrated the effectiveness of LBBAP, but LBBAP could be performed using lumen-less pacing leads (LLLs) with fixed helix (SelectSecure 3830 pacing lead, Medtronic Inc., Minneapolis, MN, USA) previously (4,6-8). Some recent studies have reported that LBBAP can be performed with standard stylet-driven leads (SDLs) supported by a new delivery system (9,10). However, there is little information on LV synchrony in LBBAP using SDLs. Therefore, in this study, we aimed to assess whether LBBAP with SDL could achieve LV synchronization comparable to LLL. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-357/rc).

Methods

Study population

We retrospectively reviewed the records of patients who underwent pacemaker implantation between March 2020 and August 2022 at Seirei Mikatahara General Hospital. Indications for pacemaker implantation were performed in accordance with the Japanese Circulation Society/Japanese Heart Rhythm Society guidelines (11).

In our hospital, we attempted LBBAP as the first-line pacing for patients with bradycardia. RVP was performed in failed LBBAP cases. We classified patients who underwent LBBAP into two groups: SDLs and LLLs. Patients with the following criteria were excluded: LVEF <35% as determined by echocardiography, history of previous cardiac device implantation such as a pacemaker or implantable cardioverter-defibrillator, lack of follow-up, and lack of adequate clinical data. This study was approved by the Ethics Committee of Seirei Mikatahara General Hospital (No. 22-40) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study is a retrospective observational study, with no new invasive procedures, and informed consent was obtained in an opt-out fashion.

Data collection

Patients' demographic characteristics, resting 12-lead electrocardiogram (ECG), and echocardiography parameters were collected before pacemaker implantation. Ventricular lead parameters, including R wave amplitude, pacing threshold, and lead impedance and ECG parameters, including paced QRS duration and the stimulus to the peak LV activation time (stim-LVAT), were recorded during the pacemaker implantation. The pacing parameters were evaluated at 1-, 6-, and 12-month follow-ups. In addition, we compared the incidence of complications between the two groups. Complications were assessed by thoracic computed tomography and transthoracic echocardiography (TTE) within a week after surgery.

Pacemaker implantation

The selection of a single-chamber pacemaker or dual-chamber pacemaker system was determined by the patients' individual circumstances. A 12-lead ECG was viewed and recorded simultaneously during the pacemaker implantation. Patients underwent pacemaker implantation following the LBBAP procedure in LLLs and SDL groups.

LBBAP implant procedure

LBBAP was performed using two delivery systems with different pacing leads and delivery sheath combinations.

In the SDL group, LBBAP was performed with a 5.6-Fr stylet-driven pacing lead with a retractable helix (Solia S60, Biotronik, SE & Co., Berlin, Germany), delivered through a pre-shaped delivery sheath (Selectra 3D, Biotronik). In the LLL group, LBBAP was performed using a 4.1-Fr LLL with a fixed helix (SelectSecure 3830 pacing lead, Medtronic Inc.), delivered through a pre-shaped delivery sheath (C315His, Medtronic Inc.). The Soria S lead was primed by exposing the expansion screw and turning the outer pin clockwise 5–10 turns. After fully exposing the 1.8 mm stretchable helix, the outer pin was rotated clockwise eight more times using the standard stylet guide tool supplied with the lead, as previously reported (10). This operation is useful to avoid partial unwinding of the extendable helix as manual rotation applied to the outer body of the lead may cause the inner coil not to follow the rotation of the outer lead body. The SelectSecure 3830 lead required no additional lead preparation and was advanced directly through the C315His. LBBAP implantation was performed as described previously (5). We performed pace mapping by lead tip to determine the lead placement site. If a W-shaped paced QRS morphology was obtained in lead V1 by pace mapping, that site was considered suitable for performing LBBAP.

The ventricular lead was screwed in the septum and advanced toward the left side after confirming that the lead tip was positioned in the septum in the left anterior oblique view. Both LLL and SDL were advanced by applying manual rotation to the outer lead body. The lead was paced intermittently, and the QRS morphology of lead V1 (the lowest point of the W-shaped notch) tapered off until the vertical R wave formed a right bundle branch block (RBBB) morphology. Lead advancement was finished when paced QRS morphology met the previously published LBBAP criteria (5,8): (I) paced QRS morphology with an RBBB-like pattern (qR or rSR' morphology in V1) and (II) stim-LVAT that prolonged abruptly with decreasing output or remained constantly short at the threshold test in different outputs. We classified patients with LBBAP into left bundle branch trunk pacing (LBTP), left anterior fascicular pacing (LAFP), left posterior fascicular pacing (LPFP), left septal fascicular pacing (LSFP), and left ventricular septal myocardial pacing (LVSP) groups depending on the location of left conduction system capture (12,13). LVSP was diagnosed if direct LBB capture criteria were not fulfilled, but qR or rSR' morphology in V1 was present. Direct LBB capture was determined according to the following criteria: (I) abrupt shortening of stim-LVAT of >10 ms during increasing output; (II) short and constant stim-LVAT and the shortest stim-LVAT <80 ms in patients with narrow QRS/isolated RBBB patients or <90 ms in patients with more advanced ventricular conduction system disease; (III) transition from nonselective LBB capture to selective LBB capture at near-threshold outputs; and (IV) V6-V1 interpeak interval >40 ms (12,14). If LBB capture was confirmed, patients were classified according to the paced QRS morphology and polarity as follows (12,13): (I) LBTP: paced QRS morphology similar to that of sinus rhythm; (II) LAFP: inferior QRS axis (leads II and III positive); (III) LPFP: superior QRS axis (leads II and III predominantly negative); and (IV) LSFP: intermediate QRS axis (lead II predominantly positive and lead III with negative component). Finally, the connection between the leads, pacemaker generator, and pocket closure was established. Azure XT (Medtronic Inc.) and Edora 8 DR-T (Biotronik) were used as pacemaker generators.

Postimplant pacemaker programming

After pacemaker implantation, ECG was performed under programming optimized for reliable ventricular capture. The atrioventricular delay was programmed short enough for DDD pacemakers to achieve the ventricular pacing capture. For VVI pacemakers, the pacing rate was programmed approximately 10 beats/min faster than the intrinsic rate to achieve complete ventricular pacing capture. The pacing lead configuration was set to bipolar mode, and the output was programmed to 5 V/0.4 ms within a week after the pacemaker implant operation. One week after the pacemaker implantation, the pacemaker programming mode was updated after confirming that lead dislodgement had not occurred. The use of managed ventricular pacing (MVP) and rate-modulated pacing algorithms were decided at the physician's discretion depending on patient's individual conditions, including expected ventricular pacing rate and underlying disease. The algorithm of MVP was the AAI/DDD switching algorithm in Azure™ XT and was the automatic atrioventricular search hysteresis in Edora 8 DR-T. An acceleration sensor was used in Azure™ XT for rate-modulated pacing, and closed-loop stimulation (CLS) was used in Edora 8 DR-T. *Figure 1* shows examples of fluoroscopy images, echocardiography, and paced ECG after implantation with both LLL and SDL.

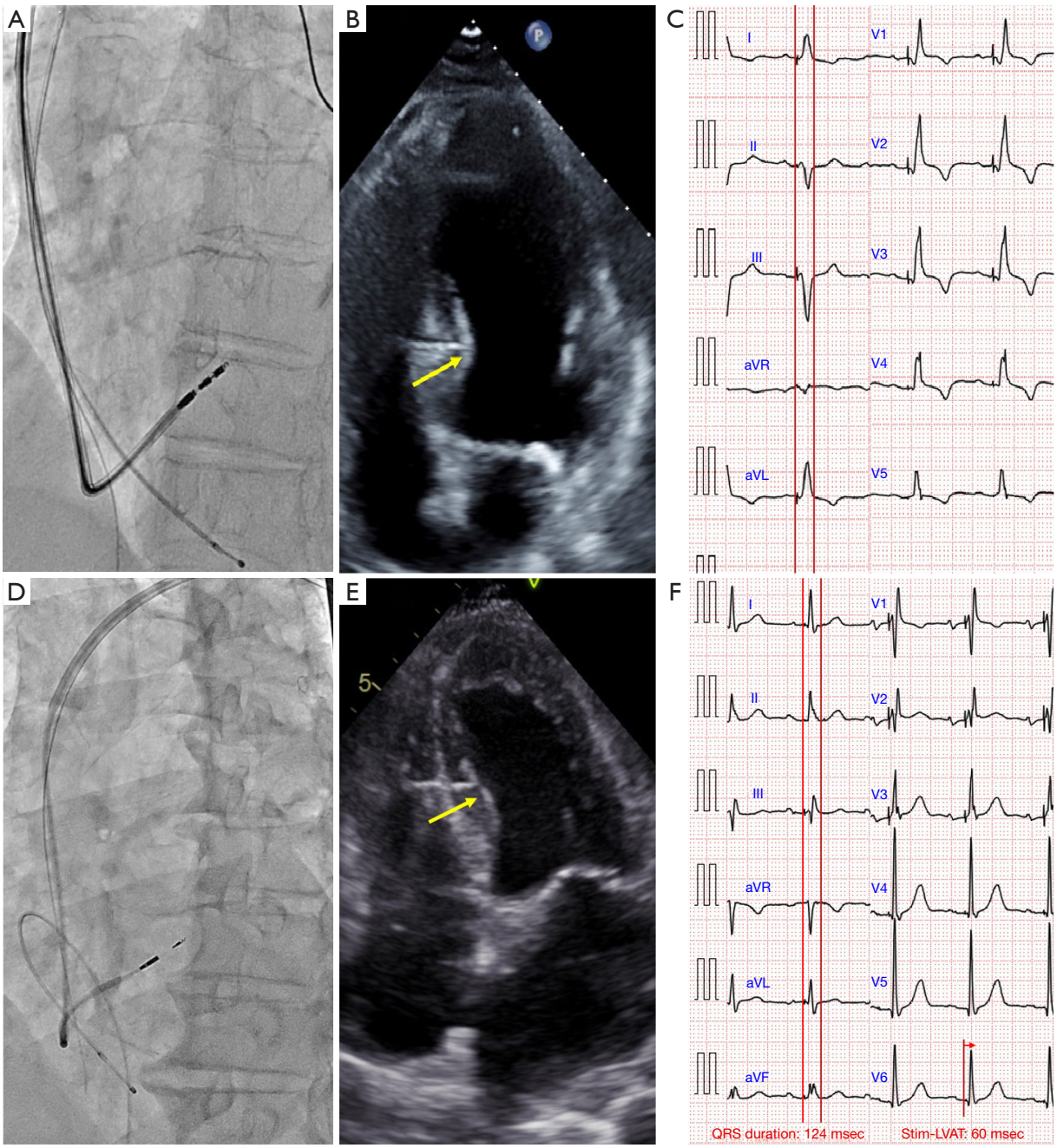

Figure 1 Fluoroscopy image, echocardiogram and electrocardiogram of representative cases in the SDL (upper) and LLL (lower) pacing groups. (A) Fluoroscopy image of SDL. (B) Echocardiogram of SDL. The yellow arrow indicates the lead tip of SDL in the septum. (C) Electrocardiogram of SDL with a paced QRS duration of 128 ms and a stim-LVAT of 70 ms. (D) Fluoroscopy image of LLL. (E) Echocardiogram of LLL. The yellow arrow indicates the lead tip of LLL in the septum. (F) Electrocardiogram of LLL with a paced QRS duration of 124 ms and stim-LVAT of 60 ms. SDL, stylet-driven lead; LLL, lumen-less pacing lead; stim-LVAT, stimulus to the peak left ventricular activation time.

ECG evaluation

Twelve-lead ECGs were obtained 1 week after the pacemaker implantation. In all patients, ECG was evaluated under programming ventricular lead output of 5 V/0.4 ms. QRS duration was defined as that of the widest complex in all leads. QT interval was measured from the QRS onset to the T offset, and the corrected QT (QTc) interval was calculated using Bazett's formula corrected for heart rate. All pacing intervals, including paced QRS duration, paced QT interval, and paced QTc interval, were measured under complete ventricular pacing capture. The differences before and after transplantation in QRS duration, QT interval, and QTc interval were also calculated and defined as ΔQRS duration, ΔQT interval, and ΔQTc interval. We further assessed stim-LVAT after transplantation in both groups.

LV mechanical synchrony evaluation

The mechanical dyssynchrony of left ventricle was evaluated within 1 week after the transplantation with phase analysis and regional wall motion analysis using technetium (Tc)-99m sestamibi ECG-gated myocardial perfusion imaging (MPI) and single-photon emission computed tomography (SPECT). Scintigraphy was performed almost simultaneously with 12-lead ECG evaluation under 5 V/0.4 ms bipolar pacing. These studies were performed entirely under ventricular pacing, and no algorithms, such as MVP, were applied. Tc-99m sestamibi (740 MBq) was administered intravenously to each patient, followed by a light meal to improve the Tc-99m sestamibi clearance from the hepatobiliary tract. One hour later, SPECT was performed using a digital gamma camera (Ventri, GE Healthcare, Little Chalfont, UK) with a low-energy, high-resolution collimator.

As previously reported, using a phase and regional wall motion analysis tool (cardioREPO, FUJIFILM RI Pharma, Tokyo, Japan, in collaboration with EXINI Diagnostics, Lund, Sweden) after gated SPECT acquisition we calculated the LV volume, LV systolic and diastolic function, such as end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF), the peak fill factor (PFR) and 1/3 mean filling rate (MFR) (15,16). Similarly, we calculated the phase analysis parameters such as the 95% width of the histogram or bandwidth (phase bandwidth), the phase standard deviation (PSD) and entropy, and regional wall motion analysis parameters, as we previously reported (17,18). The time to the end-systolic frame (TES) was calculated in regional wall motion analysis using SPECT. We also evaluated the maximum differences between segmental TES (MDTES), the standard deviation of TES (SDTES), and the difference in the TES between the lateral wall and septum (DTES-LS) using cardioREPO (18). LV synchrony was compared using all phase analysis and regional wall motion analysis parameters between both groups.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median (interquartile range) and were compared using an unpaired *t*-test or Mann-Whitney *U* test according to data distribution. All categorical variables are expressed as raw numbers and percentages and analyzed using Fisher's exact test. Statistical significance was defined as a two-tailed P value of <0.05. All analyses were performed by R v3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

This study included 99 patients, and the overall implant success rate of LBBAP was 95% (*Figure 2*). The implant success rates in the SDL and LLL groups were not significantly different: 47/48 (98%) *vs.* 47/51 (92%), respectively (P=0.36). In the LLL group, LBBAP failed in four patients.

Three patients had a history of myocardial infarction in the left anterior descending artery region, and one had cardiac sarcoidosis. Lead advancement into the septum failed due to a hard endocardium in these patients. In the SDL group, LBBAP failed in one patient because of severe right atrial enlargement.

More females were in the SDL group than in the LLL group (66% *vs.* 40%, P=0.02). The underlying arrhythmias included atrioventricular block in 74 (79%) patients, sick sinus syndrome (SSS) in 19 (20%), and atrial fibrillation bradycardia in 1 (1%). The proportion of patients with atrioventricular block did not differ between groups (74% *vs.* 83%, P=0.30). Other than sex, no significant differences existed between groups in patients' baseline characteristics data (*Table 1*). Regarding the LBBAP subtype, LAFP was significantly higher in the SDL group than in the LLL group (17% *vs.* 0%, P=0.006). Other subtypes, LBTP, LPFP, LSFP, and LVSP, did not differ between the two

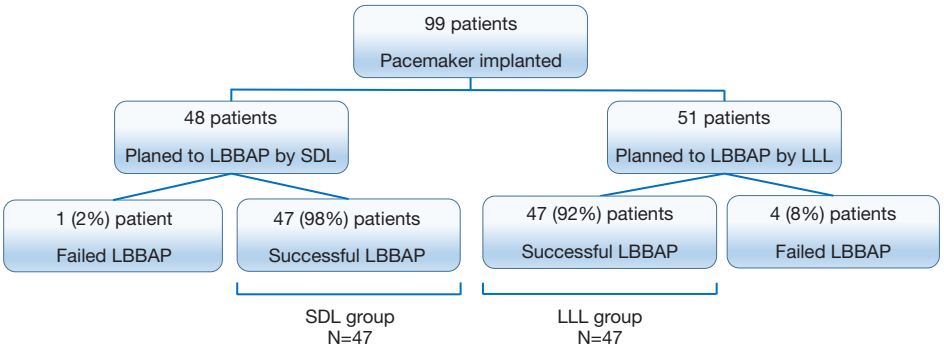

Figure 2 Flow chart of the study population. We retrospectively reviewed 99 consecutive patients who underwent pacemaker implantation and were divided into two groups: those who underwent LBBAP with SDLs and those who underwent LBBAP with LLLs. In the SDL group, 48 patients underwent LBBAP and the surgery was successful in 47 patients (98%). In the LLL group, 51 patients underwent LBBAP and the surgery was successful in 47 patients (92%). LBBAP, left bundle branch area pacing; SDL, stylet-driven lead; LLL, lumen-less pacing lead.

Table 1 Patients' baseline characteristics

Variable	SDL group (n=47)	LLL group (n=47)	P value
Age, years	80±11	79±10	0.60
Female sex	31 [66]	19 [40]	0.02
Arrhythmia			0.30
SSS	12 [26]	7 [15]	
AV block	35 [74]	39 [83]	
AF bradycardia	0 [0]	1 [2]	
Dual-chamber pacemaker	45 [96]	45 [96]	>0.99
Comorbid disease			
Hypertension	33 [70]	29 [62]	0.51
Diabetes mellitus	14 [30]	9 [19]	0.34
Dyslipidemia	14 [30]	20 [43]	0.28
Chronic kidney disease	17 [36]	19 [40]	0.83
Hemodialysis	4 [8.5]	1 [2]	0.36
Coronary artery disease	13 [28]	9 [19]	0.47
AF	15 [32]	16 [34]	>0.99
Medication			
Antiplatelet	17 [36]	16 [34]	>0.99
Anticoagulant	10 [21]	13 [28]	0.63
β-blocker	11 [23]	12 [26]	>0.99
ACE-I or ARB	20 [43]	15 [32]	0.39

Table 1 *(continued)*

Table 1 *(continued)*

Variable	SDL group (n=47)	LLL group (n=47)	P value
Laboratory parameters			
Hemoglobin, g/dL	12.6±1.8	11.9±2.1	0.09
Serum creatinine, mg/dL	0.88 [0.69–1.23]	0.89 [0.75–1.42]	0.44
LDL-cholesterol, mg/dL	99±29	99±33	0.93
HbA1c, %	6.0±1.2	6.0±1.1	0.82
B-type natriuretic peptide, pg/mL	174 [62–357]	154 [71–359]	0.89
Echocardiographic parameters			
LAD, mm	35±5.3	36±8.9	0.47
LVDD, mm	45±5.9	48±5.6	0.11
LVDS, mm	29±6.2	31±5.0	0.19
LVEF, %	66±8.7	65±8.6	0.58
LBBAP capture subtypes			
LBTP	7 [15]	11 [23]	0.43
LAFP	8 [17]	0 [0]	0.006
LPFP	15 [32]	16 [34]	>0.99
LSFP	11 [23]	10 [21]	>0.99
LVSP	6 [13]	10 [21]	0.41
Complications			
Hematoma and reoperation	0 [0]	0 [0]	>0.99
VSP (intraoperative fluoroscopy)	2 [4]	3 [6]	>0.99
VSP (TTE within 1 week)	0 [0]	0 [0]	>0.99
Macrodislodgement	1 [2]	0 [0]	>0.99
Microdislodgement	0 [0]	0 [0]	>0.99

Values are reported as mean ± standard deviation, median [interquartile range], or n [%]. SDL, stylet-driven lead; LLL, lumen-less pacing lead; SSS, sick sinus syndrome; AV, atrioventricular; AF, atrial fibrillation; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; LDL, low-density lipoprotein; HbA1c, glycated hemoglobin; LAD, left atrial dimension; LVDD, left ventricular end-diastolic diameter; LVDS, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; LBBAP, left bundle branch area pacing; LBTP, left bundle branch trunk pacing; LAFP, left anterior fascicular pacing; LPFP, left posterior fascicular pacing; LSFP, left septal fascicular pacing; LVSP, left ventricular septal myocardial pacing; VSP, ventricular septal perforation; TTE, transthoracic echocardiography.

groups. In both groups, some ventricular septal perforation (VSP) cases occurred during the pacemaker implantation procedure. However, no VSP was observed by TTE performed within 1 week.

ECG findings and pacemaker parameters

There was no difference between SDL and LLL groups regarding the distribution of intrinsic QRS morphologies (P=0.69) (*Table 2*). Intrinsic QRS duration did not differ between SDL and LLL groups (114±27 *vs.* 109±29 ms, P=0.42). The paced QRS duration and delta QRS duration did not differ [122±10 *vs.* 119±12 ms, P=0.21; 7 (–13 to 32) *vs.* 20 (–9 to 29) ms, P=0.62]. There were also no differences in the paced QTc interval and the delta QTc interval [453±30 *vs.* 445±23 ms, P=0.15; 14.5 (–22 to 42) *vs.* –1.0 (–32 to 24) ms, P=0.21]. Stim-LVAT did not differ between groups (69±12 *vs.* 66±13 ms, P=0.31).

Table 2 Twelve-lead electrocardiographic parameters before and after pacemaker implantation

Variable	SDL group (n=47)	LLL group (n=47)	P value
Intrinsic QRS morphologies			0.69
QRS without bundle branch block	21 [45]	21 [45]	
Right bundle branch block	21 [45]	24 [51]	
Left bundle branch block	5 [11]	2 [4]	
Intrinsic QRS duration, ms	114±27	109±29	0.42
Paced QRS duration, ms	122±10	119±12	0.21
Delta QRS duration, ms	7 [−13 to 32]	20 [−9 to 29]	0.62
Intrinsic QT interval, ms	491±74	482±83	0.57
Paced QT interval, ms	423±36	414±31	0.21
Delta QT interval, ms	−49 [−141 to 10]	−68 [−140 to 9]	0.96
Intrinsic QTc interval, ms	448±50	452±51	0.71
Paced QTc interval, ms	453±30	445±23	0.15
Delta QTc interval, ms	14.5 [−22 to 42]	−1.0 [−32 to 24]	0.21
Stim-LVAT, ms	69±12	66±13	0.31

Values are reported as mean ± standard deviation, median [interquartile range], or n [%]. SDL, stylet-driven lead; LLL, lumen-less pacing lead; Delta QRS duration, the difference between the paced and intrinsic QRS durations; Delta QT interval, the difference between the paced and intrinsic QT intervals; Delta QTc interval, the difference between the paced and intrinsic QTc intervals; QTc, corrected QT; stim-LVAT, the stimulus to the peak left ventricular activation time.

There was no significant difference in the frequency of MVP use between SDL and LLL groups (15% *vs.* 30%, P=0.14). The frequency of rate-modulated pacing was higher in the SDL group than in the LLL group (43% *vs.* 4.3%, P=0.002). The reasons for rate-modulated pacing and CLS in the SDL group included SSS in six patients, AF-complicated SSS in six patients, and hemodialysis in four patients.

Lead parameters at implantation and 1-, 6-, and 12-month follow-up periods are summarized in *Table 3*. There were no differences in mean thresholds between the groups during the follow-up period. The mean thresholds at implant (n=47) and after 1 month (n=47), 6 months (n=36), and 12 months (n=20) were 0.66±0.18 V at 0.4 ms, 0.82±0.26 V at 0.4 ms, 1.01±0.26 V at 0.4 ms, and 1.05±0.25 V at 0.4 ms in the SDL group, respectively (*Figure 3*). The mean thresholds at implant (n=47) and after 1 month (n=47), 6 months (n=41), and 12 months (n=37) were 0.57±0.17 V at 0.4 ms, 0.74±0.30 V at 0.4 ms, 0.89±0.45 V at 0.4 ms, and 0.94±0.37 V at 0.4 ms in the LLL group, respectively. The R-wave amplitude and lead impedance also did not differ between the groups during the follow-up period, as shown in *Table 3* and *Figure 3*. No lead revisions were required in either group.

Synchronization parameters assessed using scintigraphy

There was no significant difference in all the LV systolic and diastolic function parameters obtained by scintigraphy in both groups (*Table 4*). Phase analysis parameters, phase bandwidth, PSD, and entropy did not differ between SDL and LLL groups (73°±37° *vs.* 86°±47°, P=0.18; 19°±8.5° *vs.* 21°±9.7°, P=0.19; 0.57±0.08 *vs.* 0.59±0.08, P=0.17; *Figure 4*). There was no difference in MDTES, SDTES and DTES-LS between both groups (19%±10% *vs.* 20±10%, P=0.885; 5.0%±2.5% *vs.* 5.0%±2.5%, P=0.995; 5.0±3.7 *vs.* 4.8%±4.2%, P=0.78, respectively).

Discussion

In this study, the implant success rate of LBBAP with SDLs was comparable to that of LLLs. Moreover, pacing characteristics, such as QRS duration, delta QRS interval, and stim-LVAT, did not differ between the SDL and LLL

Table 3 Ventricular lead parameters at implantation and during the follow-up period

Variable	SDL group (n=47)	LLL group (n=47)	P value
Pacing algorithm			
Minimized ventricular pacing	7 [15]	14 [30]	0.14
Rate-modulated pacing	16 [34]	2 [4]	0.002
Pacing threshold, V/0.4 ms			
At implantation	0.66±0.18	0.57±0.17	0.05
1-month follow-up	0.82±0.26	0.74±0.30	0.07
6-month follow-up	1.01±0.26	0.89±0.45	0.17
12-month follow-up	1.05±0.25	0.94±0.37	0.35
R-wave amplitude, mV			
At implantation	13±5.0	12±5.7	0.39
1-month follow-up	14±5.3	14±5.0	0.61
6-month follow-up	14±5.5	15±5.3	0.60
12-month follow-up	14±5.4	16±5.1	0.34
Lead impedance, Ω			
At implantation	637±99	641±91	0.81
1-month follow-up	562±61	555±75	0.64
6-month follow-up	551±53	541±73	0.49
12-month follow-up	532±66	510±72	0.36

Values are reported as mean ± standard deviation or n [%]. SDL, stylet-driven lead; LLL, lumen-less pacing lead.

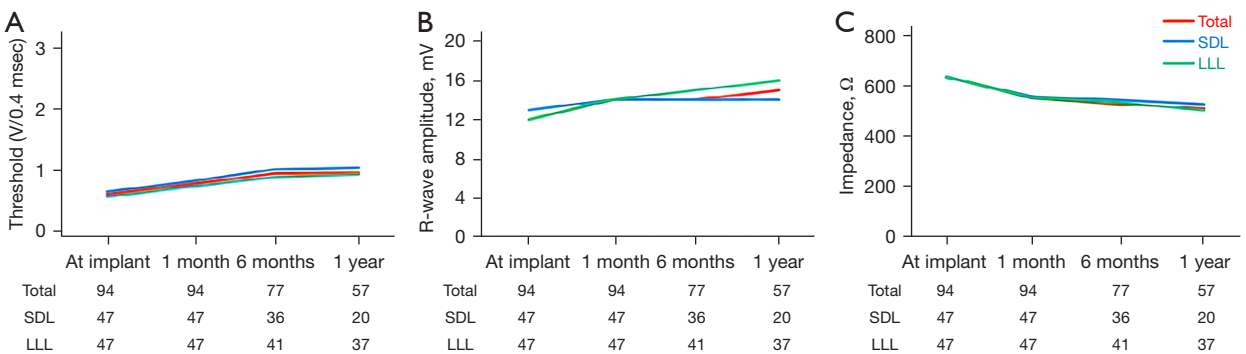

Figure 3 Serial changes of ventricular lead parameters. (A) Capture threshold; (B) R-wave amplitude; (C) impedance at implantation and during the follow-up period. SDL, stylet-driven lead; LLL, lumen-less pacing lead.

groups. We also observed no significant difference in all ventricular lead parameters, including pacing threshold, R-wave amplitude, and lead impedance, until 12-month follow-up. Lastly, the LV mechanical synchrony of the SDL group was preserved similarly to that of the LLL group. This would be the first study demonstrating that LBBAP with SDL can maintain electrical and mechanical LV synchrony in detail. LBBAP is a new conduction system pacing method to avoid non-physiological harmful RV pacing. Some reports revealed that LBBAP reduces

Table 4 Parameters of left ventricular function and dyssynchrony assessed by SPECT MPI

Variable	SDL group (n=47)	LLL group (n=47)	P value
LVEF, %	62±9.1	58±12	0.12
LVEDV, mL	72±29	83±26	0.08
LVESV, mL	28±18	35±17	0.08
PFR, /s	2.1±1.0	2.2±0.8	0.62
1/3 MFR, /s	1.1±0.6	1.2±0.5	0.50
TPFR, ms	159±72	162±72	0.85
TPFR/RR	0.19±0.09	0.20±0.09	0.78
Phase bandwidth, °	73±37	86±47	0.18
PSD, °	19±8.5	21±9.7	0.19
Entropy	0.57±0.08	0.59±0.08	0.17
MDTES, %	20±10	20±10	0.98
SDTES, %	5.1±2.4	5.0±2.5	0.87
DTES-LS, %	4.9±3.5	4.8±4.2	0.89

Values are reported as mean ± standard deviation. SPECT, single-photon emission computed tomography; MPI, myocardial perfusion imaging; SDL, stylet-driven lead; LLL, lumen-less pacing lead; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; PFR, peak filling rate; 1/3 MFR, one-third mean filling rate; TPFR, time to PFR; TPFR/RR, the ratio of TPFR to the R-R interval; PSD, phase standard deviation; TES, time to the end-systolic frame; MDTES, the maximum difference between segmental TES; SDTES, the standard deviation of TES; DTES-LS, TES difference between the lateral wall and septum.

electrical and dyssynchrony compared to RVP (18,19). Furthermore, the effectiveness of LBBAP in narrowing paced QRS duration and improving LVEF is comparable to that of HBP and biventricular pacing (7,8). Therefore, LBBAP may be the best pacing method for bradycardia.

LBBAP was performed using LLLs with SelectSecure 3830 and C315His until now. However, it has become possible to perform LBBAP using SDLs with Solia S60 supported by Selectra 3D in recent years. Zanon *et al.* reported the first two cases of LBBAP with SDLs (9). De Pooter *et al.* reported that LBBAP with SDLs was feasible and yielded comparable implant success to LBBAP with LLLs (10). Our study also achieved high success rates in using LBBAP with SDLs. De Pooter *et al.* reported that the larger outer diameter of the Solia S 60 (5.6 Fr) allowed for more grip on the lead body when applying manual rotations, and the screw of the Solia S60 into the septum was further facilitated by the extra support of the stylet and the wider (8.7 Fr) and sturdier Selectra 3D sheath. In addition, we assumed that the larger outer diameter and more rigid leads of Solia S 60 were less likely to produce the "entanglement effect" as reported by Jastrz-bski *et al.*'s study, which describes that when the pacing lead does not penetrate the interventricular septum beyond its helix length, despite substantial driving force, it results in lead spiraling and lead sleeve wrinkling (20). Since SelectSecure 3830 is a thinner and softer lead, the "entanglement effect" may occur due to spiraling and wrinkling. Regarding the location of left conduction system capture, LAFP was increased in the SDL group in our study. This may be related to the fact that Selectra 3D is wider and sturdier than C315His, and tends to be directed upward to the right ventricle, especially in smaller hearts.

Our study showed no significant differences in ventricular lead parameters in both groups for one year. The usefulness of HBP as a conduction system pacing method has been established. HBP reduces LV dyssynchrony and decreases the risk of LVEF, hospitalization associated with heart failure, and cardiovascular mortality compared with RVP (3). However, HBP presents several clinical problems, including lead dislodgement, late capture threshold increase, and the need for lead revision (21). Conversely, the stability of the lead parameter of LBBAP is reportedly comparable with that of right ventricular septal pacing (RVSP). Su *et al.* reported the long-term safety and feasibility of LBBAP using LLLs for 2 years (22). A multicenter prospective study of LBBAP using SDL in 353 patients also reported that LBBAP using SDL resulted in stable lead parameters during 12-month follow-up (23). Our study revealed that the midterm safety and feasibility of LBBAP using SDLs were not inferior to those of LLLs. In our study, intraoperative VSP occurred in 4% of the SDL group and 6% of the LLL group. VSP is a unique complication in LBBAP. The Multicentre European Left Bundle Branch Area Pacing Outcomes Study (MELOS) reported a VSP incidence of 3.8%, similar to our results (12). LBBAP guided by continuous, uninterrupted monitoring of unipolar pacing was recently reported as a method to avoid VSP, which may be an advantage of LBBAP using SDL (24).

Moreover, we report that the LV electrical and mechanical synchrony of LBBAP using SDLs was similar to that of LLLs using scintigraphy. LV synchrony has been evaluated by various modalities, such as echocardiography, magnetic resonance imaging, and scintigraphy. Several

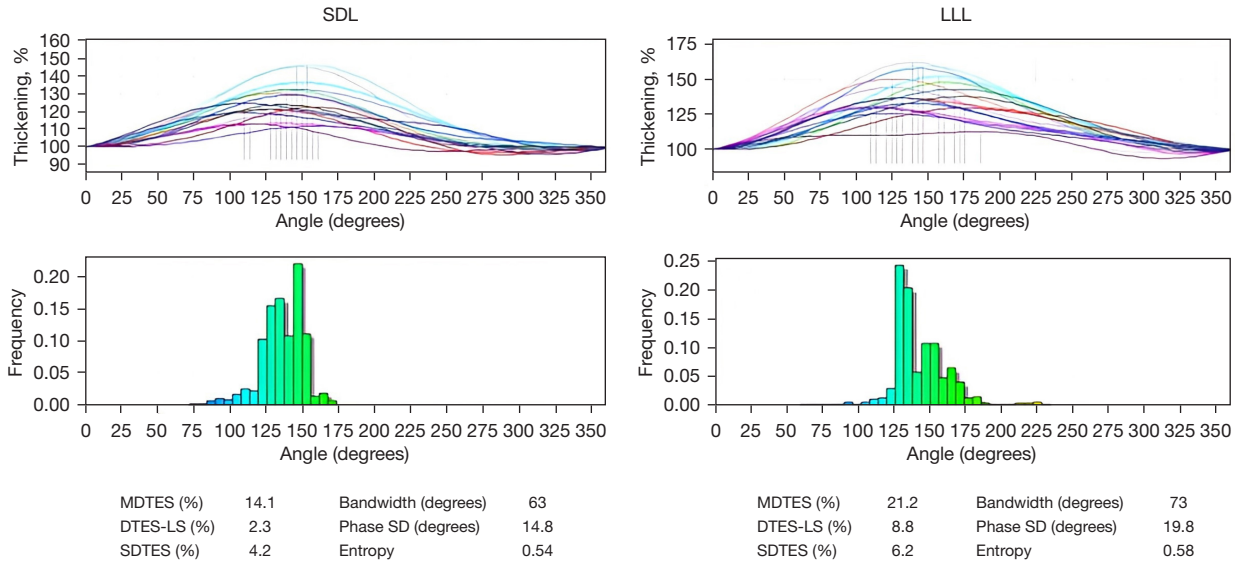

Figure 4 Phase analysis and regional wall motion analysis parameters of representative cases in the left bundle branch area pacing by SDL (left) and by LLL. The left ventricular synchrony of the SDL was maintained similarly to the LLL group. SDL, stylet-driven lead; LLL, lumen-less pacing lead; TES, time to the end-systolic frame; MDTES, maximum differences between segmental TES; DTES-LS, difference in the TES between the lateral wall and septum; SDTES, the standard deviation of TES; SD, standard deviation.

studies have demonstrated the preservation of LV synchrony in LBBAP using echocardiography. These studies evaluated LV synchrony in LBBAP using two-dimensional echocardiography tissue Doppler and speckle tracking imaging (25,26). Echocardiography is a useful noninvasive modality for assessing cardiac function, but it risks inter- and intra-observer variability, as shown in the PROSPECT trial (27). MRI myocardial tagging can accurately evaluate LV synchrony without inter- and intra-observer variability, but it is difficult to evaluate in patients with implanted devices such as pacemakers (28). Scintigraphy is not as convenient as echocardiography, but it has no inter- and intra-observer variability and can be performed in patients with implanted devices (29). Therefore, we used scintigraphy as the evaluation modality for LV synchrony in LBBAP. We previously reported that LBBAP using LLLs reduced mechanical dyssynchrony compared to RVSP and comparable to healthy control participants using myocardial perfusion scintigraphy (18). This indicates that LBBAP using SDLs may also reduce LV mechanical dyssynchrony compared with RVSP.

These results suggest that LBBAP using SDLs is as useful as LLLs, and contributes to new possibilities for LBBAP as an innovative pacing method. Pacemakers use various pacing algorithms for different pathologies. Until now, LBBAP was only feasible with certain generators such as Azure XT. However, this study revealed that LBBAP is also feasible with other generators, such as Edora 8 DR-T. In addition, recent studies reported the possibility of LBBAP using SDLs with the new delivery sheath system, Site Selective Pacing Catheter (Boston Scientific, Marlborough, MA, USA) and Agilis His Pro (Abbott, Chicago, IL, USA) (28,30,31). This enables the selection of pacing algorithms for various pathological conditions in LBBAP. In our study, there was no difference in usage frequency of minimized ventricular pacing, but there was a significant difference in the rate of rate-modulated pacing between the SDL and LLL groups. The PROVIDE study demonstrated that the CLS was associated with significantly higher heart rates than the acceleration sensor during the stress test and that the CLS and the acceleration sensor performed similarly during the physical stress test (32). CLS is also considered effective for patients who require an increase in heart rate at rest; for example, patients undergoing hemodialysis (33). In addition, Ikeda *et al.* reported that CLS was associated with reduced atrial fibrillation/atrial tachyarrhythmia (AF/AT) burden after pacemaker implantation in patients with sinus node dysfunction and a history of AF (34). The results of these studies led to the high usage frequency of rate-modulated pacing in the SDL group in our study. The usefulness of various pacing algorithms aside from CLS has also been reported. Atrial anti-tachycardia pacing and

MVP lowered through the reduction of the progression of atrial tachyarrhythmias to permanent AF in patients with bradycardia and atrial tachyarrhythmias in the MINERVA study (35). The addition of minute ventilation to rate-response pacing improves heart rate scores compared to using an accelerometer alone (36). In the future, these pacing algorithms should be optimized for patients' individual pathologies, even in LBBAP. The choice of SDL or LLL should also be made according to the underlying arrhythmias.

This study has several limitations. First, this is an observational retrospective analysis and it should be considered a hypothesis-generating study rather than a definitive trial. In particular, the choice of SDL or LLL was determined by physicians. Therefore, the selection of pacing leads may have been biased. Second, this was a single-center study with relatively few patients. Third, LBBP definitions, evaluation criteria, and operational procedures are not standardized or uniform, and success rates and outcomes may vary. Fourth, only the information on phase and regional wall motion analyses after pacemaker implantation were included in this study. If this study included these parameters before and after pacemaker implantation, it would be possible to more precisely assess the change in LV dyssynchrony in both groups. Finally, this study only included patients with preserved EF. Therefore, similar results may not be obtained in patients with severely impaired cardiac function. Large multicenter randomized studies are needed to overcome these limitations and validate our findings.

Conclusions

LBBAP using SDLs was comparable to LV electrical and mechanical synchrony with LLLs. Therefore, the choice between SDL and LLL should be made according to the patients' individual pathologies.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Seirei Mikatahara General Hospital (Approval No. 22-40) and was conducted according to the Declaration of Helsinki (as revised in 2013). The study is a retrospective observational study, with no new invasive procedures, and informed consent was obtained in an opt-out fashion.

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