

Complications with Left Bundle Branch Area Pacing: The Flip Side of the Coin

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Left bundle branch area pacing has been a breakthrough in pacing therapy and is being increasingly adopted. It delivers a more physiological form of pacing compared with right ventricular and biventricular pacing and also avoids the risk of perforation of the left ventricular free wall. However, the therapy comes at the price of new complications related to the transseptal route for placing the lead. This article provides an update on these complications and discusses how to avoid and manage these adverse events.

Keywords

Cardiac pacing, complications, conduction system pacing, left bundle branch area pacing, management, perforation

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Conduction system pacing (CSP) is being increasingly adopted as a more physiological alternative to right ventricular and biventricular pacing and is an integral part of the European Heart Rhythm Association (EHRA) core curriculum for the device specialist.^{1–6} Left bundle branch area pacing (LBBAP) has become the dominant form of CSP due to its greater perceived ease of implantation and superior electrical parameters compared with His bundle pacing.^{7,8} The implantation technique of LBBAP has been standardized in a recent EHRA consensus document, where it is recognized that the transseptal route is associated with a number of complications, which are summarized in *Table 1*.^{9–36}

Complications Intraoperative perforation

Septal perforation is the most common acute complication encountered during LBBAP implantation and has been reported in up to 14% of patients.^{9–19} Overt perforation is easy to recognize due to loss of capture and drop in sensing and impedance values, sometimes even with fluoroscopic visualization of the lead moving freely in the left ventricular cavity. Recognizing microperforation is much more problematic, as only part of the screw perforates with the proximal part still being in contact with the myocardium, with preserved thresholds.³⁷ In 95 patients with successful LBBAP implantation, postoperative echocardiography at 1 week revealed partial perforation in 26% of patients, without any differences in sensing and capture amplitudes compared with the group without perforation.³⁷ As many as 42% of patients have tenting of the endocardium on postoperative echocardiography.³⁸

Although the lead design is stiffer and thicker with stylet-driven leads (SDLs) as compared to lumenless leads (LLs), their rates of perforation are similar.^{16,17,39,40} Perforation is related to how much the operator strives to achieve conduction system capture, and whether parameters for diagnosing its occurrence are properly monitored. The myocardial substrate may also play a role, with some patients having a ‘cheesy septum’ with relatively friable tissue. Finally, torque buildup within the guiding catheter may result in continued screwing, even after the operator has released the lead. SDLs with a fully inserted stylet and backup by the guiding catheter applied against the septum may also result in continuous forward pressure, which may result in perforation. It is therefore advisable to withdraw the guiding catheter and the stylet by a few centimetres once the final lead position has been reached, to avoid this complication.

Several intraoperative parameters may indicate lead depth and distance from the left ventricular subendocardium (summarized in *Table 2*). Probably the most useful parameter for identifying impending perforation is the unipolar sensed myocardial current of injury (COI) amplitude, with amplitudes of <5 mV being associated with perforation.^{19,34,35,41,42} The best evidence for this cutoff comes from a report where LBBAP perforations were monitored by intracardiac echocardiography in a swine model, with continuous measurement of electrogram and lead parameters.³⁵ Interestingly, a drop in the COI amplitude was not visible on the pacing system analyser with microperforation (only when the screw had perforated entirely). Furthermore, a QS, RS or rS morphology of the ventricular electrogram is visualized.^{15,34–37} Of note, a fall in the COI over 10 minutes following lead deployment can be considered to be normal.¹⁹ There are less

Table 1: Complications with left bundle branch area pacing^{9–36}

Intraoperative complications
Septal perforation (0.0–14.1%) ^{9–19}
Right bundle branch block (19.9% with 6.3% permanent) ⁹
Complete heart block (9.4% acute with 2.6% permanent) ⁹
Intraoperative lead dislodgment (3.0%) ¹²
Acute coronary syndrome (0.4–0.7%) ^{16,20}
Coronary artery fistula (1.4–2.0%) ^{13,17}
Coronary vein fistula/injury ^{18,21}
Septal haematoma ²²
Helix damage/fracture (0.8–5.0%) ^{17,23,24}
Postoperative complications
Delayed septal perforation (0.1–0.3%) ^{16,17,25,26}
Worsening tricuspid regurgitation (7.3–32.6%) ^{9,12,27,28}
Lead macro-dislodgment (0.3–4.3%) ^{9,10,14,16,18,25,29–31,10,11,15,17,19,33–36}
Rise in threshold by >1V (0.3–1.8%) ^{9,10,16,18,29}
Lead micro-dislodgement with loss of LBBP or LVSP (0.3–13.5%) ^{9,16,18,31–33}

LBBP = left bundle branch pacing; LVSP = left ventricular septal pacing.

data on how the COI of *paced* QRS complexes correlates with lead depth and perforation. It should be borne in mind that amplitudes of paced and sensed COI may differ.⁴³ As it is useful to deploy the LBBAP lead during continuous pacing to monitor QRS morphology, periodic interruption of pacing is useful to check the sensed COI as soon as the paced COI falls to approximately 10 mV. Furthermore, high-pass filter settings also impact COI amplitude (the higher the value, the lower the COI amplitude). A setting of 0.5 Hz is advised as it has been validated in clinical studies (the low-pass filter does not impact COI amplitude and can be set to 300 or 500 Hz).^{15,34,35} Another reason to intermittently interrupt pacing is to check for the presence of a fascicular potential. If visualized, further rotations should be performed with extreme caution and should not be done in case of COI of the fascicular potential.^{34,44} Another sign is tip<ring COI amplitude, but the positive predictive value for perforation is only about 60%, so it should not be used alone.¹⁹

Unipolar pacing impedance has also been used to monitor lead depth, as impedances typically rise and then fall when approaching the left ventricular subendocardium, with impedances of <450 Ω or falls by >20% being associated with perforation.¹⁵ However, it should be borne in mind that pacing impedance depends on lead model, length, laboratory setup, etc., and can be highly variable.

Septal perforation may also be confirmed by contrast injection from the guiding catheter into the left ventricular cavity, but caution must be

Table 2: Features indicating possible intraoperative microperforation

- Sensed COI <5 mV - Sensed COI of QS or rS morphology - High or rise in capture threshold - Loss of fascicular potential in sensed EGM (if previously present) - Impedance <450 Ω with LLL leads and <400 Ω with SDLs, or fall by >20% (but impedance may vary with other factors)

COI = current of injury; EGM = electrogram; LLLs = lumenless leads; SDLs = stylet-driven leads.

paid as thrombotic material from nonperfused sheaths may end in the systemic circulation.⁴⁵

Acute perforation is asymptomatic, and if recognized promptly and the lead is repositioned, there are no further consequences.^{16,17,25} While microperforation has not been shown to be related to thromboembolic complications, it is advisable to recognize it during implantation and reposition the lead due to the risk of dislodgement and possibly to delayed perforation to the left endocardial cavity.³⁷ On the other hand, if microperforation is suspected on postoperative cardiac imaging, but electrical parameters are satisfactory, reoperation is not needed.

Postoperative (delayed) perforation

Delayed septal perforation is rare, with an incidence of 0.1–0.3%, and is usually diagnosed within a month of implantation.^{9,16,17,25} Case reports have described late perforations being complicated by left ventricular thrombus formation and ventricular arrhythmias.^{46–48} A study investigated the stability of LBBAP leads with computed tomography performed within 2 days of implantation and after 6 months in 67 patients with a cardiac resynchronization therapy indication, who had proof of conduction system capture at implantation.⁴⁹ In 16 (24%) patients, the helix tip was noted to cross the left ventricular subendocardium by >2 mm into the blood pool on postimplantation imaging. Of these patients, nine continued to have a protrusion of >2 mm at 6 months (the lead had retracted to within the septum or to <2 mm in seven patients), whereas another seven patients had migration of the lead to >2 mm into the blood pool. None of the patients had an increase in capture thresholds of >1V or thromboembolic events. Overall, 27% of the patients had displacement (either retraction or migration into the blood pool) by >2 mm from the implantation site, but 94% had consistent LBB capture at 6-month follow-up.

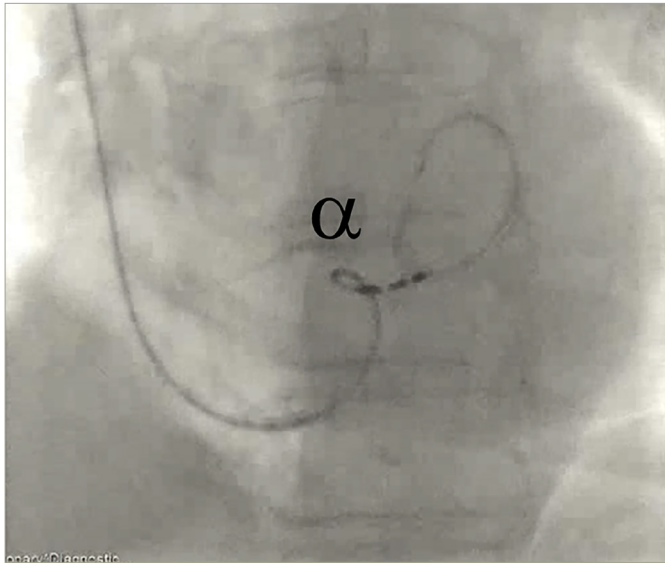
Although not proven, a likely mechanism of delayed perforation is unnoticed microperforation of the helix at implantation. Forward forces resulting from myocardial contraction cycles may result in progression of the lead within the septum.³⁶ A septal ‘endocardial barrier’ effect due to stiff tissue may be a protective factor against further advancement in some patients.^{50,51}

All cases of overt late perforation should be managed with lead repositioning, and if delayed, oral anticoagulation should be initiated to prevent thromboembolism.

Lead dislodgement

Lead dislodgment is a dreaded complication with LBBAP, as it is potentially lethal in pacemaker-dependent patients and also due to the risk of infection associated with revision. One needs to distinguish macro-dislodgment, where there may be complete loss of myocardial capture or a radical change in paced QRS morphology, from micro-dislodgment, where only conduction system capture or left ventricular septal pacing is lost while myocardial capture is usually preserved, usually resulting in only deep septal pacing.

The incidence of lead dislodgment in cardiac implantable electronic devices (CIEDs) is reported to be between 1.2 and 3.3% of implantations, with a higher incidence of atrial leads.⁵² Macro-dislodgment of LBBAP leads has been reported in 0.3–4.3% of patients and usually occurs within hours or days of implantation.^{9,10,14,16,18,25,29–31} Micro-dislodgment is more difficult to diagnose and is probably underreported in most reports as a careful analysis of a 12-lead electrocardiogram is required. The incidence

Figure 1: Stability testing using the 'α-loop' technique

The lead stylet has been withdrawn to the level of the right atrium, and the guiding catheter is pushed forward to render extra slack before resuming the original position and retesting the lead.

is reported to be 0.3–13.5%, and it is usually diagnosed within weeks to months.^{9,16,18,31–33}

There are several factors that can contribute to lead dislodgment in LBBAP. A major factor is the undesirable 'drill' effect, where the lead shows little progress in the septum despite insistent rotations, resulting in mincing of myocardial tissue with poor anchoring by the screw.⁵³ Jastrzębski et al. showed in cadaver hearts that a drill effect was present in 9.8% of attempts.⁵¹ Lead stability should be tested by withdrawing the guiding catheter to the right atrium and checking paced QRS morphology, persistence of a fascicular potential (if present initially) and a lack of rise in the COI amplitude. Further testing may be performed by forming an 'α-loop' (Figure 1) or by gently pulling on the lead and feeling some resistance.

Other causes of lead dislodgment are perforation, inadequate slack, or backspin caused by the release of tension of preconditioned SDLs. It is therefore important to avoid excessive pin rotations when preconditioning, and to release the tension maintained by the locking tool before testing the lead.

Figure 2: Result of lead entanglement of a stylet-driven lead (top), with screw damage and tissue tearing, and of a lumenless lead (below), with stretching of the screw

Postoperative macro-dislodgment with loss of capture almost always requires repositioning, whereas with micro-dislodgment, if the electrical parameters are acceptable, repositioning depends on the clinical context and the need to achieve conduction system capture.

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Lead damage

Lead deployment for LBBAP inflicts greater mechanical stress at implantation than for standard right ventricular positions, due to forceful rotations of the lead body with torque buildup, kinking at hinge points and entanglement of the screw in fibrous tissue.

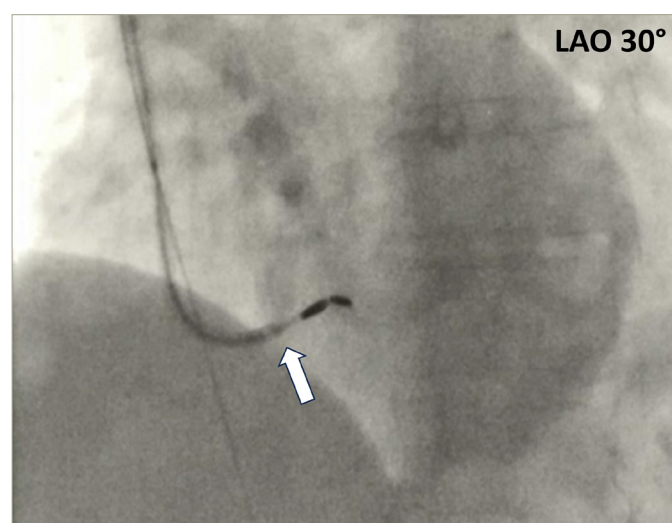
Helix damage occurs in 0.8–5% of LBBAP implantations.^{17,23,24} A study even reported an incidence of 25% with SDLs, but this occurred at the beginning of the operators' learning curve with these leads and before the entanglement effect had been recognized.²⁴ Examples of helix damage after entanglement are shown in Figure 2. It is crucial to recognize entanglement by excessive torque buildup and reposition the lead elsewhere before the lead becomes trapped in the subendocardial tissue and requires forceful traction to be released. Unipolar electrocautery (40 W for 3 s) may be applied to the lead pin, which can facilitate retrieval of the lead, which should then be replaced.⁵⁴

A recent study evaluated LBBAP lead integrity in 8,255 patients across 17 centres worldwide (68% LLLs and 32% SDLs). A higher fracture rate was observed in SDLs (0.4%) compared with LLLs (0.04%) with a median follow-up duration of 19.5 and 10.3 months, respectively. The fractures in SDLs were exclusively observed with Solia S (Biotronik, Berlin, Germany), which, however, comprised 86% of the SDLs of the study (and were thus overrepresented). The fractures were primarily located in the distal interelectrode segment between the tip and ring electrode of the Solia lead, while the few LLL fractures occurred just proximal to the ring electrode.⁵⁵ Özpak et al. showed that excessive angulation between the interelectrode spacing and excessive preconditioning were associated with a higher risk of lead fracture.⁵⁶ It is therefore important to avoid excessive pretensioning of the lead, to fully insert the stylet and to immediately stop lead rotations if kinking of the lead tip is observed during lead deployment (Figure 3). Coverage by the delivery sheath up to the septal entry site can provide protection against kinking. Continuous screening in the left anterior oblique view during lead deployment is essential to monitor coaxial lead deployment and avoid kinking.

Myocardial injury

Myocardial injury following LBBAP occurs in as many as 49% of patients when defined as a >3× increase in troponin levels above the upper reference limit (URL) at 6–12 hours, but is less than or comparable to that seen with other electrophysiology procedures (right ventricular pacing, radiofrequency ablation of atrial fibrillation or supraventricular tachycardia).⁵⁷ It occurs in up to 55% of patients when defined as an increase in high-sensitivity troponin T to >99% percentile of the URL, with 20% exhibiting elevations by >4× the URL, with the highest levels at 12 hours of implantation.⁵⁸ Multiple (>2) lead reposition attempts, the use of septography and SDLs were independent predictors of higher risk of this latter category.^{57,58} However, although there were more admissions for acute coronary

Figure 3: Kinking of a Solia (Biotronik) lead between the distal and proximal electrodes during deployment



Lead rotations were immediately stopped, the stylet was fully inserted and the catheter tip (white arrow) was advanced to cover and stabilize the lead tip.

syndrome in these patients, no significant associations were found with mortality or heart failure hospitalizations, suggesting that the beneficial effect of LBBAP may counterbalance the potential detrimental impact of myocardial injury.⁵⁸

The pathophysiological mechanisms remain uncertain but may involve direct myocardial trauma due to lead fixation, coronary microvascular dysfunction and vasospasm.

Septal haematoma and vascular complications

While LBBAP is generally considered a safe procedure, several potential vascular complications have been reported, such as interventricular septal haematoma, coronary artery spasm, injury and fistula and venous perforation.³⁴

Interventricular septal haematoma is a rare but significant complication following LBBAP, the incidence of which is not well established.⁵⁹ The likely mechanism involves injury to a septal perforating arterial branch. Patients with septal haematoma can present with chest pain, dyspnea, signs of heart failure or even hemodynamic collapse with 'dry tamponade' (due to reduced ventricular filling), which may require mechanical circulatory support.⁶⁰ Cardiac biomarkers levels are significantly higher than those expected following routine LBBAP, suggesting extensive myocardial injury. Echocardiography typically reveals a hypoechogenic mass within the thickened interventricular septum, sometimes with pericardial effusion. The management of interventricular septal haematoma depends on the severity of the condition. In hemodynamically stable patients, a conservative approach with symptomatic management, close echocardiographic monitoring and withholding anticoagulation and antiplatelet therapy may be sufficient.⁶¹ Coil embolization of the septal perforator artery has been performed to stop active bleeding.^{22,60}

Several considerations may help prevent interventricular septal haematoma during LBBAP. First, excessive anticoagulation should be avoided. Second, an anterior position may bring the lead closer to critical septal coronary branches. Third, minimizing the number of lead placement attempts or early repositioning in case of a

'drill' effect while the lead is still relatively superficial may reduce mechanical trauma and risk of septal injury. Postprocedural routine echocardiography should be performed in patients with suggestive symptoms to ensure early detection and appropriate management.

Case reports of coronary artery fistula have been reported, with multiple lead placement attempts being performed in all cases.^{62,63} Direct trauma to the septal branches of the left anterior descending artery during lead fixation can potentially disrupt the integrity of small perforator arteries, creating an abnormal communication between the coronary circulation and the ventricle. Cases were usually asymptomatic and detected incidentally on imaging, without any requirement for specific measures.

Extrinsic compression of the left anterior descending artery has been described in a case report with a highly anterior lead.⁶² Furthermore, aborted ST-elevation myocardial infarction attributed to coronary artery spasm of the left anterior descending artery induced by proximity of the LBAP lead to a septal perforator (which resolved upon repositioning of the lead) has also been reported.²⁰

Septal venous perforation may also be encountered, with visualization of the coronary sinus when injecting contrast through the guiding catheter.^{21,64} A study showed that septal venous perforation occurred in as many as 13.1% of patients undergoing LBBAP, with an increased prevalence in superior/anterior lead positions.⁴⁵ The phenomenon usually does not have any clinical impact.

Conduction system injury

Transient right bundle branch block occurs in approximately 20% of patients, but it may be rarely permanent.⁹ Transient complete heart block may occur in 9% of patients.⁹ In patients with left bundle branch block, placement of an atrial lead in the right ventricle for temporary backup pacing may be advised. To the best of our knowledge, injury to the left-sided conduction system has not yet been reported.

Tricuspid valve dysfunction

Tricuspid regurgitation (TR) is a recognized complication following pacemaker implantation, with both mechanical interference with the valve leaflets and/or subvalvular apparatus and pacing-induced dyssynchrony contributing to its progression. Severe TR is associated with worsened heart failure outcomes and reduced survival.⁶⁵

Worsening TR with LBBAP has been reported to affect 7–33% of patients^{9,12,27,28} and is comparable to that reported for right ventricular pacing.⁶⁵ More basal LBBAP implantation has been associated with worsening of TR, with a lead-annulus distance of <16–24 mm being an independent predictor of TR deterioration.^{27,28,66} A case report described the successful implantation of an LBBAP lead in a patient who had undergone tricuspid edge-to-edge repair, underscoring the feasibility of LBBAP even in complex clinical scenarios.⁶⁷

Conclusions

As with any invasive therapy, LBBAP is associated with a number of complications, some of which are avoidable and others which may occur unexpectedly. Evolution in hardware, such as leads designed specifically for LBBAP, may mitigate these complications. Nevertheless, proper technique and appropriate clinical judgment will always be necessary ingredients to enable patients to derive the greatest benefit from therapy, at the lowest risk. □

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