Long-term Safety and Feasibility of Left Bundle Branch Pacing in A Large Single Center Study

Running title: Su & Wang et al.; Feasibility and Safety of LBBP

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Abstract:

Background: Left bundle branch pacing (LBBP) is a novel pacing method and has been observed to have low and stable pacing thresholds in prior small short-term studies. The objective of this study was to evaluate the feasibility and safety of LBBP in a large consecutive diverse group of patients with long-term follow up.

Methods: This study prospectively enrolled 632 consecutive pacemaker patients with attempted LBBP from April 2017 to July 2019. Pacing parameters, complications, ECG, and echocardiographic measurements were assessed at implant, and during follow-up of 1, 6, 12 and 24 months.

Results: LBBP was successful in 618/632 (97.8%) patients according to strict criteria for LBB capture. Mean follow-up time was 18.6±6.7 months. 231 patients had follow-up over 2 years. LBB capture threshold at implant was 0.65±0.27 mV@0.5ms and 0.69±0.24 mV@0.5ms at 2-year follow-up. A significant decrease in QRS duration was observed in patients with LBBB (167.22 ± 18.99ms vs. 124.02 ± 24.15ms, p<0.001). Post implantation left ventricular ejection fraction improved in patients with QRS≥120ms (48.82±17.78 % vs. 58.12±13.04 %, p<0.001). The number of patients with moderate and severe tricuspid regurgitation decreased at 1-year. Permanent right bundle branch injury occurred in 55 (8.9%) patients. LBB capture threshold increased to more than 3 V or loss of bundle capture in 6 patients (1%), 2 patients of them had loss of conduction system capture. Two patients required lead revision due to dislodgement.

Conclusions: This large observational study suggests that LBBP is feasible with high success rates and low complication rates during long term follow up. Therefore, LBBP appears to be a reliable method for physiological pacing for patients with either a bradycardia or heart failure pacing indication.

Key words: pacing; left bundle branch block; sick sinus syndrome; atrioventricular block; feasibility; left bundle branch pacing; left bundle branch block; sick sinus syndrome; atrioventricular block; physiological pacing
Nonstandard Abbreviations and Acronyms

HBP        His bundle pacing
LBBB       Left bundle branch block
LBBP       Left bundle branch pacing
LBB        Left bundle branch
CRT        Cardiac resynchronization therapy
Sti-LVAT    Stimulus to left ventricular activation time
LVEF       Left ventricular ejection fraction
LVEDd      Left ventricular end-diastolic dimension
TR         Tricuspid regurgitation
AVB        Atrioventricular block
AF         Atrial fibrillation
AVN        Atrioventricular node
SSS        Sick sinus syndrome
RBB        Right bundle branch
RBBB       Right bundle branch block
LBBBAP     Left bundle branch area pacing
COI        Current of injury

Introduction

His bundle pacing (HBP) delivers physiological ventricular activation which results in interventricular and intraventricular electrical synchrony.\(^1,2\) Data from observational studies suggests that HBP results in symptomatic benefit to patients who require ventricular pacing.\(^3-5\) HBP can also be used to correct left bundle branch block (LBBB) and may deliver more effective ventricular resynchronization than biventricular pacing.\(^1,6,7\) However, HBP has some limitations. Conduction system capture can be challenging with His pacing in patients with infra-Hisian block.\(^8\) In some patients with LBBB a more distal conduction system pacing target is required.\(^9\) Late increases in capture thresholds continue to be a problem with current His pacing.
techniques with lead re-intervention rates of 2.7%-7.5% reported.\textsuperscript{10-12} Reports of high pacing thresholds and low R wave amplitudes as well as the long learning curve for HBP has limited the widespread adoption of this technique.

Left bundle branch pacing (LBBP) has emerged as an alternative to HBP. Huang et al.\textsuperscript{13} described the first case of successful cardiac resynchronization with LBBP. Data from subsequent case reports and small observational studies suggest that LBBP is a promising method for delivering physiological pacing.\textsuperscript{14-16} However, these observations have been limited by relatively short follow up, lack of prospective recruitment and in many cases LBB capture was not well defined and thus some patients may not have had capture of the conduction system.

The aim of the present study is to evaluate the feasibility and safety of LBBP in patients with a bradycardia or CRT indication for pacing, in a large consecutive patient population with long-term follow up and strict criteria for defining left conduction system capture.

\textbf{Methods}

The study was a single-center, prospective registry of patients with indications for pacemaker implantation in whom LBBP was attempted. The approval of the Ethics Committee of the first affiliated hospital of Wenzhou Medical University was obtained before patient enrollment, and informed consent was obtained from all recruited patients. The trial was conducted in accordance with the principles of the Declaration of Helsinki. The data from our study is available from the corresponding author upon request.
Study Patients

This study enrolled 632 consecutive patients with an indication for treatment of bradycardia or cardiac resynchronization therapy. We included all patients in whom LBBP was attempted between April 2017 to July 2019 at the first affiliated hospital of Wenzhou Medical University. Thirty patients received LBBP before April 2017 were considered part of the learning curve and were therefore not included in the study.

Implantation Procedure

The procedural steps and tips for delivering LBBP have recently been reported by our group. The Select Secure (model 3830, 69cm, Medtronic Inc, Minneapolis, MN) pacing lead was introduced through a fixed curve sheath (C315 HIS, Medtronic Inc). We have previously defined criteria for successful capture of the left conduction system.

Data Collection

Baseline patient characteristics, indications for pacing, and procedural details are all summarized in Table 1. Fluoroscopy times for LBBP lead placement and procedure duration was recorded. Pacing thresholds, R wave amplitudes and impedance was measured. Patients underwent regular follow-up at 1, 3, and 6 months and then annually post implantation. At the follow-up visit, bipolar R-wave amplitude, unipolar LBB capture threshold and unipolar pacing impedance were collected. Electrocardiographic and echocardiographic parameters were also collected, including QRS duration, Sti-LVAT, the presence of selective and nonselective left bundle capture, QRS axis, QRS transition zone, left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDd) and degree of tricuspid regurgitation (TR, mild TR as first degree, moderate...
TR as second degree and severe TR as third degree). NYHA functional class was documented. Complications such as significant increases in pacing threshold, RBB injury, loss of capture, and lead dislodgement were tracked during follow-up visits.

**Statistical Analyses**

Continuous variables were expressed as mean ± standard deviation (SD) or median (1st quartile, 3rd quartile). Independent two sample t-tests were performed to compare the differences between the two groups, and paired t-test were used to compare the differences between two-time points within the same group during follow-up if they were normally distributed. Analysis of covariance was used to compare the data (echocardiography, pacing threshold, sensed R-wave amplitude) that were collected at baseline and subsequent follow up time points. The categorical data were described as numbers (%) and chi-square test or Fisher’s exact test were used to examine the above-mentioned differences. The data analyses were performed using SPSS version 23.0 (SPSS, Chicago, IL, USA). All tests were 2-sides and P ≤0.05 was set as the level of statistical significance.

**Results**

**Baseline characteristics**

A total of 632 patients were enrolled into the study. In 618 (97.8%) patients LBBP was successfully achieved with a mean follow-up of 18.6±6.7 months. In fourteen patients LBBP pacing was unsuccessful due to either septal scarring or hypertrophy. The indication for pacing was CRT in patients with LBBB in 88 (14.2%), AVB or AF requiring AV node ablation in
371 (60.0%) and sick sinus syndrome (SSS) in 159 (25.7%) of patients. Baseline characteristics are summarized in Table 1.

**Electrophysiological characteristics**

The final unipolar paced QRS duration was 112.94±16.81ms, compared to 114.20±32.40ms at baseline (p=0.305). A significant decrease in QRS duration was observed in patients with LBBB (167.22 ± 18.99ms vs. 124.02 ± 24.15ms, p<0.001). In patients with AVB or AF with AVN ablation, the QRS duration increased slightly (108.41±26.69ms vs. 111.35±14.41ms, p=0.030). The QRS duration also increased in patients with SSS (98.75±19.13ms vs. 110.59±14.83ms, p<0.001). (Table 2)

The Sti-LVAT remained stable at low and high output when LBB was captured. In patients with LBBB, the mean Sti-LVAT was 79.40±11.34ms. In patients with AVB or AF with AVN ablation and patients with SSS the Sti-LVAT was 73.78±11.89ms and 71.04±8.80ms respectively.

Pre-implant mean QRS axis of all patients was 20.50° (1st quartile, -16.00°; 3rd quartile, 56.00°) and remained stable after LBBP 20.00° (1st quartile, -17.00°; 3rd quartile, 54.00°). However, in patients with LBBB who had left axis deviation, the mean QRS axis was corrected by LBBP. In patients with normal QRS duration, the mean QRS axis remained stable at baseline and during follow-up. Meanwhile, the QRS transition zone from pre to post-LBBP showed counterclockwise rotation. (Figure 1)

A LBB potential was recorded during the procedure in 476 (77.0%) of patients with successful LBBP. In the LBBB group, LBB potentials were recorded during restoration of left
bundle conduction by HBP in 37 (42.0%) patients undergoing a dual lead approach and during RBBB morphology escape rhythm from the LBB fascicles in 11 (12.5%) patients. Four hundred and sixty-six (75.4%) patients were observed to have selective left bundle capture during procedure, while only 191 (30.9%) has selective capture during follow-up. Electrophysiological parameters for all the patients are shown in Table 2.

**Pacing parameters**

Unipolar LBB capture thresholds remained stable during follow up. The mean thresholds at implant (n=618), 1-month (n=608), 6-months (n=580), 1-year (n=560) and 2-years (n=231) were 0.65±0.27V@0.5ms, 0.65±0.16V@0.5ms, 0.65±0.20V@0.5ms, 0.68±0.23V@0.5ms and 0.69±0.24V@0.5ms (Figure 2). The sensed R wave amplitude increased slightly at 1-month post implantation and remained stable during 2-years of follow up (11.45±5.52 mV vs. 13.78±5.28 mV vs. 14.66±65.35 mV vs. 13.93±5.50 mV vs. 13.98±6.00 mV/0.5ms). Unipolar pacing impedance decreased rapidly over the first month post implantation and thereafter remained stable during follow up (606.73±133.21Ω vs. 386.15±49.30Ω vs. 367.01±45.54Ω vs. 362.16±45.14Ω vs. 366.78±48.56Ω). Stability in LBB capture, sensed R wave and impedance were stable regardless of pacing indication. (Figure 2).

**Echocardiographic parameters**

Changes in TR are shown in Figure 2. At 1-year follow-up (n=560), TR developed or worsened by at least 1 grade in 62 (11.1%) patients and by 2 grades in 7 (1.3%) patients. We did not observe echocardiographic evidence of mechanical perforation or damage to valve leaflets. In 248 (44.3%) patients there was no change in tricuspid valve function and in 176 (31.4%) patients
the degree of TR improved following implantation. We observed an improvement in LVEF (57.08±16.60% vs. 62.36±12.20%, p<0.001) and decrease of LVEDd (52.27±7.51mm vs. 50.73±6.71mm, p<0.001) after 1-year follow up (n=560). (Figure 2)

Complications

No serious complications including procedure-related death, cardiac arrest, septal hematoma, coronary artery injury or LV thrombosis occurred. Other pacing complications such as increasing LBB thresholds, loss of conduction system capture, lead dislodgement and RBB injury are summarized in Table 3 and Table 4.

Complete loss of pacing capture

In 2 patient there was complete loss of pacing capture due to lead dislodgement to the right ventricle the day after implantation.

Loss of conduction system capture

In 2 patients there was loss of LBB capture, but maintained RV septal capture, this was likely to have occurred due to dislodgement of the lead to the right ventricular septum, the paced QRS demonstrated a QS pattern in lead V1 with a mean QRS duration >120ms.

Increase in LBB pacing capture threshold

In 11 patients LBB capture threshold increased by more than 1V@0.5ms during follow up (Supplement Table 1), but left bundle capture could be achieved at higher output. In six patients the LBB capture threshold was>3V/0.5ms, but local LV septal capture was achieved at a lower output (1.00±0.16V@0.5ms). In these patients LV septal capture resulted in mild prolongation in
Sti-LVAT and QRS duration compared to direct left bundle capture, (Sti-LVAT 78.00±7.77ms vs. 92.00±6.72ms, p<0.001, QRS duration 104.83±7.86ms vs. 123.00±10.10ms, p=0.001).

One hundred eighty-one patients (29.3%) developed RBB injury during the procedure. In thirty-nine of these patients RBBB pattern persisted during follow-up. Forty-two patients (6.7%) had transient complete AV block during the implant procedure, 26 had baseline LBBB. A total of 16 patients developed permanent complete AV block during follow-up, 12 of these patients had LBBB. (Table 4)

13 patients died during follow up, the causes of death are the listed in Supplement Table 2.

Discussion
We present the findings from the largest prospective study of LBBP to date. We report the feasibility and long-term safety of this new pacing technique in a diverse population of patients which included both bradycardia and cardiac resynchronization indications for pacing. The main findings of our study are: (1) LBBP was feasible in 97.8% of patients; (2) LBBP maintained physiological left ventricular activation in patients with a narrow QRS and was able to normalize activation in LBBB patients. (3) LBBP demonstrated low and stable pacing thresholds; (4) Complication rates were low during long term follow up.

Success rate of permanent left bundle branch pacing
Left bundle branch area pacing (LBBAP), where the pacing lead is positioned at LBB area, includes LBBP (pacing the left bundle trunk or its proximal fascicles usually with local
myocardial capture) and LVSP (deep septal pacing without LBB capture). Encouragingly we observed a high implant success rate in this study (97.8%), despite using very strict criteria for LBB capture, which is comparable to our previous studies. However, this compares favorably with reports from previous studies without strict criteria for LBB capture, where the acute success rates was reported to be between 90.9% to 93% and these studies may include patients with LBBAP. The reason for our high implant success rate may be related to our implant technique which included mapping the His bundle location which can be used as a reference prior to deploying the left bundle pacing lead. In addition, recruitment in the study began after 30 LBBP implantation procedures were performed, therefore our study excluded our learning curve.

**Ventricular activation during LBBP**

The aim of conduction system pacing is to deliver normal physiological ventricular activation during pacing. Our findings suggest that the technique of LBBP is able to reliably achieve this objective.

**Bradycardia indication for pacing**

In patients with a bradycardia indication for pacing the objective of physiological pacing is to allow ventricular pacing while maintaining normal ventricular activation. We found that LBBP resulted in only a very modest increase in QRS duration (delta 2 ms). The mean QRS duration during LBBP in patients with AVB indication for pacing was 111.35±14.41 ms suggesting rapid ventricular activation.

Left bundle pacing does not deliver entirely normal physiological ventricular activation since the conduction system is stimulated distal to the His bundle. This approach allows left
ventricular activation to occur via the conduction system but does mean that left ventricular activation precedes right ventricular activation, which is reflected in the 12 lead ECG since the precordial lead QRS transition zone usually moves to lead V1 or V2. The mild increase in QRS duration occurs because of delayed right ventricular activation, especially in patients with LBBB and/or RBBB. Whether the non-physiological right ventricular activation has important clinical consequences requires further study. It is however, reassuring that we observed that LBBP delivered to patients with a normal QRS duration maintained a normal QRS axis (Figure 1), suggesting that the left ventricular activation pattern is preserved. We also did not observe a decline in ventricular function during follow up, which suggests that preserving physiological left ventricular activation is sufficient to avoid right ventricular pacing induced cardiomyopathy.

Whether a normal QRS axis can be maintained with LBBP is determined by the pacing site. Most LBBP case reports showed left axis deviation because the pacing site is located in the left posterior branch area, which is more easily located using the current pre-shaped sheath. Our approach differs to these case reports since we deliberately target the more proximal left bundle, which means that more of the left ventricle is activated via the conduction system and therefore a normal QRS axis is maintained. (Supplement Figure 1)

Cardiac resynchronization therapy

In patients with LBBB during intrinsic conduction we observed a significant reduction in QRS duration during LBBP compared to intrinsic conduction. The mean reduction in QRS duration was 43 ms, which suggests that this approach results in cardiac resynchronization. The magnitude of cardiac resynchronization compares favorably with the QRS reduction achieved
with biventricular pacing (mean 26 ms reduction).\textsuperscript{25,26} We observed significant improvements in LVEF and LVEDd patients with baseline QRS≥120ms, which suggests that this more rapid ventricular activation translates into improved left ventricular function and reverse ventricular remodeling.

The mechanism for QRS reduction is likely to be that by pacing distal to the site of LBBB we were able to correct LBBB and restore normal physiological left ventricular activation. This conclusion is supported by our finding that left axis deviation was corrected with LBBP in patients with underlying LBBB. (Supplement Figure 2)

**Stimulus to left ventricular activation time**

Sti-LVAT is often used to reflect the lateral precordial myocardium depolarization time. LBBP resulted in synchronization of left ventricular, so it brings short and constant Sti-LVAT. Meanwhile, compared to patients with non-LBBB, patients with LBBB had prolonged Sti-LVAT. Stim-LVAT that shortens abruptly with increasing output or remains short and constant both at low and high outputs suggests LBB capture. 533 (86.2\%) of patients recorded abrupt change of Sti-LVAT in our present study. However, the abrupt change of Sti-LVAT can be recorded in almost all patients by early and multiple tests at the same site and continuous pacing with low and high output.

**Selective Vs non-selective capture**

Four hundred and sixty patients showed selective LBBP at implant, 191 of the patients showed selective LBB capture during follow-up. The reason for QRS reduction in patients with selective capture is likely to be the septal myocardial capture threshold decreased in the acute post implant
period, so it became lower than the threshold for left bundle capture. Left bundle capture threshold remained stable which supports our conclusion that this reduction was due to a decrease in local myocardial capture threshold.

**Advantages of LBBP compared to HBP**

Several studies have found that HBP is able to deliver effective ventricular resynchronization by correcting LBBB. HBP also allows normal physiological ventricular activation to be preserved in patients with a bradycardia indication for pacing. While HBP can deliver physiological activation of both ventricles, it is limited by increases in pacing thresholds over time. Our findings suggest that left bundle pacing is a very promising alternative to HBP as a method for delivering physiological pacing. It appears to overcome the limitations of high capture threshold with HBP, as we found low and stable capture thresholds over long term follow-up with LBBP. The LBB fans out to form a wide target for pacing below the membranous septum and there is less fibrous tissue surrounding the left bundle and its branches compared to the His bundle which is a narrow target surrounded by a fibrotic sheath. A further advantage of LBBP is that the lead is in close proximity to the ventricular septal myocardium providing back-up septal pacing in case of loss of LBB capture if more distal conduction system disease develops. The influence of RBB delay caused by LBBP on cardiac function and arrhythmia during follow-up requires further investigation.

**Right bundle branch injury**

We observed transient RBB injury in 20.4 % of patients and in 8.9% of patients this persisted during long term follow up. The right bundle may be injured during mapping of the distal His
bundle since there is no clear anatomic demarcation between the distal His and RBB on the right septum. Usually, the RBB is relatively thin at the anatomic bifurcation of the distal His bundle as it crosses the tricuspid valve even at the proximal site of atrioventricular junction region, so it is easy to damage the RBB when mapping near the distal His bundle. Right bundle injury occurring during mapping is usually transient. However, in patients with LBBB, temporary backup pacing is recommended prior to mapping.

To avoid RBBB during deployment of the left bundle pacing lead, we recommend avoiding placing the lead at sites where there is a right bundle potential and at sites where the lead has caused transient injury to the RBB during mapping.

Tricuspid regurgitation

With left bundle pacing there is the potential risk of causing or worsening TR\textsuperscript{15,31} since the lead crosses the tricuspid septal valve leaflet and is fixed into the septum near the valve annulus. We found that TR was caused or worsened by left bundle lead implantation in 11.1% of patients. In the majority of these patients this was a change in one grade of TR severity. However, unexpectedly we observed a decrease in TR severity in 31.4% of patients after LBBP lead implantation. The possible mechanisms for this improvement are: (1) left ventricular electrical resynchronization with LBBP which resulted in ventricular remodeling and improvement in left and right ventricular function; (2) restoration of normal AV conduction sequence in patients with AVB.
Septal perforation

Two patients had septal perforation during the implantation procedure. This was detected by changes in the current of injury (COI) of LBB potential and related ventricular COI, combined with a sudden reduction in pacing impedance. In these two patients the lead was moved to a different location without adverse sequlae.

We observed septal perforation during follow up in 1 patient. This required lead removal and re-implantation but did not result in other adverse consequences. Lead tension should be adjusted properly to prevent the lead from pushing perpendicular to the septum and causing late perforation during heart contraction.20, 32

Increased bundle capture threshold and lead micro dislocation after operation

During follow-up, in 7 patients the threshold for LBB capture increased more than 1V@0.5ms, while the absolute threshold of left bundle capture remained less than 2.5V@0.5ms. Possible explanations for an increase in LBBP capture thresholds may be: 1. local tissue fibrosis; 2. increase in lead tension; 3. possible lead micro dislodgement; 4. progression of conduction system diseases. In these patients, left ventricular endocardial pacing becomes a reliable backup for pacing which kept a relatively narrow QRS (Figure 3).

None of patients required re-intervention due to loss of capture, which is comparable with the re-intervention rates observed in studies of right ventricular pacing.33

Limitations

This study was a single-center prospective registry. The rate of incomplete follow-up of the entire cohort number was relatively high due to the COVID-19 and patients’ poor compliance.
Randomized controlled multicenter trials should be conducted to verify its long-term safety and clinical benefits. The high degree of success and proximal LBBP was achieved by implanters - highly experienced in this technique.

Conclusions

LBBP is feasible and safe in patients with a pacemaker indication. It has a high implant success rate with low and stable pacing thresholds and few complications during long-term follow-up. LBBP produces a narrow QRS, suggesting synchronized ventricular activation and is a promising method for delivering physiological pacing.

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**Table 1** Baseline characteristics

| Total no. of successful patients, N | 618 |
|------------------------------------|-----|
| Age, y, mean ± SD                 | 69.92±11.19 |
| Male sex, n(%)                    | 346(56.0) |
| LBBB with HF, n(%)                | 88(14.2) |
| AVB or AF with AVN ablation, n(%)  | 371(60.0) |
| AVN block, n(%)                   | 255(41.3) |
| Infranodal block, n(%)            | 116(18.8) |
| SSS, n(%)                         | 159(25.7) |
| Diabetes mellitus, n(%)           | 160(25.9) |
| Hypertension, n(%)                | 377(61.0) |
| Previous MI, n(%)                 | 30(4.9) |
| CAD, n(%)                         | 124(20.1) |
| NICM, n(%)                        | 173(28.0) |
| ICM, n(%)                         | 27(4.4) |
| NYHA functional class – mean ± SD | 1.18±1.31 |
| LVEF(%) - mean ± SD               | 57.12±16.47 |
| LVEDd(mm) - mean ± SD             | 53.67±8.00 |
| Procedure time (mins) - mean ± SD | 86.4±43.5 |
| Fluoroscopy time of lead placement(mins) - mean ± SD | 5.1±4.6 |

LBBB, left bundle branch block; HF, heart failure; AVB, atrioventricular block; AF, atrial fibrillation; AVN, atrioventricular node; SSS, sick sinus syndrome; MI, myocardial infarction; CAD, coronary artery disease; NICM, non-ischemic cardiomyopathy; ICM, ischemic cardiomyopathy; NYHA, new York heart association; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic dimension.
Table 2 Electrophysiological characteristic

|                          | All patients | LBBB  | AVB/AF+AVNA | SSS  |
|--------------------------|--------------|-------|-------------|------|
| N                        | 618          | 88    | 371         | 159  |
| Pre-implant QRS(ms)      | 114.20±32.40 | 167.22±18.99 | 108.41±26.69 | 98.75±19.31 |
| Post-LBBP QRS(ms)        | 112.94±16.81 | 124.02±24.15 | 111.35±14.41 | 110.59±14.83 |
| Sti-LVAT(ms)             | 73.87±11.36  | 79.40±11.34 | 73.78±11.89 | 71.04±8.80 |
| Pre-implant mean QRS axis| 20.50(-16.00,56.00) | -9.00(-39.00,42.25) | 27.00(-15.00,61.00) | 28.00(-2.50,53.00) |
| Post-LBBP mean QRS axis  | 20.00(-17.00,54.00) | 35.50(-3.00,54.75) | 16.00(-18.00,55.00) | 18.00(-15.25,52.50) |
| Pre-implant QRS transition zone | 3.50(1.50,3.50) | 4.50(3.50,4.50) | 2.50(1.50,3.50) | 2.50(1.50,3.50) |
| Post-LBBP QRS transition zone | 1.50(1.50,2.50) | 1.50(1.50,3.50) | 1.50(1.50,2.50) | 1.50(1.50,2.50) |

**LBB capture characteristic**

|                          | All patients | LBBB  | AVB/AF+AVNA | SSS  |
|--------------------------|--------------|-------|-------------|------|
| RBBB pattern (n)         | 618(100%)    | 88(100%) | 371(100%)   | 159(100%) |
| LBB Potential (n)        | 476(77.0%)   | 48(54.5%)* | 283(76.3%)  | 147(92.5%) |
| Selective LBBP at implant (n) | 460(74.4%)     | 81(92.0%) | 265(71.4%) | 114(71.7%) |
| Selective during follow-up (n) | 191(30.9%)      | 43(48.9%) | 113(30.5%) | 35(22.0%) |
| Sti-LVAT shortens abruptly, n(%) † | 533(86.2%)  | 80(90.9%) | 316(85.2%) | 137(86.2%) |

LBBB, left bundle branch block; AVB, atrioventricular block; AF, atrial fibrillation; AVN, atrioventricular node; SSS, sick sinus syndrome; LBBP, left bundle branch pacing; Sti-LVAT, stimulus to left ventricular activation time; RBBB, right bundle branch block; LBB, left bundle branch.

* LBB potentials were recorded during restoration of left bundle conduction by HBP in 37 patients and during RBBB morphology escape rhythm from the LBB fascicles in 11 patients.
† Sti-LVAT shortens more than 10ms in procedure during change of the output or deep screwing.
### Table 3 Complications of Left Bundle Branch Pacing

| Complications during procedure | Patients(n) |
|-------------------------------|-------------|
| Septal perforation            | 2           |
| Intravenous puncture-related arterial injury | 2 |
| Coronary artery injury        | 0           |

| Complications during follow-up | Patients(n) |
|--------------------------------|-------------|
| Increase of capture threshold >2V/0.5ms | 6           |
| Loss of conduction system capture | 2           |
| Lead revision                   | 2           |
| Pocket infection                | 2           |
| Hematoma                        | 1           |
| Septal perforation              | 1           |
Table 4  RBB injury during procedure

| Patients (n)                      | RBBB pattern | Complete AVB |
|----------------------------------|--------------|--------------|
|                                  | Transient    | Permanent    | Transient | Permanent |
| LBBB with HF(n=88)               | /            | /            | 26(29.5%) | 12(13.6%) |
| AVB(n=270)                       | 31(11.5%)    | 17(6.3%)     | 10(3.7%)  | 2(0.7%)   |
| AF & AV node ablation(n=101)     | 21(20.7%)    | 13(12.9%)    | 2(2.0%)   | 1(1.0%)   |
| SSS(n=159)                       | 32(20.1%)    | 9(5.7%)      | 4(2.5%)   | 1(0.6%)   |
| Total(n=618)                     | 84(13.6%)    | 39(6.3%)     | 42(6.8%)  | 16(2.6%)  |

LBBB - left bundle branch block; HF - heart failure; AVB - atrioventricular block; AF - atrial fibrillation; AV - atrioventricular; SSS - sick sinus syndrome
Figure Legends:

Figure 1 Change of mean QRS axis and QRS transition zone. A. Mean QRS axis of patients pre and post-LBBP; B. QRS transition zone of patients pre and post-LBBP.

LBBB, left bundle branch block; LBBP, left bundle branch block.

Figure 2 Pacing and echocardiographic parameters. A. LBB capture threshold of patients; B. R-wave amplitude of patients; C. Impedance of patients. D,E,F. LVEF, LVEDd and degree of TR of patients pre-LBBP and 1-year after LBBP.

LBBB, left bundle branch block; HF, heart failure; AVB, atrioventricular block; AF, atrial fibrillation; AVN, atrioventricular node; SSS, sick sinus syndrome; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic dimension; TR, tricuspid regurgitation. LBB, left bundle branch.

Figure 3. Cases of LBBP with lead dislocation. Case A: A1, intrinsic ECG of patient with narrow QRS; A2, LBBP at 0.75V/0.5ms at implant; A3, LSP at 7.5V/0.5ms at; Case B: B1, intrinsic ECG of patient with LBBB; B2, LBBP at 0.5V/0.5ms at implant; B3, LSP at 8.0V/0.5ms at 9 months follow-up;

LBBP, left bundle branch pacing; LSP, left ventricular septal pacing.
What Is Known?

- Case studies suggest that LBBP is a promising method for delivering physiological pacing, but it has been limited by relatively short follow up and small sample size.
- LBB capture was not well defined in previous studies and thus some patients enrolled may not have had capture of the conduction system.

What the Study Adds?

- Prospective single center clinical data of left bundle branch pacing according to strict criteria for LBB capture with long term follow-up and large sample size.
- The characteristics of LBB pacing including electrocardiographic characteristics and pacing parameters in patients with LBBB, and AVB or SSS group. We showed stable and excellent pacing thresholds over time as well as maintaining and improvement in cardiac function in both patient groups.
- The major complications related to LBBP including tricuspid regurgitation, right bundle branch injury, lead dislodgement and septal perforation were analyzed and discussed, and low complication rates was observed during long term follow up.
A1: Intrinsic

A2: LBBP 0.75V/0.5ms at implant

A3: LSP 7.5V/0.5m at 9 months

B1: Intrinsic

B2: LBBP 0.5V/0.5ms at implant

B3: LSP 8.0V/0.5m at 3 months
**Study Population and Method**

- **Total 632 patients attempted LBBP**
- **Success rate is 97.8%**
  - According to strict criteria for LBB capture
- **LBBB**
  - n=88
- **AVB or AF & AVN ablation**
  - n=371
- **SSS**
  - n=159

**Follow-up**

- **Mean follow-up was 18.6±6.7 months**
- **Pacing parameters**
- **ECG**
- **Echocardiography**

**Results**

- **Threshold (V@5Ma)**
  - LBBB and HF (n=84)
  - AVB or AF post AVN ablation (n=337)
  - SSS (n=139)

- **QRS duration (ms)**
  - SSS (n=139)
  - AVB or AF post AVN ablation (n=337)
  - LBBB and HF (n=84)

- **LVEF (%)**
  - SSS QRS=120ms (n=139)
  - AVB/AF/AVNA QRS=120ms (n=233)
  - QRS≥120ms (n=192)

**Complications**

- LBB capture threshold increased to more than 3 V in 4 patients
- Loss of bundle capture in 2 patients