Electrophysiological characteristics of septal perforation during left bundle branch pacing

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BACKGROUND Left bundle branch pacing (LBBP) provides a low and stable threshold by direct capture of left bundle fibers on the left ventricular subendocardium. As the procedure involves the deployment of the pacing lead deep inside the septum, septal perforation is a potential complication.

OBJECTIVES The purpose of this study was to analyze the morphology of intracardiac electrograms and unipolar pacing parameters to identify septal perforation in patients undergoing LBBP.

METHODS Patients who had undergone successful LBBP between January 2020 to November 2021 were retrospectively included in the study.

RESULTS LBBP was attempted in 219 patients and was successful in 212 (96.8% success rate). Septal perforation during lead deployment was identified in 30 patients (14.1%). Peak troponin release was 188 ± 162 pg/mL. Mean unipolar impedance during septal perforation was 404.6 ± 19.9 Ω (400–450 Ω in 16 patients [53.3%]; <400 Ω in 14 patients [46.7%]). A cutoff <450 Ω for diagnosing septal perforation had high sensitivity (100%) and specificity (96.6%). Current of injury amplitude reduced from 15.4 ± 11.6 mV just before perforation to 0.9 ± 0.6 mV after perforation. Based on morphology, unfiltered unipolar electrograms were classified into 2 patterns: (1) type I (QS) seen in 20 patients (67%) due to complete perforation (mean unipolar impedance 402.5 ± 20.4 Ω); and (2) type II (RS/rS) seen in 10 patients (33%) due to partial perforation, with 80% showing capture (mean impedance 411 ± 21.3 Ω). All 30 patients underwent successful reimplantation at a new site. No patient developed lead dislodgment during mean follow-up of 9.9 ± 6.7 months.

CONCLUSION Although considered one of the concerns of LBBP, septal perforation, when recognized promptly during implantation by unipolar parameters and treated by reimplantation, would be benign and not associated with an unfavorable outcome.

KEYWORDS Current of injury; Left bundle branch pacing; Pacing impedance; Septal perforation; Template beat; Unfiltered unipolar electrogram

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Introduction

His-Purkinje conduction system pacing aims to directly capture the cardiac conduction system, resulting in synchronized activation of the ventricles with the goal of preventing right ventricular (RV) pacing–induced cardiomyopathy.1–3 Permanent His-bundle pacing (HBP) has been shown to reduce the risk of heart failure hospitalizations, atrial arrhythmias, and mortality compared to conventional RV pacing.4 However, HBP is associated with variable procedural success rates (65%–92%),5,6 late rise in capture threshold, and increased risk of lead revisions. Since the original report by Huang et al7 of deep septal left bundle branch pacing (LBBP) to overcome the limitations of HBP, LBBP has gained significant momentum in the last few years.8–11 Several multicenter observational studies have demonstrated the feasibility and efficacy of LBBP as an alternative to cardiac resynchronization therapy (CRT).12–14 Early observations suggest that confirmation of left bundle branch (LBB) capture is essential to achieve maximal electrical resynchronization in patients with heart failure.14 The left bundle and its branches spread in a fanlike pattern on the left ventricular (LV) septal subendocardium.15 Successful LBBP lead placement and capture of the LBB involve deployment of the lead in the LV subendocardium. During lead implantation, there is a potential risk of perforation into the LV cavity. Recognizing the septal perforation (SP) during implantation is essential to avoid long-term thromboembolic complications and has to be managed immediately by repositioning the lead at a different site. A drop in unipolar impedance to <500 Ω, sudden rise in capture threshold, and
loss of myocardial current of injury (COI) are considered markers of SP. The morphology of intracardiac electrograms and unipolar pacing impedance during SP have not been well studied. The aim of our study was to analyze the morphology of intracardiac electrograms and unipolar impedances to identify SP in patients undergoing LBBP.

Methods
This retrospective, single-center, observational study included consecutive patients who underwent successful LBBP for symptomatic bradyarrhythmia or as an alternative to CRT between January 2020 and November 2021 (Figure 1). Patients in whom definite LBB capture could not be confirmed were excluded. The study was approved by the Institutional Review Board of Velammal Medical College Hospital and Research Institute and adhered to the guidelines of the Helsinki Declaration. All patients provided informed consent after understanding the nonstandard nature of the procedure. LBBP was performed using C315 sheath and 3830 SelectSecure™ lead (Medtronic Inc., Minneapolis, MN) by deploying the lead 1–1.5 cm below the His bundle along an imaginary line connecting the distal His signal to the RV apex. Continuous monitoring of intracardiac electrograms were done using the Workmate Claris (Abbott, Plymouth, MN) electrophysiology system. The pacing lead electrogram was recorded simultaneously by the electrophysiology recording system and pacing system analyzer.

Pacing lead tip was connected in unipolar configuration with high- and low-pass filter settings of 0.5 and 500 Hz, respectively, to obtain unfiltered electrogram (LB-U) for monitoring the COI. Filtered unipolar electrogram (LB-F) was obtained with high- and low-pass filter settings of 30 and 300 Hz, respectively, to record the LB potential. Notch filtering was done at 50 Hz. Capture of the LBB was confirmed by the presence of right bundle branch conduction delay pattern (qR/rSR in lead V1) along with demonstration of LBB potential, abrupt shortening and then short and constant peak LV activation time in lead V6, nonselective to selective/nonselective to septal capture transition, programmed deep septal stimulation, physiology-based electrocardiographic criteria, or V6–V1 interval. SP during lead implantation was identified by unipolar pacing impedance <500 Ω, associated with abrupt increase in capture threshold and loss of COI in the unfiltered electrograms. Once perforation was identified, the lead was gently withdrawn while monitoring unipolar electrograms to demonstrate recovery of myocardial COI, thereby confirming perforation (Figure 2). Bipolar pacing parameters were not used to identify SP. The lead then would be repositioned at a different site to complete the procedure rather than just withdrawing it back, which might predispose to lead dislodgement during follow-up.

Data collection
Baseline characteristics of the study population and indication for pacing were collected. Pacing parameters at the time of implantation and electrocardiographic parameters were documented. If SP was identified, the unfiltered unipolar lead electrogram and the unipolar pacing impedance were recorded. The morphology of the unfiltered unipolar lead electrogram at the site of perforation was analyzed. Pacing parameters after successful repositioning of the lead were recorded. Echocardiography was performed before and after the procedure to assess septal thickness, LV systolic function, valvular regurgitation, and depth of the lead inside the septum. Serum high-sensitivity cardiac troponin I measurement was done at baseline and 12 hours after the procedure. Patients underwent follow-up in the device clinic at 15 days, 1 month, and every 3 months thereafter.

Statistical analysis
Categorical variables are given as frequency (percentage) and compared with the χ² test. Continuous variables are given mean ± SD and were compared with the Student t test. Statistical analysis was performed using SPSS Version 25 (SPSS, Chicago, IL). P < .05 was considered significant.

Results
Baseline characteristics
LBBP was attempted in 219 patients using the C315 sheath and 3830 SelectSecure lead. The pacing lead has an open helix (1.8 mm in length) as the cathode and a radiopaque anode separated by 9 mm. LBBP was successful in 212 patients (96.8% acute procedural success rate). LBB capture could not be confirmed in the remaining 7 patients, who were excluded from the study. SP during lead deployment was identified in 30 patients (14.1%) (Table 1). The indications for pacing were symptomatic sinus node dysfunction (n =
2), atrioventricular block (n = 14), as an alternative to CRT (n = 13), and atrioventricular junction ablation (n = 1). Patients were asymptomatic for SP during implantation. Mean fluoroscopy duration for the procedure was 16.3 ± 4.7 minutes. Mean duration of follow-up was 10 ± 7 months. Mean age of the patients who had SP was similar to those without SP (60.1 ± 11.2 years vs 62.3 ± 11.3 years, respectively; P = .32). There was no difference between patients who had SP compared to those without SP with regard to interventricular septal thickness (10.1 ± 1.6 mm vs 10.5 ± 1.4 mm; P = .15) and LV ejection fraction (44.1% ± 16.2% vs 47.8 ± 15.7%; P = .23).

Unipolar pacing impedance
Mean unipolar pacing impedance during SP was 404.6 ± 19.9 Ω (range 360–440 Ω) (n = 30). Pacing impedance between 400 and 450 Ω was noted in 16 patients (53.3%) and <400 Ω in the remaining 14 patients (46.7%). Mean unipolar pacing impedance of patients without SP was 612.1 ± 113.2 Ω (n = 182). In this group, pacing impedance between 450 and 500 Ω was noted in 18 patients (9.9%), 400–450 Ω in 5 patients (2.7%), and <400 Ω in 1 patient (0.5%). For identification of SP, a cutoff <500 Ω had high sensitivity (100%) but low specificity (86.6%). Similarly, a cutoff <400 Ω had high specificity (99.4%) and low sensitivity (46.6%). A cutoff <450 Ω would be an optimal value as it has sensitivity of 100%, specificity of 96.6%, positive predictive value of 83.3%, and negative predictive value of 100% (Table 2). Serial monitoring of COI during lead deployment showed significant drop in amplitude from 15.4 ± 11.6 mV just before perforation to 0.9 ± 0.6 mV after perforation into the LV cavity. Fifteen patients (50%) had demonstrable capture during perforation, with mean threshold of 3.02 ± 0.7 V (0.5-ms pulse width). R-wave peak time (RWPT) measured in lead V6 was 75.9 ± 17.3 ms (n = 15) during perforation.

All 30 patients underwent successful repositioning of the lead at a new site. Extreme care was taken to avoid entering the same site, which would predispose to subsequent lead dislodgments. We then utilized the following parameters to confirm a new entry site: (1) fluoroscopic landmark; (2) pacing on the right side of the septum to show change in QRS morphology of inferior leads (R/RS/R/S/S pattern) compared to the original site; (3) premature ventricular complexes (template/fixation beats)20,21 during rapid lead deployment; and (4) movement of lead during deployment in the left anterior oblique fluoroscopic view. Absent template/fixation beats during rapid deployment and hypertransmission of rotations to the lead tip inside the septum would favor a same site and thus was avoided. A different paced QRS morphology in the inferior leads would confirm a new site before deployment. Unipolar pacing impedance after successful lead repositioning was 606.8 ± 101.1 Ω, with capture threshold of 0.4 ± 0.1 V at 0.5-ms pulse width (n = 30). RWPT after reimplantation was less than during perforation, although not statistically significant (n = 15; 71 ± 12.4 ms vs 75.9 ± 17.3 ms; P = .38).

Unipolar electrogram during perforation
Based on the morphology, unfiltered unipolar electrograms were classified into 2 different patterns: (1) type I (QS...
pacing impedance was 402.5 Ω. Steep negative deflection would be recorded. Mean unipolar pacing impedance was 411 ± 21.3 Ω. The amplitude of COI dropped from 19.7 ± 10.5 mV before perforation to 1.3 ± 0.9 mV after perforation. Eight of 10 patients (80%) with type II pattern showed capture of myocardium during perforation, with mean capture threshold of 2.8 ± 0.8 V (0.5-ms pulse width). Due to partial contact, both unipolar pacing impedance and amplitude of COI during perforation were greater in the type II (“RS/rS”) pattern group compared to the type I (“QS”) pattern group, although not statistically significant (P = .29 and .15, respectively). Similarly, 80% of patients with type II pattern showed capture during perforation compared to 35% with type I pattern (P = .02). Irrespective of the type of perforation pattern, the lead was removed and reimplanted at a different site with good COI. Peak troponin release was 188 ± 162 pg/mL. There were no incidence of coronary artery injury, septal hema-
toma, or systemic embolism. Postprocedure transthoracic echocardiography showed no evidence of lead perforation or ventricular septal defects. Follow-up echocardiography showed no evidence of residual ventricular septal defect; an increase in LV ejection fraction from 44.1% ± 16.2% to 49.6 ± 14.7%; and a reduction in LV end-diastolic diameter from 54.5 ± 9.8 mm to 51.2 ± 9.2 mm, although not statistically significant (P = .17 and .18, respectively). No patient developed lead dislodgment during mean follow-up of 9.9 ± 6.7 months. Two patients in the group without SP (1.09%; n = 182) during implantation had dislodgment (into RV) requiring repositioning in the LBB area (mean follow-up 10.9 ± 6.7 months).

Discussion

The major findings of our study were as follows. (1) SP with significant drop in COI occurred in 13.9% of patients during LBBP. (2) Two patterns of unfiltered unipolar electrograms (67% QS, 33% RS/rS) due to complete or partial SP were observed. (3) Unipolar pacing impedance <450 Ω predicted SP with sensitivity of 100% and specificity of 96.4%. The procedural technique of LBBP involves deep septal deployment of the lead below the LV subendocardium to capture the left bundle or its branches. The number of rotations required to reach the LBB area varied depending on septal

| Table 1 | Baseline characteristics of patients with septal perforation |
|-----------------|-----------------|--------|--------|
| Total no. of patients | 30 |
| Age (y) | 60.1 ± 11.2 |
| Male/female | 14/16 |
| Septal thickness (mm) | 10.1 ± 1.6 |
| Indication for pacing | Atioventricular block | 14 |
| CRT alternative | 13 |
| Sinus node dysfunction | 2 |
| AV junction ablation | 1 |
| LV ejection fraction (%) | 51.2 ± 9.2 |
| RWPT (ms) | 71.1 ± 11.2 |
| QRS duration (ms) | 152.1 ± 31.6 |
| Post-LBBP | 116.2 ± 11.1 |
| COI amplitude (mV) | 45.1 ± 16.1 |
| Before perforation | 15.4 ± 11.6 |
| During perforation | 0.9 ± 0.6 |
| After repositioning | 606.8 ± 101.01 |
| Sensed R wave (mV) | 0.4 ± 0.1 |
| Peak troponin release (pg/mL) | 188 ± 162 |

Values are given as mean ± SD or n (%) unless otherwise indicated.

AV = atioventricular; COI = current of injury; CRT = cardiac resynchroni-
zation therapy; LBBP = left bundle branch pacing; LV = left ventricle; RWPT = R-wave peak time.

| Table 2 | Unipolar pacing impedance cutoff value for diagnosing septal perforation |
|-----------------|-----------------|--------|--------|
| Impedance cutoff (Ω) | No perforation (n = 182) | Perforation (n = 30) | Sensitivity | Specificity | Positive predictive value | Negative predictive value | Accuracy |
| <500 | 24 (13.2) | 30 (100) | 100 | 86.6 | 55.5 | 100 | 88.5 |
| <450 | 6 (3.3) | 30 (100) | 100 | 96.6 | 83.3 | 100 | 97.13 |
| <400 | 1 (0.5) | 14 (46.6) | 46.6 | 99.4 | 93.3 | 91.7 | 91.8 |

Values are given as n (%) or %.

An optimal cutoff <450 Ω showed high sensitivity and specificity.

pattern); and (2) type II (RS or rS pattern) (Figure 3). Type I pattern was noted in 20 patients (67%) and was characterized by predominantly negative deflection (QS pattern) with or without notches (Figure 4). As the cathode (helix) of the lead would be placed within the LV cavity away from the septal myocardial depolarization wavefront after perforation, steep negative deflection would be recorded. Mean unipolar pacing impedance was 402.5 ± 20.4 Ω. The amplitude of COI dropped from 12.7 ± 9.3 mV before perforation to 0.9 ± 0.6 mV after perforation. Seven of 20 patients (35%) with type I pattern showed capture of myocardium during perforation, with mean capture threshold of 3.3 ± 0.4 V (0.5-ms pulse width)

Type II pattern was noted in 8 patients (33%) and was characterized by an initial positive deflection without notches (RS pattern). We hypothesize that a subtotal perforation with a small part of the cathode in contact with the septal myocardium as the mechanism of the "RS" pattern. With partial contact, the proximal end of the helix would record an initial positive deflection, followed by a negative deflection ("RS") as the wavefront travels across the septal myocardium (Figure 5). Mean unipolar pacing impedance was 411 ± 21.3 Ω. The amplitude of COI dropped from 19.7 ± 10.5 mV before perforation to 1.3 ± 0.9 mV after perforation. Eight of 10 patients (80%) with type II pattern showed capture of myocardium during perforation, with mean capture threshold of 2.8 ± 0.8 V (0.5-ms pulse width). Due to partial contact, both unipolar pacing impedance and amplitude of COI during perforation were greater in the type II ("RS/rS") pattern group compared to the type I ("QS") pattern group, although not statistically significant (P = .29 and .15, respectively). Similarly, 80% of patients with type II pattern showed capture during perforation compared to 35% with type I pattern (P = .02). Irrespective of the type of perforation pattern, the lead was removed and reimplanted at a different site with good COI. Peak troponin release was 188 ± 162 pg/mL. There were no incidence of coronary artery injury, septal hema-
toma, or systemic embolism. Postprocedure transthoracic echocardiography showed no evidence of lead perforation or ventricular septal defects. Follow-up echocardiography showed no evidence of residual ventricular septal defect; an increase in LV ejection fraction from 44.1% ± 16.2% to 49.6 ± 14.7%; and a reduction in LV end-diastolic diameter from 54.5 ± 9.8 mm to 51.2 ± 9.2 mm, although not statistically significant (P = .17 and .18, respectively). No patient developed lead dislodgment during mean follow-up of 9.9 ± 6.7 months. Two patients in the group without SP (1.09%; n = 182) during implantation had dislodgment (into RV) requiring repositioning in the LBB area (mean follow-up 10.9 ± 6.7 months).

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thickness, sheath support, yield of the septal myocardium, and presence or absence of scar. Jastrzebski et al.\textsuperscript{22} showed 4 unique lead behaviors during deployment in a cadaver simulation study: (1) helix-only penetration due to endocardial entanglement effect (43.1%); (2) helix-only penetration due to endocardial barrier effect (19.6%); (3) shallow or moderate penetration with drill effect (9.8%); and (4) progressive penetration resulting in deep septal deployment due to screw-driver effect (27.4%). They also demonstrated LV endocardium to be an effective barrier that protects against penetration despite additional rotations by the cadaver model. The reported incidence of SP during implantation varied between 0.3% and 3.2%.\textsuperscript{11,23} The incidence in our study (14.1%) was higher than the previously reported data. The reasons for this higher incidence can be attributed to concerted efforts to achieve selective LBB capture by sub-endocardial deployment of the lead, narrower interventricular septal thickness (mean 10.1 mm in our study), and likely ethnicity of the study population. In all patients, the lead was safely repositioned at a new site without any complication.

Unipolar electrograms are generated by connecting the lead tip to the negative input of the recording amplifier (Workmate Claris, Abbott) (Figure 6). The positive input of the amplifier is connected to the Wilson central terminal.\textsuperscript{24} The morphology of the unipolar electrograms from the lead tip indicates the direction of the wavefront. A positive deflection will be produced by a wavefront moving toward the recording electrode and a negative deflection as it moves away from the electrode. Depolarization of the tissue beneath the electrode coincides with maximum negative slope ($-\frac{dV}{dt}$) of the signal. During catheter ablation of tachyarrhythmias, unipolar electrograms are used to identify the site of origin, as “QS” complexes typically are recorded at the site of origin.\textsuperscript{25,26} However, QS complexes also can be recorded if the exploring electrode is not in contact with the myocardium, as in our patients with perforation. In these patients,
the initial negative deflection will be slurred due to far-field activation. The potential disadvantage of the unipolar electrogram is the simultaneous recording of far-field signal. Nevertheless, a unipolar electrogram from the lead tip would provide better information than a bipolar electrogram about the SP, as the proximally positioned anode would mask the features of perforation.

Previous studies have suggested unipolar pacing impedance $<500 \, \Omega$ to be a marker of SP. In our study, we showed that a cutoff $<500 \, \Omega$ had low specificity (86.6%), whereas $<400 \, \Omega$ had low sensitivity (46.6%). An optimal value would be $<450 \, \Omega$, which provided 100% sensitivity, 96.4% specificity, 82.3% positive predictive value, and 100% negative predictive value. Significant drop in the amplitude of COI in the unipolar electrogram (from 15.4 ± 11.6 mV to 0.9 ± 0.6 mV in our study) would indicate a possible SP. Hence, monitoring the amplitude of COI might help in identifying perforation during implantation. SP could be complete (helix into the LV cavity) or partial (proximal portion of the helix in contact with the septum). Accordingly, the unipolar electrogram would produce 2 different patterns: type I (QS) indicating complete perforation; and type II (RS) indicating partial helix contact with the septum. Although intracardiac echocardiography was not performed in our study, we hypothesize type II pattern to be a marker of partial contact by (1) demonstration of initial positive deflection due

Figure 5 A: Type II perforation pattern with unfiltered unipolar electrogram (LB-U) showing RS pattern. B: Repositioning the lead at a new site showed good current of injury in the unfiltered electrogram. There was no significant injury pattern change in filtered unipolar electrogram (LB-F) for diagnosing septal perforation.

Figure 6 A: Setup for unfiltered unipolar electrogram in the electrophysiology system. Lead tip is connected to the negative input of the recording amplifier (Abbott). The positive input of the amplifier is connected to the Wilson central terminal. B: Type I pattern due to complete perforation would show QS (with or without notch) due to loss of contact with the myocardium. C: Type II pattern due to partial perforation would show an initial R wave due to wavefront traveling toward the proximal helix.
to wavefront traveling toward the proximal helix (RS pattern); (2) higher unipolar impedance and COI amplitude compared to type I, although not statistically significant; and (3) 80% of patients with type II showed capture during perforation compared to 35% with type II pattern.

LV subendocardium acts as a fibrous and elastic barrier while the lead moves from the right side to left side of the septum. When the protection is breached by excessive rotations, perforation into the LV cavity occurs. Complete penetration of the helix into the cavity can be identified by loss of capture, absent COI, and drop in unipolar pacing impedance. Partial perforation (type II pattern in our study) has to be suspected in patients with "RS/rS" unipolar electrogram pattern with low-amplitude COI. Although associated with myocardial capture during pacing, the capture threshold would be high as demonstrated in 8 of 10 patients with type II pattern. All 30 patients underwent successful repositioning at a new site. Lead entry into the same site during reimplantation could be diagnosed by flourescent landmark, absent template/fixation beats, similar paced QRS morphology and hypertransmission of rotations to the lead tip inside the septum. Presence of COI alone would not confer a new implantation site, as it can be seen reappearing while retracting the lead back into the septum from the LV cavity (Figure 2) after perforation.

The novel findings of our study would help in the diagnosis of SP using unipolar pacing parameters and avoid long-term complications. Although considered one of the concerns of LBBP, SP—when recognized promptly during implantation and treated by reimplantation—would be benign and not associated with unfavorable outcome.

Study limitations
This is the first study to analyze electrogram morphology and pacing impedance in patients with SP. This was a retrospective, single-center study using intracardiac electrograms and pacing parameters to identify SP. Intracardiac echocardiography was not used to demonstrate lead perforation during implantation and can be considered a major limitation of our study. Electroanatomic mapping during native rhythm was not performed to delineate the septal activation wavefront, so the "RS" pattern hypothesis requires further validation by electroanatomic mapping studies.

Conclusion
LBBP involves placement of the lead in the LV subendocardium, and the risk of complete or partial SP must be considered if pacing parameters are suboptimal. Prompt identification using unipolar electrograms and immediate repositioning at a different site will help in avoiding long-term thromboembolic complications.

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