Electrophysiological Insights into Three Modalities of Left Bundle Branch Area Pacing in Patients Indicated for Pacing Therapy

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Summary
Left bundle branch pacing (LBBP) has been adopted as a new pacing therapy whether in routine pacing or patients with heart failure, but the criteria for a completely captured LBBP are too complicated and have a low success rate in routine clinical practice.

Consecutive patients with pacing therapy indications were enrolled. Left bundle branch area pacing (LBBAP) was conducted, and the presence of LBB potential, paced QRS duration, stimulus to left ventricular activation time (Stim-LV AT), and LBB potential to left ventricular activation time (LBB po-LV AT) were determined and utilized to characterize LBBAP modalities. Pacing parameters and safety were assessed at 6-month follow-up. LBBAP succeeded in 95.6% of patients (103/106) who completed the 6-month follow-up. Complete LBBP was achieved in 21 (20%) patients, characterized with a short Stim-LV AT equal to LBB po-LV AT. Incomplete LBBP was achieved in 58 (56%) patients with a short Stim-LV AT equal to LBB po-LV AT at a high pacing output and a relatively longer Stim-LV AT at a low pacing output. Deep septal pacing (DSP) characterized with no LBB potential and a longer Stim-LV AT (83.3 ± 7.7 ms) than that in LBBP (71.37 ± 7.1 ms, \( P < 0.01 \) versus DSP) was observed in 24 (23%) patients. Complete LBBP had a longer total procedure time and longer fluoroscopic time than the other two groups.

This study describes the similarities and differences in electrophysiological characteristics and the possible mechanisms of the different types of LBBAP, classified into 3 modalities in routine clinical practice, each with narrow paced QRS duration and stable parameters, indicating LBBAP can be a near-physiological pacing modality.

Key words: Left ventricular activation time, Left bundle branch potential, Deep septal pacing

Left bundle branch pacing (LBBP) is recognized as one of the physiological pacing modalities.1) LBBP that is achieved by left bundle branch area pacing (LBBAP) in the left side of the basal ventricular septum is characterized by a low and stable capture threshold, and a relatively narrow QRS duration (QRSd) with a right bundle branch block (RBBB) pattern due to rapid left ventricular activation and direct excitation of the left bundle branch.2,3) The pattern of left ventricular activation and mechanical synchrony during LBBP is similar to that during His bundle pacing.4,5) Recent studies have demonstrated the procedural feasibility and clinical benefits of LBBP in certain patients,5-7) especially in those with pathological changes in AV node, His bundle, and proximal left bundle branch.8) However, the criteria of LBB area pacing remain unclear. Recently, Huang, et al summarized the general operating procedures and standards of LBBP.9) However, the minuscule difference in capture threshold of the LBB and surrounding myocardium and the low chance of recording LBB potential make the judgement of LBBP complicated at implantation, which likely leads to multiple, and sometimes unnecessary, attempts for a successful LBBP by an operator. In addition, multiple attempts of lead re-position inside of the ventricular septum can cause local tissue injury or damage.

Methods

Patient selection: A total of 103 consecutive patients who met pacing therapy indications according to 2013 ESC
ECG judgment ready to advance inside of the septum. tricular septum (Figure 1C-E), making the pacing lead tip sheath was perpendicular against the superior interven-
30° (Figure 1D). In both methods, the distal part of the ventricle, and then the 3830 lead was advanced through the sheath with the lead helix exposed. We slightly pulled and rotated the delivery sheath along the right side of the RV to the right side of the interventricular septum. Once the paced QRS morphology showed a right bundle branch block pattern, we started to screw the pacing lead towards the left side of the interventricular septum. Once the paced QRS morphology showed a right bundle branch block or delay (RBBB/RBBD) in ECG lead V1 (Figure 1A-5), which indicated that the tip of the lead was already located near the sub-
endocardium of the left ventricular septum, we stopped the advancement of the pacing lead. In this process, the left bundle branch potential could be recorded during intrinsic rhythm. 2) Once the LBB potential was observed, the interval from the LBB potential to the left ventricular activation time (LBB po-LVAT) was measured. The LVAT is defined as the time of the peak QRS upstroke in V5/V6 (Figure 1A-5). We then delivered the decremental pacing outputs from 5V to the capture threshold, and measured the interval from the stimulus to left ventricular activation time (Stim-LVAT). During incremental pacing output, an abrupt shortening of Stim-LVAT that was equal to the LBB po-LVAT and remained constant both at low and high outputs was indicative of direct LBB capture (also termed as complete LBBP). 3) If no LBB potential was observed during screwing of the lead, paced QRS morphology showed RBBB in lead V1, but the Stim-LVAT was relatively longer and could not be shortened by increasing the output, which we defined as deep septal pacing (DSP, Figure 1C). 2) Single-lead technique: The delivery sheath C315HIS was directly placed into the right ventricle, and then the 3830 lead was advanced through the sheath with the lead helix exposed. We slightly pulled and rotated the delivery sheath along the right side of the interventricular septum under a fluoroscopic view of RAO 30° (Figure 1D). In both methods, the distal part of the sheath was perpendicular against the superior interventricular septum (Figure 1C-E), making the pacing lead tip ready to advance inside of the septum.

**ECG judgment during operation** 1) Pacing with 5V@0.5 ms was delivered intermittently, and ECG QRS morphology was closely monitored. Once we observed a QRS “W” morphology in lead V1 (Figure 1A-2, 3), which is an indication of pacing the right ventricular septum that caused the left bundle branch block pattern, we started to screw the pacing lead towards the left side of the interventricular septum. Once the paced QRS morphology showed a right bundle branch block or delay (RBBB/RBBD) in ECG lead V1 (Figure 1A-5), which indicated that the tip of the lead was already located near the sub-
endocardium of the left ventricular septum, we stopped the advancement of the pacing lead. In this process, the left bundle branch potential could be recorded during intrinsic rhythm. 2) Once the LBB potential was observed, the interval from the LBB potential to the left ventricular activation time (LBB po-LVAT) was measured. The LVAT is defined as the time of the peak QRS upstroke in V5/V6 (Figure 1A-5). We then delivered the decremental pacing outputs from 5V to the capture threshold, and measured the interval from the stimulus to left ventricular activation time (Stim-LVAT). During incremental pacing output, an abrupt shortening of Stim-LVAT that was equal to the LBB po-LVAT and remained constant both at low and high outputs was indicative of direct LBB capture (also termed as complete LBBP). 3) If no LBB potential was observed during screwing of the lead, paced QRS morphology showed RBBB in lead V1, but the Stim-LVAT was relatively longer and could not be shortened by increasing the output, which we defined as deep septal pacing (DSP, Figure 1C). 2) Single-lead technique: The delivery sheath C315HIS was directly placed into the right ventricle, and then the 3830 lead was advanced through the sheath with the lead helix exposed. We slightly pulled and rotated the delivery sheath along the right side of the interventricular septum under a fluoroscopic view of RAO 30° (Figure 1D). In both methods, the distal part of the sheath was perpendicular against the superior interventricular septum (Figure 1C-E), making the pacing lead tip ready to advance inside of the septum.

**Table 1. Baseline Patient Data of Three Types of LBBAP**

| Parameters                        | Complete LBBP (n = 21) | Incomplete LBBP (n = 57) | Deep septal pacing (DSP) (n = 25) | P value |
|-----------------------------------|------------------------|--------------------------|-----------------------------------|---------|
| Age (years)                       | 70.7 ± 10.6            | 71.3 ± 9.7               | 71.6 ± 9.7                        | 0.9432  |
| Male (%)                          | 57%                    | 54%                      | 64%                              | 0.7263  |
| Height (cm)                       | 162.5 ± 9.3            | 161.2 ± 8.8              | 164.9 ± 8.4                      | 0.2260  |
| Weight (kg)                       | 62.8 ± 12.9            | 59.9 ± 9.9               | 65.8 ± 10.1                      | 0.0763  |
| Diabetes (%)                      | 19%                    | 23%                      | 28%                              | 0.7729  |
| Hypertension (%)                  | 71%                    | 58%                      | 64%                              | 0.5448  |
| Persistent atrial fibrillation (%)| 33.0%                  | 42%                      | 48%                              | 0.6691  |
| Sinus node dysfunction (%)        | 33.3%                  | 24.6%                    | 12%                              | 0.2259  |
| AV block (%)                      | 28.6%                  | 26.3%                    | 32%                              | 0.8728  |
| Pre-implantation LVEF (%)         | 56.1 ± 17.2            | 58.4 ± 12.9              | 53.5 ± 16.3                      | 0.3637  |
| Pre-implantation LVEDD (mm)       | 49.0 ± 8.2             | 47.3 ± 6.7               | 50.7 ± 8.7                       | 0.1599  |
| Pre-implantation IVST (mm)        | 10.8 ± 2.3             | 11.3 ± 2.5               | 11.0 ± 1.9                       | 0.7104  |
| Pacing percentage (%)             | 75.8 ± 24.7            | 77.7 ± 21.3              | 71.4 ± 25.1                      | 0.5871  |

BMI indicates body mass index; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; ICM, ischemic cardiomyopathy; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; and IVST, interventricular septum thickness.
angiography in the left anterior oblique (LAO) 30° view, showing the depth of the lead inside of the septum (Figure 3A); (2) local capture by the ring electrode, which indicates the distal part of the ring electrode in the septum; and (3) an abrupt drop of impedance, which is indicative of the helix in the LV chamber. Usually, unipolar pacing impedance between 400-1200 Ω is normal. If the impedance suddenly decreases along with a higher capture threshold in the process, however, this suggests that the lead may break through the left ventricular septal surface. Post-operation cardiac ultrasound and chest CT scans can be used to display the depth of the lead inside of the septum (Figure 3B, C). If any of the above methods can exclude lead perforation and make sure the lead helix is located at the left ventricular septum, and simultaneously meet the electrophysiological LBBAP standard, the operation can be judged as successful.

Statistical analysis: Continuous variables are expressed as the mean ± SD. Independent two-sample t-tests were performed to compare the differences between groups, and the data of the 3 subgroups were evaluated by the one-way ANOVA. A P-value of ≤ 0.05 was considered statistically significant. All data analyses were performed using SPSS version 20 (SPSS Statistics 20, IBM Corp., Armonk, NY, USA).

Programming: The LBBAP lead was connected to the device atrial port in patients with persistent atrial fibrillation (AF). A right ventricular septal (RVS) pacing lead was connected to the RV port as a backup pacing. In patients with sinus node dysfunction and atroventricular block (AVB), we connected the LBBAP lead to the RV port or LV port if a CRT device was used. AV delay programming should be individualized, taking AV conduction into consideration. Ventricular safety pacing was turned on in non-AF patients. The automatic AV search function was routinely turned on in patients with sinus node dysfunction and AVB. The lower rate for LBBAP was initially set at 70 beats/minute, and then programmed to 60 beats/minute at 1-month follow-up. The pacing output was programmed at the device-default value (mostly 3.5 V@0.5 ms as a working output), and unipolar pacing mode was usually chosen.
Figure 2. Electrocardiogram characteristics of complete LBBP, incomplete LBBP, and deep septal pacing (DSP). A: Complete LBBP with LBB potential. LBB po-LVAT is 78 ms and Stim-LVAT is also 78 ms at pacing outputs of 5V/0.5 ms, 3V/0.5 ms, and 1V/0.5 ms. B: Incomplete LBBP, in which potential could be recorded. LBB po-LVAT is 74 ms, and Stim-LVAT gradually shortened as pacing output increased. Stim-LVAT equals to LBB po_LVAT at 5V/0.5 ms. C: DSP without LBB potential. Stim-LVAT is relatively long at pacing outputs of 5V/0.5 ms, 3V/0.5 ms, and 1V/0.5 ms. In all 3 cases, ECG QRS morphology exhibits the pattern of the right bundle branch block.
EGM signatures.

LBBAP were observed with corresponding ECG and side of the basal ventricular septum. Therefore, 3 types of with excitation of local tissue (LBB area) (Figure 2C). In

advanced deeply into left inside of the septum but no LBB

terminated (Figure 2B). When the pacing lead helix was ad-

vanced at working output, incomplete LBB pacing (icLBBP) was de-

scribed as performed (Figure 2A). When the Stim-LVAT was equal to LBB po-LVAT and the Stim-LVAT remained constant at different pacing

outputs, complete LBB pacing (cLBBP) was achieved (Figure 2A). If the Stim-LVAT was longer at low pacing output and could be shortened to LBB po-LVAT at high

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termined (Figure 2B). When the pacing lead helix was ad-

vanced deeply into left inside of the septum but no LBB

potential was recorded, a relatively long Stim-LVAT was

present and remained constant irrespective of whether low

or high pacing output was applied, which indicated DSP

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all cases, the pacing lead helix was confirmed in the left

side of the basal ventricular septum. Therefore, 3 types of

LBBAP were observed with corresponding ECG and

EGM signatures.

Results

Electrocardiographic signatures of 3 LBBAP patterns:
The most evident signature of the LBBAP was ECG QRS

morphology with RBBB. Specifically, lead V1 demonstrated an incremental R wave amplitude following a Q or S wave when the pacing lead was advanced towards the left side of the septum (Figure 1A-5). With the electrode at the LBB area, LBB potential could be recorded (Figure 2A). When the Stim-LVAT was equal to LBB po-LVAT and the Stim-LVAT remained constant at different pacing

outputs, complete LBB pacing (cLBBP) was achieved (Figure 2A). If the Stim-LVAT was longer at low pacing output and could be shortened to LBB po-LVAT at high

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QRS duration The overall paced QRS duration was 120.7 ± 12.7 ms (all measured at working output) and was longer than intrinsic rhythm (109.1 ± 14.9 ms, \( P < 0.01 \)). There was a difference in paced QRS duration between patients with LBB potential and those without LBB potential (118.7 ± 12.5 ms versus 125.0 ± 13.0 ms, \( P = 0.0296 \)). Of the 3 groups, there was no significant difference in paced QRS duration between the cLBBP and icLBBP groups (115.0 ± 9.4 ms versus 120.1 ± 12.9 ms, \( P = 0.11 \)). However, paced QRS duration in both of the above groups was shorter than that during DSP (126.6 ± 12.5 ms, \( P < 0.05 \)) (Table II).

LBB potential and LVAT LBB potential was recorded in 78 of 103 patients (75.7%). The overall LBB po-LVAT was 71.6 ± 6.9 ms, and Stim-LVAT at working output was 76.8 ± 8.9 ms. There was no significant difference between LBB po-LVAT (70.4 ± 6.2 ms) and Stim-LVAT (70.8 ± 5.7 ms) in patients with cLBBP at working output. In patients with icLBBP, there was no significant difference between LBB po-LVAT and Stim-LVAT at high pacing output, but LBB po-LVAT was significantly shorter than the Stim-LVAT at capture threshold (LBB po-LVAT = 71.7 ± 7.4 ms, Stim-LVAT = 71.9 ms at 5V, 76.2 ± 8.7 ms at 3V and 85.3 ± 7.6 ms at 1V). In patients with DSP, Stim-LVAT was 83.3 ± 7.8 ms at working output, which

| Classification of LBBAP patterns | Complete LBBP \((n = 21)\) | Incomplete LBBP \((n = 57)\) | DSP \((n = 25)\) | \(P\) value (ANOVA) |
|--------------------------------|----------------|----------------|----------------|----------------|
| Intrinsic QRSd                | 106.2 ± 10.2   | 108.9 ± 15.8   | 111.8 ± 16.4   | > 0.1          |
| Paced QRSd (3V/0.5 ms)        | 115.0 ± 9.4    | 120.1 ± 12.9   | 126.6 ± 12.5   | < 0.01*        |
| LBB po-LVAT                   | 70.4 ± 6.2     | 71.7 ± 7.4     | None           | > 0.1          |
| Stim-LVAT (3V/0.5 ms)         | 70.8 ± 5.7     | 76.2 ± 8.7     | 83.3 ± 7.8     | < 0.01*        |
| R-wave amplitude (unipolar)   | 9.5 ± 4.7mV    | 10.9 ± 5.1mV   | 10.3 ± 4.2mV   | > 0.1          |
| Pacing thresholds (unipolar)  | 0.9 ± 0.3V     | 0.9 ± 0.3V     | 0.8 ± 0.3V     | > 0.1          |
| Lead impedance (unipolar)     | 602.9 ± 144.1Ω | 650.5 ± 167.2Ω | 641.4 ± 133.4Ω| > 0.1          |

QRSD indicates QRS duration; LBB po-LVAT, left bundle branch potential to left ventricular activation time; and Stim-LVAT, stimulus to left ventricular activation time. \(P\) value: the comparison of the data of the 3 subgroups was performed using ANOVA. Least Significant Difference (LSD) pairwise comparison methods were applied to compare results between each group. Paced QRSd: cLBBP versus icLBBP group, \(P > 0.1\); cLBBP versus DSP group, \(P < 0.01\); icLBBP versus DSP group, \(P < 0.01\); Stim-LVAT: cLBBP versus icLBBP group, \(P < 0.01\); cLBBP versus DSP group, \(P < 0.01\); icLBBP versus DSP group, \(P < 0.01\).
achieved in 21 (20.4%) patients, icLBBP was achieved in those with RBBB potential. LBB indicates left bundle branch; Stim-LVAT, stimulus to left ventricular activation time; LBB po-LVAT, left bundle branch potential to left ventricular activation time; RBBB, right bundle branch block; and RBBD, right bundle branch delay.

Table III. Characteristics of Three LBBAP Modalities

| Conduction system pacing | Complete LBB capture pacing | Incomplete LBB capture pacing | Deep septal pacing (DSP) |
|--------------------------|-----------------------------|-------------------------------|--------------------------|
| LBB potential            | Yes                         | Yes, with high output         | No                       |
| Stim-LVAT                | Constant, shortest,         | Variable, high output shortens it | Constant, long |
| QRS morphology           | RBBB or RBBD                | RBBB or RBBD                  | RBBB or RBBD             |
| Myocardium captured      | By a high pacing output     | By a low pacing output        | By a low pacing output   |
| Micro-perforation         | High possibility             | Low possibility                | Low possibility           |

Figure 4. The hypothesized association between the Stim-LVAT and the lead location by different LBBAP modalities. A: Deep septal: relatively long Stim-LVAT at the high pacing output of 5V and the low pacing output of 1V. B: Incomplete LBBP: short Stim-LVAT at the high pacing output (5V) and long Stim-LVAT at the low pacing output (1V). C: Complete LBBP: short Stim-LVAT at the low or high pacing output. The red-colored stars represent the possible impact area of the pacing current.

is significantly longer than LBB po-LVAT (71.6 ± 6.9 ms, \( P < 0.001 \)) observed in the other two LBBAP patterns (Table II).

**Definition of classification and implant results:** LBBAP can capture the LBB and/or its surrounding myocardium with the following characteristics: (1) trans-ventricular septal placement of the pacing lead tip into the LV septal sub-endocardial region; (2) paced ECG QRS morphology with RBBB; (3) the presence of LBB potential; and (4) LVAT at different pacing outputs. We then defined the complete LBBP, incomplete LBBP and DSP, as shown in Table III. Potential mechanisms for the 3 LBBAP patterns are illustrated in Figure 4.

LBBAP succeeded in 97.2% of patients (103/106). In patients who had failed LBBAP following 3 attempts for LBBAP lead placement, the pacing lead was placed at the conventional location of the right ventricular septum. According to the classification described above, cLBBP was achieved in 21 (20.4%) patients, icLBBP was achieved in 57 (55.3%) patients, and DSP in 25 (24.3%) patients. The mean total procedure time was 128.3 ± 23.8 minutes, 98.2 ± 26.2 minutes and 89.3 ± 31.0 minutes, and fluoroscopic time was 13.2 ± 5.16 minutes, 9.1 ± 3.8 minutes and 7.8 ± 2.8 minutes in the 3 groups, respectively. Concerning both the total procedure time and fluoroscopic time, significant differences were found between the cLBBP group and the other two groups, but no significant difference was present in the icLBBP group and the DSP group.

**Follow-up:**

**Pacing parameters** Pacing capture thresholds measured at implantation (0.87 ± 0.3V) remained stable during 6-month follow-up (0.77 ± 0.3V, \( P > 0.05 \) versus at implantation, Figure 5A). There was no difference in pacing capture threshold among the 3 LBBAP modalities (Table II, Figure 5D-F). The sensed R-wave amplitude was 10.5 ± 2.8 minutes in the 3 groups, respectively. Concerning both the total procedure time and fluoroscopic time, significant differences were found between the cLBBP group and the other two groups, but no significant difference was present in the icLBBP group and the DSP group.
Figure 5. Electrical parameters of LBBAP during the follow-up period. A: Pacing capture threshold. B: Sensed R-wave amplitude. C: Pacing impedance. D-F: Pacing capture threshold among 3 LBBAP modalities at baseline and 6-month follow-up. BL indicates baseline value; 1M, 1-month follow-up visit; 3M, 3-month follow-up visit; 6M, 6-month follow-up visit; cLBBP, complete LBBP; IcLBBP, incomplete LBBP; and DSP, deep septal pacing.

study cohort was 77.9 ± 26.9%, and there was no difference among the 3 LBBAP modalities. Safety assessment In the current study, among the 103 patients who completed the 6-month follow-up, one patient with LBBP had left ventricular perforation of the pacing lead helix, which was detected by post-operative echocardiography. At the 3-month follow-up, echocardiographic examination indicated that the tip appeared to be covered with intima. Another patient with LBBP experienced a worsening tricuspid valve regurgitation. No lead dislocation, infection, valve injury, or increasing of the pacing capture threshold were observed during the follow-up periods.

Discussion

In recent years, LBBAP has been adopted as a new pacing therapy, and is thought to involve recruitment of the left bundle branch. The present study, for the first time, reported 3 pacing modalities when the pacing lead helix was placed at the left side of the ventricular septum for LBBAP, i.e., complete LBB pacing, incomplete LBB pacing, and deep septal pacing (DSP). A conclusion was drawn: For patients with pacing indication, the 3 modalities have no differences in long-term parameters and safety. There was no significant difference in paced-QRS duration between IcLBBP and cLBBP. The paced QRS duration of DSP is slightly wider than the first two. Under the working output, the Stim-LV AT of icLBBP and cLBBP has no obvious difference; DSP is longer than the first two. But the advantages of DSP and icLBBP are the significantly shortened fluoroscopic time and total procedure time. In addition, the study simplified techniques for achieving LBBAP, and proposed feasible criteria for confirming LBBAP in routine clinical settings that could lead to less fluoroscopic exposure time and fewer attempts of lead placement inside of the septum.

LBB and its fascicles widely distribute beneath the endocardium of the left side of the ventricular septum. As a consequence, a promising opportunity exists to place the pacing lead helix at or near the LBB by using the transventricular approach.2,3) This is especially the case when compared to His bundle pacing implantation, which is performed in a narrow region with certain procedural difficulties. For this reason, pacing the LBB has rapidly emerged as a viable type of physiological or near-physiological pacing.1) Recent clinical investigations have demonstrated the procedural feasibility of LBBP implantation, similarity in left ventricular activation, synchrony between LBBP and His bundle pacing,5,7,10) and potential clinical benefits in heart failure patients.11) Criteria for LBBP have been recently proposed,2,3) including ECG QRS morphology of RBBB, LBB potential, short LVAT, and selective and non-selective nature of LBBP. These criteria were advanced based on a setting of clinical investigation. In a routine clinical practice, once the pacing lead helix is placed in the LBB area, different electrical characteristics of pacing the LBB area can be observed. For example, LBB potential is observed in approximately 50-70% of studied patients,5,7,30) and potential clinical benefits in heart failure patients.11)
LVAT to confirm LBB pacing. Therefore, it may be difficult to meet all of the criteria of LBBP at implantation in every patient, as proposed by Huang, et al.3 Indeed, Li, et al.10 demonstrated that LBBP was achieved in only 80% of patients studied when no more than 3 attempts were made for LBBP lead placement, suggesting that more attempts would have been needed for achieving a higher success rate of LBBP. Multiple attempts in a small region of the ventricular septum, however, would certainly increase the risk of local tissue damage and left ventricular perforation when the pacing lead is advanced and maneuvered inside of the septum. This raises the question of whether multiple attempts of lead placement are necessary in most cases in a routine clinical practice.

Although the LBB widely spreads in the left side of the ventricular septum in comparison with the narrow path of the His bundle, most of the ventricular septum still lacks LBB fascicles. As the LBB travels immediately beneath the sub-endocardium, the placement of the pacing lead helix in this thin region can potentially lead to left ventricular perforation. Therefore, we hypothesize that the pacing lead helix may not be precisely placed at the LBB in every case, but rather near the LBB in most cases. Based on our hypothesis, we proposed the following 3 scenarios (Figure 4): (1) the pacing lead helix at the LBB, leading to a true LBBP-icLBBP; (2) the pacing lead helix close to the LBB, part of LBB fascicles may be captured, leading to no LBB capture at low pacing output that captures only local tissue and LBB capture at a higher pacing output, e.g., icLBBP; and (3) the pacing lead helix around the LBB, although the pacing lead is in the left side of the septum, but no LBB capture regardless of how high the pacing output is, only local tissue is captured, e.g., DSP. However, DSP is different from traditional right ventricular septal pacing (RVSP). The lead helix is located on the left ventricular septum in DSP which was confirmed by cardiac ultrasound or chest CT scan in our study, and paced ECG QRS showed RBBB morphology and the QRS duration is relatively shorter than RVSP. Consistent with our hypothesis, the present study demonstrated that when the pacing lead helix was placed in the left side of the ventricular septum, LBBP was achieved in 20.4% of patients, incomplete LBBP in 55.3% of patients, and DSP in 24.3% of patients.

Based on our hypothesis and clinical observations, we thus proposed classification criteria of LBBAP that is achieved by placing the lead tip in the left side of the ventricular septum, in which LBBAP shows the paced ECG QRS morphology with RBBB (Table III). (1) if LBB potential is recorded and Stim-LVAT at different pacing outputs remains constant and essentially equals to LBB po-LVAT, LBB pacing modality is achieved; (2) if Stim-LVAT can be shortened to LBB po-LVAT at high pacing output but lengthened at a low pacing output, LBBP is partially achieved and this is termed incomplete LBBP; and (3) if no LBB potential is recorded and Stim-LVAT remains relatively long at low or high pacing output, the pacing is termed deep septal pacing (DSP). Different from previous criteria of LBBP by Huang, et al.,5 we proposed to compare LBB po-LVAT and Stim-LVAT to differentiate LBBP from incomplete LBBP and DSP, which constitutes a relatively simple method to judge LBBP in routine clinical practice.

Clarification of LBBP and DSP may be important in clinical practice. LBBP can provide rapid left ventricular activation, similar to native left ventricular synchrony, but LBBP may not be easily achieved in certain situations, such as a large right atrium, especially with a hypertrophic ventricular septum and the lead placement with an angle during lead advancement inside of the septum. Moreover, advancing the pacing lead to the sub-endocardium of the septum likely leads to LV perforation, which may cause thrombosis. On the other hand, DSP, which is easier to achieve at implantation, may not generate as rapid of an LV activation as does LBBP, but the LVAT in DSP lags by only approximately 10 ms. This then raises the question of whether the impact of DSP on clinical outcomes would be similar to LBBP. Left ventricular septal pacing (LVSP) by a transvenous approach through the interventricular septum (IVS) with favorable electrical and mechanical effects in animals was explored in the past12,13 and in humans more recently.14,15 However, definitive outcome studies remain warranted.

**Study limitations:** While the present study prospectively enrolled consecutive patients for LBBAP implantation, 3 patterns of LBBP and corresponding criteria for classifying these 3 LBBAP modalities were identified and developed retrospectively based on ECG characteristics and pacing outputs. The non-selectivity of the study cohort is the limitation of this study, and was performed in a limited patient population. Consequently, the findings in the present study and the criteria of LBBAP should be confirmed in multi-center studies in broad patient populations. While the present study found different LBBAP modalities, clinical outcomes should be investigated for each of the LBBAP modalities, and especially to test whether a significant difference exists in clinical outcomes between LBBP and DSP.

**Conclusion**

The current study reported on LBBAP performed in patients in a routine clinical setting, and identified 3 unique modalities of LBBAP: (1) complete LBBP; (2) incomplete LBBP; and (3) deep septal pacing (DSP). The present study proposed a new concept of LBB po-LVAT in comparison with Stim-LVAT to confirm LBB pacing, based on which criteria were developed to classify each of the LBBAP modalities. Furthermore, the study simplified the LBBAP implant process and criteria, making it easier to be promoted to primary hospitals. Large prospective randomized studies are requisite to further confirm the procedural feasibility of LBBAP, as well as the long-term safety and clinical benefits of each of the LBBAP modalities.

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Disclosure

Conflicts of interest: The authors declare that there are no conflicts of interest.

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