Prospective evaluation of clinical safety and efficacy of left bundle branch area pacing in comparison with right ventricular septal pacing

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Research Article

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Abstract

Background

Left bundle branch area pacing (LBBaP) has recently emerged as alternative a new physiologic strategy of pacing to His-bundle pacing (HBP) associated with difficulty of lead implantation, His bundle damage, high and unstable thresholds.

Objective

The purpose of this study is to compare clinical safety and efficacy of LBBaP with right ventricular septal pacing (RVSP).

Methods

From February 2019 to May 2020, consecutive pacing-indicated patients were prospectively enrolled and divided into two groups. Ventricular synchrony index such as QRS duration (QRSd), interventricular mechanical delay (IVMD) and septal-posterior wall motion delay (SPWMD), left ventricular function such as left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF), pacing parameters, and complications were evaluated in perioperative period and during follow-up.

Results

LBBaP was successful in 45 patients (88.2%), and finally 46 patients underwent RVSP. With LBBaP, the ventricular electrical-mechanical synchrony were similar with the native-conduction system (P = .784). However, the ventricular electrical synchrony (QRSd, 108.47 ± 7.64 vs 130.63 ± 13.63 ms, P < .0001) and mechanical synchrony (IVMD, 27.68 ± 4.33 vs 39.88 ± 5.83, P < .0001; SPWMD, 40.39 ± 23.21 vs 96.36 ± 11.55, P < .0001) in the LBBaP group were significantly superior to the RVSP group. No significant differences in LVEDD (46 [44-48.5] vs 47 [44–52] mm, P = .488) and LVEF% (66 [62.5–70] vs 64 [61–68], P = .759) were noted in both two groups at last follow-up. But, in the subgroup analysis, LVEDD was shorter (46 [44–49] vs 50 [47–58] mm, P = .032) and the LVEF% was higher (65 [62–68] vs 63 [58–65], P = .022) in the LBBaP-H (high ventricular pacing ratio > 40%) group compared with RVSP-H group at last follow-up. There was lower capture thresholds (0.59 ± 0.18V vs. 0.71 ± 0.26V, P = 0.011) at implantation in the LBBaP group than RVSP group, and R-wave amplitudes and pacing impedances did not differ between the two groups. No serious complications were found in both two groups at implantation and follow-ups.

Conclusion

This study confirms the clinical safety and efficacy of LBBaP, and that produces better ventricular electrical-mechanical synchrony than RVSP. The event of pacing-induced left ventricular dysfunction is lower in the LBBaP-H group than RVSP-H group.

Trial registration
Trial registration Chinese Clinical Trial Registry, ChiCTR2100046901, Registered 30 May 2021—Retrospectively registered, http://www.chictr.org.cn/searchproj.aspx?regstatus=1008001.

**Background**

Pacemaker therapy has been used for more than half a century in patients with bradycardia arrhythmias. Conventional right ventricular apical pacing (RVAP) is easily successful, good pacing parameters, and less lead dislodgement, but it is related to high risk for heart failure and atrial fibrillation\[1, 2\] due to ventricular electromechanical dyssynchrony. Pursuit of alternate right ventricular pacing sites (septum or outflow tract) do not lead to ventricular synchrony and has not been confirmed to be superior to RVAP\[3\]. Cardiac resynchronization Therapy (CRT) based on biventricular pacing (BVP) can shorten the left and right ventricular delays and improve ventricular systolic function, however, approximately 30 and 40% of patients have no clinical benefit or no response to conventional biventricular CRT\[4\], moreover there was no significant improvement in cardiac function in patients with right bundle branch block (RBBB)\[5\], even leading to deterioration of cardiac function in patients with narrow QRS duration\[6\]. His bundle pacing (HBP) can maintain ventricular synchronized contraction via pacing the native His-Purkinje system directly, emerging as a viable alternative for CRT with physiological restoration of electrical synchrony\[7\]. However, there are still some challenges of HBP, including high capture thresholds, electrode dislocation and lower success rates particularly in patients with bundle branch block (BBB) or infranodal block\[8, 9\].

Thus, left bundle branch area pacing (LBBaP) as another physiological pacing form was firstly proposed in 2017\[10\]. Subsequently, the narrow paced QRS duration (QRSd), good ventricular mechanical synchrony and a low capture threshold of LBBaP has been confirmed by several studies\[11, 12\]. However, the results of comparison of left ventricular (LV) function such as left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF) between LBBaP and right ventricular pacing (RVP) were inconsistent in several studies\[13, 14\]. In this study, we aimed to evaluate the clinical safety, efficacy and LV function of LBBaP compared to RVSP.

**Methods**

**Study design**

This study was performed in Xiangtan Central Hospital with consecutive pacemaker-indicated patients who received LBBaP or RVSP from February 2019 to May 2020, according to 2013 ESC/EHRA Guidelines on cardiac pacing. Exclusion criteria consisted of (a) previously implanted with cardiac devices (b) underwent cardiac resynchronization therapy (CRT) (c) moderate to severe valvular diseases (d) acute or old myocardial infarction (e) severe liver, kidney or lung dysfunction. All surgical methods were performed in accordance with relevant guideline\[15\] and hospital regulations. And the protocol of this prospective was approved by the Research Ethics Committee of Xiangtan central Hospital, and all patients had submitted written informed consent.

**Procedure**
LBBaP: Axillary vein angiography was performed through the left cubital vein to guide the axillary vein puncture (Fig. 1a). If this method failed, the loach guide wire (Merit Medical Systems, Inc.) was sent through the femoral vein to the left subclavian vein to guide the axillary vein puncture under X-rays (Fig. 1b). Then, the 6-pole ventricular electrode of Synaptic Medical was implanted into the right ventricle through the right femoral vein, of which the purpose was to provide protective pacing and to predetermine the His bundle region by intracardiac electrogram (EGM) with the 6-pole ventricular electrode and fluoroscopic image (Fig. 2a). The C315 HIS sheath (Medtronic Inc., Minneapolis, MN) with the lead (model 3830, Medtronic Inc., Minneapolis, MN) was inserted into the His bundle region through the left axillary vein access under the guidance of position of the 6-pole ventricular electrode to mark the His bundle potential (Fig. 2a). Using the His bundle region as a marker, subsequently, the C315 sheath with the 3830 lead was advanced 1 to 1.5 cm toward right ventricular (RV) apex in right anterior oblique (RAO) 30° projection (Fig. 2b). The morphology of QRS wave at baseline in LBBaP was shown in Fig. 3a. Unipolar paced QRS morphology in lead V1 appeared W-shaped at an output of 2V/0.42 ms, which was acted as the ideal point for lead implantation (Fig. 3b). Next, the pacing lead tip was screwed towards the left side of septum perpendicularly with 8 to 10 clockwise rotation. During the lead screwing process, the cathode ring of the lead was intermittently paced and the W-shaped “notch” morphology in V1 lead gradually shifted and finally disappeared and the paced QRS morphology changed from left bundle branch block (LBBB) to RBBB, and the lead advancement was stopped (Fig. 3b, 3c, 3d), and left bundle branch (LBB) could be recorded (Fig. 3e). At the same time, we closely monitored output threshold and pacing impedance to avoid septum lead perforation. The stimulus to peak left ventricular activation time (S-PLVAT) in lead V5 was also measured. Finally, successful LBBaP manifested as a paced QRS morphology of RBBB pattern with short QRSd, and S-PLVAT was no change with low and high output (Fig. 3f, 3g). In addition, LBB potential or premature ventricular contraction (PVC) originated from the left side of septum could be observed during the lead screwing procedure (Fig. 2b). Postoperative images of LBBaP and contrast injection through the sheath showed in Fig. 4.

RVSP: The loach guide wire (Merit Medical Systems, Inc.) was sent to the right ventricular outflow tract (RVOT) through the left axillary vein access, and the C315 S10 sheath (Medtronic Inc., Minneapolis, MN) was inserted into the RVOT. Then, the guide wire and inner sheath was pulled out and slowly retracted the delivery sheath to the middle or low septum of the right ventricle. Next, the lead (model 3830, Medtronic Inc, Minneapolis, MN) was delivered through the sheath to the RV septum. Finally, the lead was screwed towards the middle site of ventricular septum perpendicularly with 4 to 6 clockwise rotation. The schematic representation of RVSP was shown in Fig. 3h, 3i and postoperative images of RVSP and contrast injection through the sheath showed in Fig. 4.

Programming

Atrioventricular (AV) delay programming should be individualized for those patients with BBB. Before discharge, a series of sensed and paced AV delays, ranging from 100 ms to intrinsic PR interval in 10 ms increment, were tested for those patients until BBB appeared. AV delay was considered optimum when
BBB was corrected and the QRSd was minimum Fig. 5. We routinely turned on the automatic AV search/VIP function in the remaining patients.

**Date collecting and follow-up**

Baseline patient characteristics were collected at enrolment. ECG and intracardiac EGM pattern, QRSd, S-PLVAT, fluoroscopy dose, procedure duration (defined as the time from sterilization to the end of the operation) and imaging data were recorded during implantation. Pacing parameters (capture threshold, sensing amplitude and impedance) were recorded at implantation and during follow-ups.

Echocardiography were performed by specialists before implantation and during follow-up. The distance from the the onset of the QRS to the blood flow starting point of the left ventricular outflow tract (LVOT) was measured as aortic pre-ejection in interval (APEI), to the blood flow starting point of the RVOT as pulmonary pre-ejection interval (PPEI), and the absolute value of the difference between APEI and PPEI was defined as the interventricular mechanical delay (IVMD). And interventricular dyssynchrony was considered present if IVMD was more than 40 ms. Intraventricular dyssynchrony was defined as the septal-posterior wall motion delay (SPWMD) of more than 130 ms, which was measured by M-mode as the difference between the time of maximum displacement of the septum and the posterior wall of the left ventricle. Complications such as pocket infection, hematoma, and late lead dislodgment were monitored during follow-up visits. Pacing parameters would be tested at 1 month and several months (6 to 24) after operation. Echocardiography would be performed at several months (6 to 24) after operation.

**Statistical analysis**

The Shapiro-Wilk normal test was applied to verify whether the data followed a normal distribution. Categorical date were described as absolute number and percentage (%). Continuous variables were expressed as mean ± standard deviation or as median with interquartile range (IQR), as appropriate based on data distribution. The χ² test or Fisher’s exact test was used for categorical data, as appropriate. Continuous variables were compared with the use of the Student t test if the data were normally distributed, and with the Mann-Whitney U test or the Wilcoxon signed rank test for nonparametric data. A two-sided P-value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics 26.

**Results**

**Participants**

Between February 2019 and May 2020, a total of 91 patients were enrolled and divided into LBBaP group and RVSP group. Among the 91 patients, LBBaP was attempted in 51 patients and successful in 45 patients (88.2%). The other 6 patients (11.8%) that failed LBBaP, received RVSP instead. The remaining 40 patients underwent RVSP as planned. Finally, 45 patients (age 74 [67.5–79.5] years; 26% male) underwent LBBaP and 46 patients (age 70.5 [63-78.3] years; 18% male) underwent RVSP. The follow-up duration in the LBBaP group was 14 (10–18) months compared to 14 (9–17) months (P = .842) in the
RVSP group, one patient complicated with acute myocardial infarction during follow-up was excluded in the LBBaP group, and four patients were lost to follow-up because of death in the RVSP group (Fig. 6). Of the patients with LBBaP, 11 patients were diagnosed with sick sinus syndrome (SSS), 33 with AVB, and 1 with permanent AF with slow ventricular rate. Compared to the RVSP group, the LBBaP group displayed higher atrium ventricular block (AVB) (73.3% vs 37%, P < .001), lower RBBB (0% vs 10.9%, P = .023) and SSS (24.4% vs 50%, P < .001). Other baseline clinical characteristics did not statistically differ between the two groups (Table 1).

**Implantation results**

LBB potential could be recorded in 31 patients (68.9%) during intrinsic rhythm, and 4 (8.9%) were implanted with single-chamber pacemaker and 41 (91.1%) was implanted with dual-chamber pacemaker in the LBBaP group. Compared to the RVSP group, the LBBaP group displayed higher Cum% VP (98 [26.3–100] vs 6 [1–95], P < .0001). The mean S-PLVAT in lead V5 was 71.80 ± 5.31ms during LBBaP in the study and that was no difference between patients with recorded LBB potential and patients without LBB potential (71.29 ± 4.53 vs 72.93 ± 6.79 ms, P = .344). Both the total surgery time (121 [110–130] vs 91 [89–98] minutes, P < .0001) and fluoroscopic dose (78 [73–81] vs 53 [48–56] mGy, P < .0001) were significantly longer and increased in LBBaP group than that in RVSP group (Table 1).
Table 1
Baseline patient characteristics and procedure outcomes

| Groups                        | RVSP(n = 46)       | LBBaP(n = 45)      | P value |
|-------------------------------|--------------------|--------------------|---------|
| Demographics                  |                    |                    |         |
| Age (years)                   | 70.5 (63-78.3)     | 74 (67.5–79.5)     | .108    |
| Male sex, n (%)               | 18 (39.1%)         | 26 (57.8%)         | .075    |
| Comorbidities                 |                    |                    |         |
| Hypertension, n (%)           | 27 (58.7%)         | 25 (55.6%)         | .762    |
| Diabetes, n (%)               | 4 (8.7%)           | 7 (15.6%)          | .316    |
| Coronary artery disease, n (%)| 5 (10.9%)          | 12 (26.7%)         | .053    |
| Paroxysmal or persistent AF, n (%) | 15 (32.6%) | 13 (28.9%)         | .701    |
| Diagnosis                     |                    |                    |         |
| SSS, n (%)                    | 23 (50%)           | 11 (24.4%)         | .012    |
| AVB, n (%)                    | 17 (37%)           | 33 (73.3%)         | <.001   |
| AF with slow ventricular rate, n (%) | 6 (13.0%) | 1 (2.3%)           | .053    |
| LBBB, n (%)                   | 2 (4.3%)           | 5 (11.1%)          | .226    |
| RBBB, n (%)                   | 5 (10.9%)          | 0 (0%)             | .023    |
| Types of pacemaker            |                    |                    |         |
| Single chamber, n (%)         | 6 (13.0%)          | 4 (8.9%)           |         |
| Dual chamber, n (%)           | 40 (87%)           | 41 (91.1%)         |         |
| LBB potential, n (%)          |                   | 31 (68.9%)         |         |
| Pacing-R wave peak of V5 lead, (ms) | 71.80 ± 5.31      |                    |         |
| Procedure duration, (min)     | 91 (89–98)         | 121 (110–130)      | <.0001  |
| Fluoroscopy dose, (mGy)       | 53 (48–56)         | 78 (73–81)         | <.0001  |

AF atrial fibrillation, AVB atrium ventricular block, LBB left bundle branch, LBBaP left bundle branch area pacing, RBBB right bundle branch block, RVSP right ventricular septum pacing, SSS sick sinus syndrome, Values are given as no. (%), median (interquartile range), mean ± (SD).

ECG and Echocardiography characteristics

A comparison of ECG and echocardiography parameters between the two groups at baseline and last follow-up are shown in Table 2. There was no significant difference in QRSd in both the two groups at native-conduction mode, and QRSd had also no difference between the LBBaP capture mode and the
LBBaP native-conduction mode (P = .784). But ECG QRSd was much shorter in the LBBaP capture mode compared with that in the RVSP capture mode (108.47 ± 7.64 vs 130.63 ± 13.63 ms, P < .0001). Furthermore, we observed patients with LBBB (n = 5) in the LBBaP group and found that those QRSd was significantly narrowed (152.40 ± 6.34 vs 120.00 ± 1.58 ms, P = .001). On the other hand, no statistical differences were noted in paced QRSd between patients with recorded LBB potential and patients without LBB potential (107.42 ± 6.84 vs 110.79 ± 9.03 ms, P = .174).

IVMD at baseline was no difference in both the two groups (29.00 ± 9.86 ms vs 27.46 ± 10.97 ms, P = 0.193). At last follow-up interventricular synchrony in LBBaP group was better than in RVSP group (27.68 ± 4.33 vs. 39.88 ± 5.83 ms, P < .0001). Intraventricular delay as expressed by SPWMD at baseline was similar in both two groups (39.62 ± 30.10 vs. 40.65 ± 32.61, P = 0.876). Intraventricular dyssynchrony was minimal in LBBaP group (40.39 ± 23.21 vs. 96.36 ± 11.55 ms, P < .0001) at last follow-up. Those indicated a good mechanical synchrony resulting from LBBaP.

LVEDD (47 [44.5–50] vs 46.5 [44-50.5] mm, P = .955) and LVEF% (65 [61.5–70] vs 67 [61-69.3], P = .896) preoperatively were similar in both LBBaP and RVSP groups. LVEDD and LVEF did not change significantly in both LBBaP and RVSP group at last follow-up (P > .05). Patients with high ventricular pacing ratio (> 40%) in the two groups were screened, and two different subgroups were formed as follows: LBBaP-H (high ventricular pacing ratio (> 40%) in left bundle branch area pacing ) and RVSP-H (high ventricular pacing ratio (> 40%) in right ventricular septum pacing ). LVEDD and LVEF preoperatively were similar in both LBBaP-H and RVSP-H groups (P > .05). However, LVEDD was shorter (46 [44–49] vs 50 [47–58] mm, P = .032) and the LVEF% was higher (65 [62–68] vs 63 [58–65], P = .022) in the LBBaP-H group compared with RVSP-H group at the end of follow-up Fig. 7.
### Table 2
Comparison of QRSd and echocardiographic parameters between the LBBaP and RVSP groups

| Parameter | RVSP               | LBBaP              | P for group |
|-----------|--------------------|--------------------|-------------|
| QRSd, (ms)| Baseline 106.04 ± 20.78 | 109.09 ± 19.88     | .447        |
|           | Post implantation 130.63 ± 13.63 | 108.47 ± 7.64      | < .0001     |
| RAD, (mm) | Baseline 36 (34–39)  | 36 (32.5–46)       | .396        |
|           | At last follow-up 36 (34–40) | 37 (34–39)  | .917        |
| LVEDD, (mm)| Baseline 46.5 (44-50.5) | 47 (44.5–50)       | .955        |
|           | At last follow-up 47 (44–52) | 46 (44-48.5)  | .488        |
| LVEF, (%) | Baseline 67 (61-69.3) | 65 (61.5–70)       | .896        |
|           | At last follow-up 64 (61–68) | 66 (62.5–70)  | .759        |
| IVMD, (ms)| Baseline 27.46 ± 10.97 | 29 ± 9.86         | .112        |
|           | At last follow-up 39.88 ± 5.83* | 27.68 ± 4.33     | < .0001     |
| SPWMD, (ms)| Baseline 40.65 ± 32.61 | 39.62 ± 30.10     | .876        |
|           | At last follow-up 96.36 ± 11.55* | 40.39 ± 23.21 | < .0001     |

IVMD interventricular mechanical delay, LBBaP left bundle branch area pacing, LVEDD left ventricular end-diastolic diameter, LVEF left ventricular ejection fraction, QRSd QRS duration, RAD right atrial diameter, RVSP right ventricular septum pacing, SPWMD septal-posterior wall motion delay, Values are given as median (interquartile range), mean ± (SD).

* P < .0001 baseline vs at last follow-up

**Pacing electrical parameters and complications**

The comparison and variation trend of lead parameters (capture thresholds, R-wave amplitudes and pacing impedances) in LBBaP group and RVSP group were shown in Fig. 8. Compared with RVSP patients, LBBaP patients had lower capture thresholds at pulse width of 0.4ms (0.59 ± 0.18V vs. 0.71 ± 0.26V, P = 0.011) at implantation, but there was no difference between the two groups during follow-up (0.59 ± 0.21V vs. 0.57 ± 0.22 V, P = 0.673) and remained stable. R-wave amplitudes and pacing impedances did not differ between the two groups (P > .05) at implantation and during follow up, but the R-wave amplitude increased, pacing impedance decreased and remained stable over the follow-up time.

During the implantation procedure, acute lead dislodgement occurred in two patient in the LBBaP group during withdrawal of the sheath, one patient developed septal lead perforation in LBBaP group (see
Additional le 1), and finally received RVSP instead. Other implantations such as pocket hematoma, loss of capture, lead removal, or late lead dislodgement were not observed.

**Discussion**

LBBaP is an other physiological pacing strategy that swiftly recruited the left ventricular His-Purkinje system by advanced activation of the LBB. The QRS duration is a characterization of ventricular activation time and has been accepted as a surrogate indicator for evaluating of ventricular electrical synchrony[16]. Our study shows that ECG QRSd was significantly shorter with LBBaP capture mode compared with the RVSP capture mode and did not prolonged in comparsion with native-conduction QRS duration, which represented better ventricular electrical synchrony resulting from LBBaP. This finding was consistent with other studies[17, 18]. Significantly, as shown in our study, the paced QRSd in the RVSP group (130.63 ± 13.63 ms) was relatively narrow compared to those two studies, which was 154.80 ± 9.85 ms in Chen's study[17], 149.38 ± 19.40 ms in Sun's study[18]. One reason for this difference is that the pacing lead was located in the interventricular septum in our RVP group, while the pacing lead was located in the right ventricular septum or the apex in the other two studies. Another reason for the difference in results may be related to the different implantation methods of RVSP. In these three studies, active fixation lead (model 5076; Medtronic Inc) was implanted into the right ventricular septum or apex, while we guided lead (3830, 69 cm, Medtronic Inc) to the middle of the right ventricular septum through delivery sheath (C315 S10, Medtronic Inc). The C315 sheath made the 3830 lead more perpendicular to the septum, and the lead could be screwed deeper into the septum than the 5076 lead. So, the paced QRSd of the RVSP group in our study was similar with the mid-septal pacing (Mid-SP) group (127.20 ± 15.36 ms) in Chen's study[17] and narrower than those of the RVSP group in the three studies. Meanwhile, we optimized AV delay, especially in patients with BBB, to make the paced QRS duration more shorter and to achieve better ventricular electrical synchronization. Interestingly, LBB potential can be recorded during the LBBap implantation procedure, an indication of direct LBBaP[19], but not all LBBaP can observe LBB potential. Our study showed that approximately 68.9% of implants can record LBB potential, which was identical to other studies (60–80%)[11, 17, 20]. S-PLVAT in V5 lead and paced QRSd were similar in patients with vs without LBB potential recorded in the LBBaP group in our study, which was consistent with Chen's[17]and Cai's results[20], but contradictory with Hou's result[11]. The specific reasons for this difference are unknown and may be related to the different diagnoses of the included patients, so large sample size and randomized multicenter study with longer term follow-up is needed to obtain conclusive evidence. However, since pacing is intended to correct conduction disease or stimulate the bundle branch to produce rapid conduction with normal or near-normal electrocardiogram, it may not be necessary to record LBB potential, which is consistent with Chen's view[17]. Consequently, Surgical method of LBBaP reported by Zhang JM et al without the guidance of intracardiac electrograms proved to be effective[21].

As is known to all that good ventricular electric synchrony associated with a narrow QRSd leads to good ventricular mechanical contraction synchronization[22, 23]. Indeed, subsequent studies have confirmed that LBPaP has better ventricular mechanical synchronization than RVSP. The LV mechanical synchrony of LBBaP was proved to be superior to that of RVSP and to be similar to that of native conduction by
using phase analysis of gated SPECT myocardial perfusion imaging in Hou's study[11], 2-D speckle tracking echocardiograph in Sun's study[13], real-time three dimensional echocardiographic (RT-3DE) and tissue Doppler image (TDI) in Cai's study[20]. Our study also demonstrated this result by measuring IVMD and SPWMD. Therefore, LBBaP maintained a good LV electrical-mechanical synchrony, which was similar to normal conduction and significantly superior to RVSP.

Theoretically, LV function in patients with LBBaP should be superior to that in patients with RVSP because of LV electrical-mechanical synchrony in LBBaP group was significantly better than RVSP group. Das's study[24] and Zhang's study[14] showed that LBBaP is associated with better LV function (higher LVEF and lower LVEDD, P < .05) during short-middle term follow-up in comparison to RVAP. However, no statistical difference existed in LVEDD and LVEF between the LBBaP and RVSP groups during middle-term follow-up in our study, which were identical to other short term follow-up studies[13, 20]. One possible reason for this difference is that patients enrolled into the two studies were different, patients with BBB or AV block were enrolled into Das's study[24] and patients with AV block were enrolled into Zhang's study[14], resulting in most of patients with high ventricular pacing ratio. By subgroup analysis, our study also showed that LV function is better (higher LVEF and lower LVEDD, P < .05) in the LBBaP-H group compared with the RVSP-H group. For those LBBB patients with heart failure, nonrandomized clinical trials have demonstrated that CRT delivered with LBBaP can correct LBBB and significantly improve LV function, even better than CRT based on BVP[25–27]. Hence, we think that LBBaP may be an option for pacemaker-induced patients requiring a high ventricular pacing ratio, complicated with heart failure or associated BBB.

In our study, the success rate of LBBaP was 88.2%, which was similar to the success rate (80.5%-100%) of LBBaP in previous studies[11, 13, 20]. The LBBaP failed in six patients, in two cases, the 3830 lead was pulled which dislocated the lead when removing the C315 delivery sheath. In other three cases, we tried three times and failed to position the lead in the left side of the septum. One patient developed septal lead perforation with a sudden loss of capture and a decrease in lead impedance from 780Ω to 350Ω. The main challenge of LBBaP is to place the lead deep enough in the septum to ensure capture of the LBB, yet not too deep to avoid acute or delayed perforation. Recent documents proposed several methods to monitor lead depth: fulcrum sign, sheath angiography, impedance monitoring, changes in the QRS notch in V1 lead, pacing from the ring electrode and observing fixation beats (the ectopic beats of qR/rsR' morphology in V1 lead)[28]. Meanwhile, fixation beats is a novel marker for reaching the LBB area. Other complications such as pocket hematoma, loss of capture, lead removal, or late lead dislodgement, ventricular septal coronary damage were not observed in both two groups. The recent study about acute myocardial damage secondary to implantation of lead for the LBBaP found that troponin T levels were significantly higher at 12 hours after LBBP surgery than before operation(96.45 ± 11.07 vs.16.59 ± 1.84 ng/L, p < .001)and the number of attempts was an independent risk factor related to the myocardial damage by correlation and regression analysis[29]. Whether the myocardial damage of LBBaP is more serious than that of RVSP, needs to be confirmed in prospective randomized clinical trials. At least, we should pay attention to the damage of ventricular septal coronary and excessive number of attempts should be avoided.
This study showed that the capture threshold with LBBaP was lower at implantation compared to RVSP, but there was no difference between the two groups during short-middle term follow-up and remained stable. R-wave amplitudes and pacing impedances did not differ between the two groups at implantation and during short-middle term follow up, but the R-wave amplitude increased, pacing impedance decreased and remained stable over the follow-up time. It may be that electrode tip of LBBaP causes more myocardial injuries, then excessive myocardial edema in the early stage made the electrode impedance high and R-wave amplitude low at implantation. When the edema was reduced, the impedance gradually decreased, R-wave amplitudes gradually increased and tended to be stable. Other studies also confirmed good pacing parameters for LBBaP [11, 14, 17].

**Limitation**

Several limitations should be mentioned. First, this is a non-randomized, a single-centre, observational study with a small sample size, therefore, the LBBaP surgery was not representative. Second, the follow-up time of patients in the two groups was not strictly limited, which may lead to bias of the results. So, randomized multicenter study with larger sample sizes, longer term follow-up is needed for conclusive evidence.

**Conclusion**

This study demonstrates the clinic safety and efficacy of LBBaP that produces better ventricular electrical-mechanical synchrony than RVSP and confirmed good, stable pacing parameters for LBBaP. The occurrence of pacing-induced left ventricular dysfunction is lower in the LBBaP-H group than RVSP-H group.

**Abbreviations**

AF: atrial fibrillation; IVMD:interventricular mechanical delay; LBBaP:left bundle branch area pacing; LVEDD:left ventricular end-diastolic diameter; LVEF:left ventricular ejection fraction; QRSd:QRS duration; RVSP:right ventricular septum pacing; SPWMD:septal-posterior wall motion delay;

**Declarations**

**Acknowledgments**

None.

**Authors’ contributions**

XL, WL and MW were responsible for the conception and design of the study. XL, WL, LW and ST were responsible for data collection. XL and WL were responsible for analysis of data; furthermore, XL and LW
were in charge of statistical analysis. XL drafted the manuscript; JZ, HH and MW revised and commented on the draft and overall responsibility. All authors read and approved the final manuscript.

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Availability of data and materials

The dataset supporting the conclusions of this article will be available upon request to the corresponding author.

Ethics approval and consent to participate

Our study was approved by the Ethics Committee of Xiangtan central Hospital. Written informed consent from every participating patient was obtained.

Consent to publish

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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**Figures**
Figure 1

Axillary vein localization. Axillary vein angiography (a), Loach guide wire in axillary vein guidance (b).

Figure 2

The implantation procedure of LBBaP. Fluoroscopic image of 6-pole RV electrode and its potential at IEGM were recorded. HB potential (the back arrow shows) was identified at IEGM and fluoroscopic image of the 3830 lead and sheath position were recorded as a reference (a). Fluoroscopic image of LBB area was preliminarily confirmed. The 3830 lead implanted in LBB area successfully and LBB potential (the back arrow shows) can be seen at IEGM, and a paced QRS morphology of RBBB pattern with short QRSd
was recorded (b). HB: His bundle; IEGM: intracardiac electrogram; LBBaP: left bundle branch area pacing; LBB: left bundle branch; RV: right ventricular

Figure 3

The morphology of QRS wave at baseline (a) in LBBaP, change of the W-shaped “notch” morphology in V1 lead during implantation (b,c,d), left bundle branch potential (e), the S-PLVAT with low and high output (f,g). The morphology of QRS wave at baseline and pacing (h,i) in RVSP; LBBaP: left bundle branch area pacing; RVSP: right ventricular septal pacing; S-PLVAT: stimulus to peak left ventricular activation time
Figure 4

Postoperative images of LBBaP (a, b) and RVSP (d, e), contrast injection through the sheath in LBBaP (c) and RVSP (f). LBBaP: left bundle branch area pacing; RVSP: right ventricular septal pacing
Figure 5

The optimization of sAV and pAV delays. With the delay of sAV interval, the self LBBB pattern appeared. When the sAV was set at 100ms, the morphology of QRS wave in V1 lead was rSr type, and the QRSd was the narrowest (120ms), and LBBB was corrected (a). With the delay of pAV interval, the morphology of QRS wave changed from RBBB to LBBB. When the pAV was set at 150ms, the QRSd was the narrowest (107ms) (b). LBBB: left bundle branch block; pAV: paced atroventricular; QRSd: QRS duration; RBBB: right bundle branch block; sAV: sensed atroventricular
Figure 6

Schematic diagram of the study. 1 Reasons for exclusion: one patient complicated with acute myocardial infarction; 2 Reasons for death: accident (n=1), cerebral hemorrhage (n=1), carcinoma of esophagus (n=1), not clear (n=1); LBBaP: left bundle branch area pacing; RVSP: right ventricular septum pacing
Figure 7

Comparison of LVEDD (a) and LVEF (b) between LBBaP and RVSP at implantation and last follow-up. Comparison of LVEDD (c) and LVEF (d) between LBBaP-H and RVSP-H subgroups at implantation and last follow-up. LBBaP: left bundle branch area pacing; LBBaP-H: high ventricular pacing ratio (>40%) in left bundle branch area pacing; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; RVSP: right ventricular septum pacing; RVSP-H: high ventricular pacing ratio (>40%) in right ventricular septum pacing.
Figure 8

Comparison of Capture threshold (a), R-wave amplitude (b), and Pacing impedance (c) between two groups at implantation and during follow-up. LBBaP: left bundle branch area pacing; RVSP: right ventricular septum pacing

Supplementary Files

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