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Comparison of synchronization between left bundle branch and his bundle pacing in atrial fibrillation patients: An intra-patient-controlled study

Xia Sheng MD ¹	Yi-Wen Pan MD ¹ \odot Chan Yu MD ² Bei Wang MD ²
Pei Zhang MD ¹	Jing Li MD ^{1,3} Jie-Fang Zhang MD ¹ \circ Shi-Quan Chen MD ¹
Min Wang MD ¹	Ya-Xun Sun MD ¹ \odot Dong-Mei Jiang MD ¹ Ying Yang MD ¹
Yang Ye MD ¹ 💿 👘	Yong-Mei Cha MD ⁴ 💿 🕴 Guo-Sheng Fu MD ¹ 💿

¹ Department of Cardiology, Key Laboratory of Cardiovascular Intervention and Regenerative Medicine of Zhejiang Province, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, China

² Department of Diagnostic Ultrasound & Echocardiography, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, China

³ Department of Cardiology, Jinhua Wenrong Hospital, Jinhua 322118, China

⁴ Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA

Correspondence

Guo-Sheng Fu, MD, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, 310016, China. Email: fugs@zju.edu.cn

Xia Sheng and Yi-Wen Pan contributed equally to the study.

Abstract

Background: His bundle pacing (HBP) is a physiological pacing strategy to preserve the electrical synchrony of ventricular conduction and left ventricular (LV) function. Left bundle branch pacing (LBBP) has emerged as an alternative physiological pacing technique.

Objective: To evaluate cardiac electrical and mechanical synchrony comparing LBBP and HBP in patients with permanent atrial fibrillation (AF).

Methods: Consecutive patients with symptomatic bradycardia and AF were enrolled from January to June of 2019. The cardiac electrical and mechanical synchrony in different pacing mode were evaluated at baseline and after implantation.

Results: Both HBP and LBBP were performed in 20 patients. LBBP significantly widened the QRS duration compared with the intrinsic conduction (113.2 \pm 14.5 vs. 96.5 \pm 16.2 ms; p = .01), while HBP did not (104.5 \pm 22.3 vs. 96.5 \pm 16.2 ms; p = .12). Both LBBP and HBP patients had similar LV myocardial strain measurements for the mechanical synchrony evaluation without significant change compared with baseline. There was no significant difference in right ventricular synchrony measurement between LBBP and HBP. Compared to HBP, LBBP had less interventricular synchrony (IMVD, 14.7 \pm 9.2 vs. 3.1 \pm 12.7 ms, p < .01; Ts-LV-RV, 37.9 \pm 10.7 vs. 18.5 \pm 10.8 ms, p < .001).

Conclusions: Although LBBP's a physiological pacing mode can achieve a similar cardiac electrical and mechanical synchronization when compared to HBP, LBBP results in modest delay in RV activation, and the clinical implication remains to be studied.

Abbreviations: AF, atrial fibrillation; BVP, bi-ventricular pacing; CRT, cardiac resynchronization therapy; GLS, Global longitudinal strain; HBP, His-bundle pacing; HF, heart failure; IMVD, Intraventricular mechanical delay; IVS, interventricular septum; LBBP, left branch bundle pacing; LVAT, the LV activation time; LVDD, left ventricular end diastolic dimension; LVEF, left ventricular ejection fraction; PSD, phase standard deviation; PW-TDI, pulsed-wave Doppler tissue imaging; RVFW, right ventricular free wall; RVP, Right ventricular pacing; TDI, tissue Doppler imaging; TTE, transthoracic echocardiography.

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KEYWORDS

atrial fibrillation, electrical synchronization, His-bundle pacing, left bundle branch pacing, mechanical synchrony

1 | INTRODUCTION

Atrial fibrillation (AF) tends to occur in atria with compromised systolic function, so the prevalence of AF is as high as 22–68% in patients with cardiac dysfunction.^{1.2} Cardiac resynchronization therapy (CRT) has emerged as an alternative choice for patients with heart failure, but evidence to date showed no significant clinical benefit from CRT implantation in patients with AF and normal QRS duration.^{3,4} HBP has emerged as a major physiological pacing strategy to preserve the ventricular electrical and mechanical synchrony.⁵ HBP may provide a better ventricular resynchronization than CRT via the biventricular pacing (BVP) in patients with heart failure (HF) and left bundle branch block (LBBB).⁶ However, HBP is limited by an elevated His bundle capture threshold, lower R-wave amplitudes, and increased risk of lead dislodgement.

Left bundle branch pacing (LBBP) is an emerging alternative physiological pacing, which was first introduced in 2017.⁷ It is a pacing modality of the left ventricular septal pacing to capture the left bundle branch (LBB). Studies have demonstrated that LBBP is feasible with high success rates and low complication rates during long-term followup,^{8,9} and could achieve cardiac resynchronization as an alternative to CRT, especially in patients with LBBB.^{10,11} However, the mechanistic studies on cardiac synchrony with LBBP are scarce. In this study, we aim to prospectively evaluate the cardiac and mechanical synchrony using LBBP versus HBP with an intra-patient-controlled study design in patients with permanent AF.

2 METHODS

2.1 | Study population

One hundred ninety-eight consecutive patients from Sir Run Run Shaw Hospital received conduction system pacing from January to June of 2019, including 58 cases for symptomatic bradycardia and permanent AF. Twenty-six of 58 patients with chronic atrial fibrillation underwent HBP and LBBP. HBP was the preferred method of pacing in our center during the study period. Additionally, LBBP was attempted in patients with the high risks for the threshold increasement of HBP lead, such as calcification, severe tricuspid regurgitation, or low sensing. Finally, these 26 cases were enrolled prospectively, and the data of 20 cases were collected for analysis because of both achievement of HBP and LBBP. The patients with LBBB, RBBB, or intraventricular conduction defect were excluded because of the effect to the assessment of the cardiac electrical and mechanical synchrony. The flow chart can be found in Figure 1. The study protocol was approved by the ethics committee of the Sir Run Run Shaw hospital, and written informed consents were collected from all the patients (Clinical trial: ChiCTR1900025952).

2.2 | Conduction system pacing

Each patient received two pacing leads (Medtronic Select Secure, model 3830, 69 cm, Medtronic Inc, Minneapolis, MN, USA), using a fixed-curve sheath (C315 His, Medtronic Inc, Minneapolis, MN, USA), one for HBP, and another for LBBP as previously described.¹²⁻¹⁵ Twelve-lead electrocardiogram (ECG) and intracardiac electrograms (EGM) were recorded via the lead tip using the electrophysiological recording system (Bard Electrophysiology Lab System, MA, USA). The first lead was advanced to the His bundle region under the fluoroscopic imaging view of the right anterior oblique (RAO) 30°, and then gently rotated counterclockwise to map the His bundle potential. If His potential (Po_{His}) steadily recorded, thresholds were tested. Successful HBP was defined as the same QRS morphology as the intrinsic QRS. Once the pacing parameters were satisfactory (HBP thereshold of < 1.5V @ 0.5 ms), the active fixation was deployed.¹⁶

The LBBP lead placement has been previously described by Huang et al.¹⁵ When the pacing lead was perpendicularly screwed into the IVS near LV endocardium, the paced QRS of a right bundle branch block (RBBB) pattern by a unipolar pacing from the lead tip was observed. Left ventricular activation time (LVAT) was defined as the time from the intracardiac pacing stimulus to the peak R-wave in leads V5 and V6 (Stim-LVAT). LBB capture was be confirmed by a recording retrograde His potential and anterograde LBB potential (Po_{LBB}), abrupt decrease in Stim-LVAT of \geq 10 ms, or demonstration of selective LBBP.¹⁷ LBB capture threshold of < 1.0V @ 0.5 ms was satisfactory. A typical case is shown in Figure 2.

2.3 Device programming

All patients received a dual-chamber pacemaker. The HBP lead was connected to the atrial port, while the LBBP lead was connected to the ventricular port. The device was programmed at the DVIR mode of 60 ppm to avoid oversensing of HBP lead with lower R-wave amplitude, while turning off the ventricular safety pacing. The atrioventricular interval was set at 120/100 ms.

2.4 Cardiac synchrony evaluation

2.4.1 Cardiac electrical synchrony

We evaluated the cardiac electrical synchrony using the QRS duration and LVAT using 12-lead ECG in HBP and LBBP. Po_{His} -LVAT and



FIGURE 1 Flow chart of study

GLS, Global longitudinal strain; HBP, His-bundle pacing; IVS, interventricular septum; IMVD, Intraventricular mechanical delay; LBBP, left bundle branch pacing; LVAT, the LV activation time; PSD, phase standard deviation; PW-TDI, pulsed-wave Doppler tissue imaging; RVFW, right ventricular free wall; RVP, right ventricular pacing; TDI, tissue Doppler imaging

Po_{LBB}-LVAT were defined as the time from the intracardiac pacing stimulus to the peak R-wave in leads V5 and V6, respectively (Figure 1E and 1F). The parameters' measurement was done by two independent experienced ECG specialists who were blinded to the study.

2.4.2 | Cardiac mechanical synchrony

The cardiac mechanical synchrony was evaluated by transthoracic echocardiography (TTE) within 7 days before implantation as baseline intrinsic rhythm and at follow-up. Echocardiography was done by an experienced specialist who was blinded to the study. The data were collected in HBP and LBBP pacing with a washout period of 2 min. The LBBP parameter was programmed to unipolar pacing for 30 min to evaluate the cardiac synchrony.

2.4.3 | Left ventricular synchrony

The left ventricular synchrony was evaluated by the speckle-tracking echocardiography (STE). The global longitudinal strain (GLS) and phase standard deviation (PSD) were used as LV mechanical synchrony parameters. GLS was obtained by averaging all 17 segments strain values. PSD was defined as standard deviation of time to peak strain in 17 segments from the apical views.

2.4.4 | Right ventricular synchrony

The right ventricular synchrony was evaluated by tissue Doppler imaging (TDI) and pulsed-wave Doppler tissue imaging (PW-TDI) echocardiography. The regional durations of time measured for the basal segments in the right ventricle (RV) and RV free walls (RVFW) and interventricular septum (IVS) were from the start of QRS to the peak velocity of S wave (Ts), respectively.¹⁸ The difference of Ts (Ts-RVFW-RV) between RVFW and RV, and difference of Ts (Ts-IVS-RV) between IVS and RV were evaluated as universal indicators of right ventricular activation pattern.

2.4.5 | Interventricular synchrony

The interventricular synchrony was also evaluated by TDI and PW-TDI echocardiography. Intraventricular mechanical delay (IVMD) is an echocardiographic index that represents the degree of interventricular contraction delay.¹⁸ IVMD was defined as the difference between the LV pre-ejection period (aortic pre-ejection time, APEI) and RV preejection period (pulmonary pre-ejection time, APEI). The pre-ejection period was the time interval form QRS onset to the beginning of the blood flow of the LV and RV outflow tracts respectively. The cutoff value of IVMD is 40 ms.¹⁸ IVMD > 40 ms indicates that the ventricular pacing site is oriented toward right ventricle (RV), and the



HBP, PSD = 25ms, GLS = -17.8% LBBP, PSD = 29ms, GLS = -17.4%

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FIGURE 2 Electrograms and lead position of HBP/LBBP. A 54-year-old female received a dual-chamber pacemaker with HBP and LBBP due to chronic atrial fibrillation with slow ventricular rate and narrow QRS wave. Intrinsic electrogram was identified (A). Left bundle branch (LBB) potential and His bundle potential were both recorded as a discrete potential before the QRS complex (B, C, black arrow). The duration of LBB potential to QRS (Po_{LBB} -QRS, PV = 28 ms) was shorter than His potential to QRS (Po_{His} -QRS, HV = 48 ms) (B, C). The LVAT remained constant at low (D) and high output (E) when the LBB was captured. A retrograde His potential could be recorded during low-output LBBP (D, black arrow) and an anterograde LBB potential could be recorded during low-output HBP (F, black arrow). Po_{LBB} -LVAT (66 ms) and Po_{His} -LVAT (76 ms) were shown in (E) and (F), respectively. The LBBP lead is located between the right ventricular apex and the HBP lead (G, H). GLS and PSD measured by speckle-tracking echocardiography in different pacing modes were shown in this figure (I). GLS, Global longitudinal strain; HBP, His-bundle pacing; LBBP, left bundle branch pacing; LVAT, the LV activation time; PSD, phase standard deviation [Color figure can be viewed at wileyonlinelibrary.com]

obvious presence of intraventricular desynchrony. The regional durations of time measured for the basal segments in the right ventricle (RV) and LV lateral walls were from the start of QRS to the peak velocity of S wave (Ts),¹⁸ respectively. The difference of Ts (Ts-LV-RV) between LV and RV was also evaluated. A Ts-LV-RV delay > 65 ms was used as a cut-off for desynchrony.¹⁹ Therefore, we used IVMD and Ts-LV-RV as universal indicators of intraventricular activation pattern, and compared interventricular synchrony in various pacing modes.

2.5 | Follow-up

The parameters of the left ventricular ejection fraction (LVEF) and LV end-diastolic dimension (LVEDD) were measured at baseline and at the follow-up. The lead parameters, including the capture thresholds, R-wave amplitudes and pacing impedances were recorded at one day, first, and third month after implantation.

2.6 | Statistical analysis

All the analyses were conducted using the SPSS software version 22.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as mean \pm standard deviation, while categorical variables were expressed as frequencies or percentages. The Fisher's exact test was used to compare the categorical data between the groups, and the paired t test was used to compare the numerical data. A p < .05 was considered to be statistically significant.

3 | RESULTS

3.1 | Patient characteristics

Among 26 patients with symptomatic bradycardia and AF, 20 (mean age of 72.9 \pm 9.0 years; 13 males) had HBP and LBBP lead placement. The baseline clinical details of the patients are shown in Table 1. LVEF at baseline was 62.0% \pm 12.0% with underlying LV dysfunction in 15% of the patients. The baseline QRS duration was 96.5 \pm 16.2 ms. All patients had normal QRS duration except three patients had RBBB due to RBB injury during LBBP lead implantation without recovering postprocedure.

3.2 | Procedure characteristics

The mean procedure time was 110.8 ± 34.9 min. In four patients with complete atrioventricular block, we were unable to place the HBP lead and the LBBP was successful with RV pacing backup; and in two patients with cardiomyopathy, HBP was successful but LBBP did not achieve significant narrowing of QRS width and the deep septal pacing lead as a backup RV lead was accepted (Figure 2). Selective HBP could be achieved in 14 out of 20 patients, while RBBB was able to be corrected in two out of three patients. Selective LBBP could be found in 10 patients.

TABLE 1 Baseline clinical and demographic characteristics of patients

Total number of patients	26
Successful HBP and LBBP	20 (76.9%)
Age, mean (SD)	72.9 ± 9.0
Male, N (%)	17(65.4%)
Body mass index (kg/m ²)	24.9 ± 4.2
QRS duration (ms), mean (SD)	96.5 ± 16.2
Hypertension, N (%)	17(65.4%)
Diabetes, N (%)	10(38.5%)
Coronary artery disease, N (%)	17(65.4%)
Ischemic stroke, N (%)	4(15.4%)
Cardiomyopathy, N (%)	4(15.4%)
Ultrasonic cardiogram	
LVEF%, mean (SD)	62.0 ± 12.0
LVDD (mm), mean (SD)	51.8 ± 5.4

Abbreviations: HBP, His-bundle pacing; LBBP, left branch bundle pacing; LVDD, left ventricular end diastolic dimension; LVEF, left ventricular ejection fraction.

Values are mean (SD), or number (%).

3.3 | Lead parameters

An intraoperative testing of the leads showed that the following parameters were significantly increased for the LBBP lead: The R-wave amplitude (9.7 \pm 4.5 vs. 3.7 \pm 3.1 mV, respectively; p < .01) and the pacing impedance (713.7 \pm 171.9 vs. 597.0 \pm 120.4 Ω , respectively; p = .01). On the other hand, the threshold did not show a significant difference (HBP vs. LBBP: 1.0 \pm 0.3 vs. 0.8 \pm 0.3 V, respectively; p = .18). The lead parameters remained stable and showed the same trend during the follow-up period (Figure 3).

3.4 Cardiac electrical synchrony measurement

There was no significant change in QRS duration after HBP compared with baseline (104.5 \pm 22.3 vs. 96.5 \pm 16.2 ms, respectively; p = .12), while the LBBP slightly widened the QRS complex (113.2 \pm 14.5 vs. 96.5 \pm 16.2 ms, respectively; p = .01), as shown in Figure 4A. The paced QRS duration of HBP and LBBP were unchanged at the follow-up.

The His potential was recorded in all cases, and a local P potential was recorded in 16 patients (80%). The mean His-ventricular (HV) interval was 47.3 ± 2.8 ms, and the mean PV interval was 21.6 ± 3.9 ms. Paced LVAT was similar in HBP and LBBP (68.5 ± 13.1 vs. 66.5 ± 11.6 ms, respectively; p = .68) (Figure 4B).

3.5 | Left ventricular synchrony measurement

The cardiac mechanical synchrony parameters (GLS and PSD) were separately evaluated in HBP and LBBP. The STE revealed no



FIGURE 3 Lead parameters of HBP and LBBP. LBBP leads had much higher R-wave amplitudes and impedance than HBP. The lead parameters of both pacing modes remained stable during 3-month follow-up. HBP, His-bundle pacing; LBBP, left bundle branch pacing

significant differences in these parameters between LBBP and HBP as follows: LV GLS ($-13.8 \pm 3.0\%$ vs. $-14.2 \pm 2.6\%$, respectively; p = .52) and PSD (51.6 ± 13.4 vs. 48.9 ± 15.5 ms, respectively; p = .61). Moreover, left ventricular synchrony parameters of LBBP is not inferior to those of intrinsic rhythm (GLS, $-13.8 \pm 3.0\%$ vs. $-16.1 \pm 4.0\%$, respectively; p = .32; PSD, 51.6 ± 13.4 vs. 44.5 ± 18.8 ms, respectively; p = .14) (Figure 5).

3.6 | Right ventricular synchrony measurement

Figure 6 shows right ventricular mechanical synchrony parameters (Ts-RVFW-RV and Ts-IVS-RV) in HBP and LBBP respectively. There were no significant differences in these parameters between the LBBP group and HBP group (Ts-RVFW-RV, 169.3 \pm 47.3 vs. 153.3 \pm 44.7 ms, respectively; p = .28; Ts-IVS-RV, 117.3 \pm 66.2 vs. 144.0 \pm 55.1 ms, respectively; p = .19). Moreover, right ventricular synchrony parameters



FIGURE 4 Comparison of QRS duration and LVAT of LBBP and HBP. Paced QRS duration of LBBP was slightly wider than that of intrinsic. No difference was found between intrinsic and paced QRS duration in HBP (A). Mean LVAT of tip-paced QRS complex in HBP (Po_{His}-LVAT) was similar to that of LBBP (Po_{LBB}-LVAT) (B). HBP, His-bundle pacing; LBBP, left bundle branch pacing; LVAT, the LV activation time

eters in LBBP were similar to the baseline (Ts-RVFW-RV, 169.3 \pm 47.3 vs. 184.3 \pm 72.3 ms, respectively; p = .49; Ts-IVS-RV, 117.3 \pm 66.2 vs. 141.4 \pm 43.0 ms, respectively; p = .32).

3.7 | Interventricular synchrony measurement

Seventeen patients with normal QRS duration were evaluated for interventricular mechanical synchrony. Figure 7 showed interventricular mechanical synchrony parameters (IMVD and Ts-LV-RV) in HBP and LBBP, respectively. LBBP had a greater IMVD and Ts-LV-RV compared with HBP pacing (IMVD, 14.7 ± 9.2 vs. 3.1 ± 12.7 ms, p < .01; Ts-LV-RV, 37.9 ± 10.7 vs. 18.5 ± 10.8 ms, p < .001).

3.8 | Follow-up outcome

During the follow-up period, none of the study patients had HF rehospitalization. None of the study patients developed complications,



FIGURE 5 Left ventricular synchrony of LBBP and HBP. GLS and PSD measured by speckle-tracking echocardiography in different pacing modes. Both LBBP and HBP mode had similar cardiac mechanical synchrony to those of intrinsic rhythm. GLS, Global longitudinal strain; HBP, His-bundle pacing; LBBP, left bundle branch pacing; PSD, phase standard deviation



FIGURE 6 Right ventricular synchrony of LBBP and HBP. Ts-RVFW-RV and Ts-IVS-RV were measured by TDI and PW-TDI echocardiograph. Both LBBP and HBP mode had similar right ventricular mechanical synchrony to those of intrinsic rhythm. GLS, Global longitudinal strain; HBP, His-bundle pacing; IVS, interventricular septum; LBBP, left bundle branch pacing; PSD, phase standard deviation; RVFW, right ventricular free wall



FIGURE 7 Interventricular synchrony of LBBP and HBP. IMVD and Ts-LV-RV were measured by TDI and PW-TDI echocardiograph. LBBP had significant more IMVD and Ts-LV-RV than HBP (A, B). HBP, His-bundle pacing: IMVD. Intraventricular mechanical delay: LBBP. left branch bundle pacing; PW-TDI, pulsed-wave Doppler tissue imaging; TDI, tissue Doppler imaging

including lead dislodgement, cardiovascular perforation, tricuspid valve injury, or loss of capture at 3-month follow-up.

DISCUSSION 4

In this study, we evaluated the feasibility, safety, and the cardiac electrical and mechanical synchrony between permanently implanted HBP and LBBP with a self-control design. The main findings of this study are (1) HBP and LBBP can be achieved in one procedure; (2) LBBP had better R-wave sensing compared with HBP; (3) LBBP and HBP had similar left and right ventricular mechanical synchrony, yet LBBP had less interventricular synchrony.

AF is the most common persistent arrhythmia. The incidence of AF increases with age and is up to 10% among people over 75 years old.¹ The prevalence of AF is high in patients with cardiac dysfunction.² Several studies have demonstrated that the applications of RVP are able to improve the quality of life of patients with AF with symptoms. However, conventional RVP could lead to unsynchronized left ventricular <u>1530 |</u> WILI

contraction, results in compromised systolic and diastolic function, ventricular remodeling, and eventually unstable hemodynamics. A number of previous studies have shown that the long-term outcome of BVP was effective in patients with AF and wide QRS morphology compared with those with RVP. Previous studies showed no significant clinical benefit from CRT implantation in patients with normal QRS duration.³ In these patients, BVP can cause iatrogenic dyssynchrony, leading to increased mortality.³ The present guidelines suggest that the indication for BVP in AF patients is only a Class IIa/b, even for those with intrinsic LBBB.

To date, HBP is considered to be a major physiological pacing strategy. HBP allows the ventricles to be activated via the His-Purkinje system. As a result, normal physiological cardiac activation is maintained when His-bundle pacing is applied to patients with a narrow QRS duration. It may even restore physiological activation sequence in patients with RBBB or LBBB.⁷ However, some recent studies showed that HBP was associated with lower implantation success rate, higher lead dislocation rate, and increased incidence of late rise in the capture thresholds. Vijayaraman et al. reported that the 5-year generator replacement rate in HBP was higher than that of RVP (9% vs. 1%, respectively).⁵ LBBP is an emerging physiological pacing technique. LBB is a wide network beneath the endomyocardium of the left septum. Thus, positioning the lead deep enough to the left septal subendomyocardium could easily capture the left conduction system, as described by the animal study.²⁰ The advantages of this method are greater pacing threshold and more stable R wave sensing than that from HBP. Accumulating evidence has demonstrated that LBBP, like HBP, produces faster and more synchronized left ventricular activation, indicated that LBBP may serve as an alternation in patients with difficulty in HBP implantation.¹⁰ A previous study indicated that AF patients with LBBB have greater improvement in LVEF and NYHA class function than patients with narrow QRS from HBP/LBBP after AVJ ablation. LBBP showed similar outcomes to patients with HBP, but with lower pacing thresholds and higher R-wave amplitude.²¹ It is reasonable to consider that HBP and LBBP are the better choice to achieve an optimal activation in the LV, especially in patients with LV dysfunction.^{22,23}

In this study, HBP and LBBP had similar QRS duration and LVAT. The feasibility of LBBP, as demonstrated in this study, suggested that this novel pacing modality is equally feasible as HBP in patients with AF. The unique finding in our study is the difference between the HBP and LBBP in interventricular synchrony. LBBP with a unipolar configuration had slightly late myocardial contraction of right ventricle compared to HBP. The capture of the LBB can ensure the fast left bundle branch and LV activation. However, the incomplete RBBB morphology as shown in 12-lead ECG renders a slight delay in RV activation and contraction. The clinical significance of this modest delay in RV contraction in the long-term remains to be learned.

4.1 | Limitations

The present study was a single-center prospective study with an intrapatient-controlled design; its main shortcomings were the limited sample size and the short follow-up period. Therefore, further multicentral and randomized controlled trials should be conducted to verify its long-time safety and clinical benefits in the ventricular synchrony. As our data have shown and according to some current studies, the novel pacing technique of LBBP is physiological, safe, and effective and can achieve cardiac synchronization.

However, there are some problems to overcome. The Select Secure 3830 lead should be deeply screwed into the IVS for LBB capture. However, no present tools, including the 3830 lead, are designed for this procedure. In addition, the long-term integrity of the pacing lead and the interaction between the lead and IVS need further evaluation. The effect of the physiological and pathological interaction between the left and right ventricles by continuous deep septal pacing is another focus.

5 | CONCLUSIONS

In this study, we demonstrated LBBP as a physiological pacing can achieve cardiac electrical and mechanical synchronization as with HBP in patients with permanent AF. Although LBBP results in modest delay in RV activation, and the clinical implication remains to be studied.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

CLINICAL TRIAL

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Yi-Wen Pan MD ^(b) https://orcid.org/0000-0003-4909-7301 Jie-Fang Zhang MD ^(b) https://orcid.org/0000-0002-0327-1987 Ya-Xun Sun MD ^(b) https://orcid.org/0000-0002-5457-7855 Yang Ye MD ^(b) https://orcid.org/0000-0002-7003-5714 Yong-Mei Cha MD ^(b) https://orcid.org/0000-0002-5897-9464 Guo-Sheng Fu MD ^(b) https://orcid.org/0000-0001-7304-7975

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