Left Bundle Branch Pacing Postatrioventricular Junction Ablation for Atrial Fibrillation: Propensity Score Matching With His Bundle Pacing

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BACKGROUND: Left bundle branch pacing (LBBP) has emerged as a promising pacing modality to preserve physiological left ventricular activation; however, prospective data evaluating its long-term safety and efficacy in pacemaker-dependent patients following atrioventricular junction (AVJ) ablation are lacking. This study aimed to examine the feasibility, safety, and efficacy of LBBP in patients with atrial fibrillation and heart failure (HF) after AVJ ablation and compare LBBP with His bundle pacing (HBP) through a propensity score (PS) matching analysis.

METHODS: We prospectively enrolled patients with atrial fibrillation and HF referred for AVJ ablation and LBBP between July 2017 and December 2019. The control group was patients selected from HBP implants performed from 2012 to 2019 using PS matching with a 1:1 ratio.

RESULTS: A total of 99 patients were enrolled in the study. The LBBP implant success rate was 100%. Left ventricular ejection fraction improved from baseline 30.3±4.9 to 1-year 47.3±14.5 in HF patients with reduced ejection fraction and from baseline 56.3±12.1 to 1-year 62.3±9.1 in HF patients with preserved ejection fraction (both \(P<0.001\)), and left ventricular ejection fraction in both groups remained stable for up to 3 years of follow-up. A threshold increase >2 V at 0.5 ms occurred in only one patient. Of 176 (81.9%) of 215 patients who received permanent HBP post-AVJ ablation, 86 were matched to the LBBP group by 1:1 PS (propensity score matched His bundle pacing, N=86; propensity score matched left bundle branch pacing, N=86). No significant differences in echocardiographic or clinical outcomes were observed between the 2 groups (\(P>0.05\)), whereas lower thresholds, greater sensed R-wave amplitudes, and fewer complications were observed in the propensity score matched left bundle branch pacing group (\(P<0.05\)).

CONCLUSIONS: LBBP is feasible, safe, and effective in patients with atrial fibrillation and HF post-AVJ ablation and has similar clinical benefits, a higher implant success rate, better pacing parameters, and fewer complications compared with HBP.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: atrial fibrillation | atrioventricular junction ablation | cardiac pacing | heart failure | His bundle pacing | left bundle branch pacing

In patients with atrial fibrillation (AF) and symptomatic heart failure (HF) despite optimal medical therapy, atrioventricular junction (AVJ) ablation and ventricular pacing is an effective therapy to slow and regularize ventricular rate. Nevertheless, these beneficial effects may be offset by ventricular dyssynchrony, which occurs with right ventricular pacing (RVP). Several studies have compared the efficacy of biventricular pacing (BVP) and...
WHAT IS KNOWN?

- While previous studies have demonstrated the safety and feasibility of left bundle branch pacing in patients with heart failure, the clinical value of this approach in patients with atrial fibrillation and heart failure post–atrioventricular junction ablation remains unknown.
- Left bundle branch pacing is considered as an alternative to His bundle pacing for delivering physiological pacing, but the advantages and disadvantages of these 2 pacing modalities in this population have not been addressed.

WHAT THE STUDY ADDS

- Left bundle branch pacing significantly improved left ventricular ejection fraction, similar to His bundle pacing, and both left bundle branch pacing and His bundle pacing had a similar impact on the composite endpoints of all-cause death or heart failure hospitalization in patients with atrial fibrillation and heart failure post-atrioventricular junction ablation.
- Left bundle branch pacing has a higher implant success rate, better pacing parameters, and fewer late lead-related complications than His bundle pacing.
- Left bundle branch pacing makes the atrioventricular junction ablation procedure technically easier and usually does not require a backup lead as is often required for His bundle pacing.

Nonstandard Abbreviations and Acronyms

| Abbreviation | Description |
|--------------|-------------|
| AF           | atrial fibrillation |
| AVJ          | atrioventricular junction |
| BVP          | biventricular pacing |
| HBP          | His bundle pacing |
| HF           | heart failure |
| HFH          | heart failure hospitalization |
| HFrEF        | heart failure with reduced ejection fraction |
| LBB          | left bundle branch |
| LBBP         | left bundle branch pacing |
| LV           | left ventricular |
| LVEF         | left ventricular ejection fraction |
| NYHA         | New York Heart Association |
| PS           | propensity score |
| PS-HBP       | propensity score matched His bundle pacing |
| PS-LBBP      | propensity score matched left bundle branch pacing |
| RBBB         | right bundle branch block |
| RVP          | right ventricular pacing |
| TR           | tricuspid regurgitation |

RVP in patients with AF post-AVJ ablation and demonstrated that BVP was superior to RVP for improving left ventricular (LV) function or reducing the incidence of HF morbidity endpoints.3–6 To avoid the adverse effects of chronic RVP, His bundle pacing (HBP) or left bundle branch pacing (LBBP) are novel methods for delivering cardiac resynchronization therapy (CRT) by facilitating conduction through the native His-Purkinje system.7–14 In observational studies, HBP combined with AVJ ablation has been observed to be effective in patients with either wide or narrow intrinsic QRS morphology.15–17 LBBP provides ample space to allow AVJ ablation with low capture threshold and high amplitude R-waves.18–20 However, there are limited prospective data evaluating LBBP as the primary pacing approach in patients with AF and HF requiring AVJ ablation and no data evaluating the advantages and disadvantages between LBBP and HBP. In this study, we aimed to (1) assess the feasibility and long-term safety and efficacy of LBBP in patients with AF and HF post-AVJ ablation and (2) compare the implant success rates, pacing parameters, complications, and clinical benefits of LBBP and HBP.

METHODS

Study population

This single-center, prospective registry study was performed at the First Affiliated Hospital of Wenzhou Medical University between July 2017 and December 2019. Patients who met the following inclusion criteria were recruited: (1) persistent or long-standing persistent AF and symptomatic HF despite optimal medical therapy and (2) AVJ ablation and attempted permanent LBBP. We excluded patients who were aged <18 years, were pregnant, had a life expectancy of <1 year, or had nonspecific intraventricular conduction delay. In addition to the primary study, we also selected patients who attended our hospital between 2012 and 2019 for HBP and AVJ ablation. These patients were recruited, and their data were retrospectively analyzed. This study was approved by the Ethics Committee of the first affiliated hospital of Wenzhou Medical University, and all patients provided informed consent. The data from our study are available from the corresponding author upon reasonable request.

Implantation Procedure

An electrophysiological recording system (GE CardioLab EP Recording System 2000; GE) was used to record the intracardiac electrograms and 12-lead electrocardiograms. We utilized the methods we have previously described for LBBP lead implantation,21 confirmation of LBBP capture22,23 and AVJ ablation.24 Figure 1 shows the study workflow. We performed LBBP and AVJ ablation during the same procedure.

Secondary LBBP was when patients in whom we first attempted acute HBP and AVJ ablation but failed to achieve permanent HBP and then switched to LBBP. Figure 2 shows the design of LBBP as a secondary alternative strategy for patients with failed HBP.
Data Collection and Follow-Up
The baseline patient characteristics were documented. Paced QRS duration (stimulus to the end of QRS), stimulus-to-peak LV activation time, total procedural time, AVJ ablation duration, number of AVJ ablation sites, and acute periprocedural complications (procedure-related deaths, septal hematoma, septal perforation, pneumothorax, pericardial effusion, and intravenous puncture-related arterial injury) were recorded. Acute and chronic pacing thresholds, R-wave amplitudes, and impedance were measured at the implantation and follow-up visits. Patients underwent regular follow-up at 1, 3, and 6 months and then annually after implantation. At the follow-up visit, the New York Heart Association (NYHA) functional class and echocardiographic parameters, such as left ventricular ejection fraction (LVEF) and mitral and tricuspid valve regurgitation graded (mild as first degree, moderate as second degree, and severe as third degree) were collected. Clinical outcomes including heart failure hospitalization (HFH) and all-cause mortality were also recorded. Late lead-related complications, including dislodgement, loss of capture, perforation, infection, and threshold increase by ≥2 V at 0.5 ms, were noted.

Statistical Analyses
Continuous data are presented as mean±SD or median (interquartile range), and categorical data are summarized as frequencies (percentages). The χ² or Fisher exact tests were used to analyze categorical data. The paired t-tests or Wilcoxon signed-rank tests were used to compare differences between the baseline and specific time points during follow-up within the group. An independent sample t test or Wilcoxon rank-sum test was used to evaluate the between-group differences. Data among multiple groups were evaluated by 1-way ANOVA with the Bonferroni post-hoc test for comparisons between groups. Statistical significance was set at P<0.05; all tests were 2-sided. Statistical analyses were performed using SPSS software (IBM Corporation).

Propensity Score Matching Analysis
To adjust for bias due to potential confounders, a propensity score (PS) matching approach was performed to match participants in HBP and LBBP groups at a ratio of 1:1. Specifically, potential confounding factors including age, sex, diabetes, renal dysfunction, ischemic cardiomyopathy, intrinsic QRS duration, intrinsic ventricular rate, LVEF, QRS morphology, NYHA functional class, and medication use for HF were fit into a multivariable logistic model with a caliper as 0.05. This procedure of PS matching was performed by SPSS software version 22 (IBM Corp, Armonk, NY). Potential different efficacy on the 2 therapies were visualized by Kaplan-Meier survival curves and further evaluated by log-rank tests in associated outcomes (all-cause mortality or HFH, whichever occurred first) and late lead-related complications.

RESULTS
Baseline Characteristics
A total of 99 patients were recruited into the prospective study, of which 76 underwent de novo LBBP, and 23 had LBBP attempted after an initial HBP attempt.
HBP threshold >1 V at 0.5 ms after AVJ ablation, N=7; His capture/corrective threshold >2 V at 0.5 ms, N=13; failure to correct left bundle branch block, N=2; His lead fixation failure, N=1), and all were successfully switched to LBBP. The success rate of permanent LBBP and AVJ ablations was 100%. The baseline characteristics of the entire study population with permanent LBBP and AVJ ablation and the subgroups are shown in Table 1.

Electrophysiological Characteristics
At implantation, the mean paced QRS duration was 130.5±13.6 ms. The mean stimulus-to-peak LV activation time was 74.8±9.5, 74.7±6.1, and 80±8 ms in patients with narrow QRS complex, right bundle branch block (RBBB), and left bundle branch block, respectively. During bipolar pacing testing in 99 patients, 40 (40.4%) patients achieved anodal capture, with complete elimination of the RBBB pattern in 23 (23.2%) patients. In those who had RBBB pattern elimination, the QRS duration was significantly decreased from 135±13.5 ms with unipolar pacing to 123.6±13.3 ms with bipolar pacing (P<0.001, N=23). The mean bipolar pacing threshold for complete RBBB pattern elimination was 3.7±2.0 V at 0.5 ms (N=23; range, 0.25 to 1 V at 0.5 ms). The pacing parameters are displayed in Figure 3. The mean capture threshold was found to be slightly increased at 1-year follow-up (0.47±0.15 vs 0.6±0.18 V at 0.5 ms, P<0.001, N=96), and no further change was observed at 2-year follow-up (0.6±0.18 vs 0.61±0.17 V at 0.5 ms, P=0.123, N=83) and within 3-year follow-up (0.64±0.19 vs 0.63±0.18 V at 0.5 ms, P=0.835, N=49). Only one patient was observed to have an increase in the threshold above 2 V at 0.5 ms during follow-up. Similar dynamic changes were observed in the sensed R-wave amplitude and impedance during follow-up (Figure 3).

Echocardiographic Data and NYHA Functional Class
Ninety-six patients completed 1-year follow-up. A total of 2 patients died within 1 year, and 1 patient was lost to 1-year follow-up. The mean LVEF increased from

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Figure 2. Case of left bundle branch pacing (LBBP) as a secondary alternative strategy performed in patients with failed His bundle pacing (HBP).
A patient diagnosed with dilated cardiomyopathy, New York Heart Association (NYHA) class IV, atrial fibrillation (AF) with rapid ventricular rate received LBBP due to the increased His capture threshold caused by atrioventricular junction (AVJ) ablation. (A) Native electrogram (EGM) showed AF. The dual-lead method (D) was used with one pacing lead placed in the His bundle region with a pacing output of 1 V at 0.5 ms for selective HBP (B) and another pacing lead (backup pacing) placed distally to the left bundle branch area where LBBP was achieved at 0.5V at 0.5 ms (C). Ablation of the AVJ was performed to achieve a complete atrioventricular block with accelerating junctional rhythm during ablation (D). After AVJ ablation, the HBP threshold increased to 5 V at 0.5ms (E), while the LBBP threshold remained unchanged (F). The His region lead was subsequently moved to the atrial septum while the LBBP lead was maintained in place (G).
Complications and Adverse Events

No acute procedure-related complications were noted. No patient showed an increase in the LBBP capture threshold post-AVJ ablation. At a mean follow-up of 27.7±8.1 months, 10.1% (10/99) of patients had experienced HFH. The all-cause mortality was 5.1% (5/99) and death was due to end-stage HF (3), pneumonia (1), or diabetic foot infection (1). One patient had an increase in capture threshold of >2.0 V at 0.5 ms at the 13-month follow-up; however, the LV septal capture remained low at 0.75 V at 0.5 ms. No other complications such as LV perforation, loss of ventricular capture, and pocket infection occurred during follow-up.

Propensity Score Matching Analysis

From 2012 to 2019, 176 of 215 patients with AF and HF successfully underwent permanent de novo HBP and AVJ ablation, the success rate of which was lower than with de novo LBBP (81.9% versus 100%; P<0.001). Detailed information on the causes of HBP failure is presented in the supplemental text (Results in Supplemental Material). A total of 176 patients with permanent HBP were matched with 99 patients who underwent permanent LBBP through PS. Subsequently, 172 patients were successfully matched (propensity score-matched His bundle pacing (PS-HBP), N=86; propensity score-matched left bundle branch pacing (PS-LBBP), N=86). Detailed information on the overall cohort is presented in Table S1. The baseline characteristics of the PS-matched cohort are presented in Table 2. Procedure and pacing characteristics, clinical events, and late lead-related complications were analyzed in the PS-matched cohort. The echocardiographic outcome and NYHA functional class at 1-, 2-, and 3-year follow ups were analyzed based on a new PS-matched cohort created in patients who had reached the target follow-up time. The baseline characteristics of the PS-HBP and PS-LBBP groups during the yearly follow-up are shown in Table S2.

Procedure and Pacing Characteristics

Table 3 shows the procedure and pacing characteristics for both the PS-HBP and PS-LBBP groups. Patients in the PS-LBBP group had a wider paced QRS duration, shorter AVJ ablation times, shorter total procedural time, fewer numbers of ablation sites, fewer additional ventricular leads, lower acute threshold, and higher acute sensed R-wave than patients in the PS-HBP group. Moreover, 97.7% (84/86) of patients were observed to have acute threshold of <1 V at 0.5 ms in the PS-LBBP group, while this was observed in 48.8% (42/86) of the patients in the PS-HBP group (P<0.001). In the PS-LBBP group, 54.7% (47/86) of patients had an additional ventricular lead for defibrillation, synchronization, or safety backup function. In the PS-HBP group, 97.7% (84/86) of patients had an additional ventricular lead for defibrillation or safety backup function. No acute peri-procedural complications occurred in either of the groups.

Echocardiographic Data and NYHA Functional Class

Echocardiographic outcomes and NYHA functional classes among the PS-HBP and PS-LBBP groups are presented in the supplemental text (Results in Supplemental Material). A total of 176 patients with permanent HBP were matched with 99 patients who underwent permanent LBBP through PS. Subsequently, 172 patients were successfully matched (propensity score-matched His bundle pacing (PS-HBP), N=86; propensity score-matched left bundle branch pacing (PS-LBBP), N=86). Detailed information on the overall cohort is presented in Table S1. The baseline characteristics of the PS-matched cohort are presented in Table 2. Procedure and pacing characteristics, clinical events, and late lead-related complications were analyzed in the PS-matched cohort. The echocardiographic outcome and NYHA functional class at 1-, 2-, and 3-year follow ups were analyzed based on a new PS-matched cohort created in patients who had reached the target follow-up time. The baseline characteristics of the PS-HBP and PS-LBBP groups during the yearly follow-up are shown in Table S2.

Table 1. Baseline Characteristics

| Number of patients | LBBP, N=99 | De novo LBBP, N=76 | Secondary LBBP, N=23 | P Value |
|--------------------|------------|--------------------|----------------------|---------|
| Age, y             | 69±9.7     | 70±8.6             | 67±12.7              | 0.207   |
| Male               | 48±13.5    | 36±47.4            | 12±52.2              | 0.886   |
| Hypertension       | 87±6.7     | 48±5.3             | 19±82.6              | 0.081   |
| Diabetes           | 28±23.3    | 20±23.3            | 8±34.8               | 0.43    |
| Renal dysfunction  | 27±23.3    | 19±25.0            | 8±34.8               | 0.256   |
| ICM                | 12±13.2    | 10±13.2            | 2±8.7                | 0.566   |
| NICM               | 87±6.7     | 49±64.5            | 18±78.3              | 0.219   |
| PCI                | 9±9.1      | 8±10.5             | 1±4.3                | 0.366   |
| Intrinsic QRS duration, ms | 116±33.1 | 120±35.1          | 105.5±22.7           | 0.059   |
| Intrinsic ventricular rate, beats/min | 90±19.3 | 90.5±19.3         | 92.2±23.7            | 0.712   |
| Baseline LVEF, %   | 40±15.2    | 40±14.9            | 38.9±16.4            | 0.874   |
| QRS morphology     | 0.1        | 0.1                | 0.1                  | 0.1     |

1ICM indicates ischemic cardiomyopathy; LBBP, left bundle branch block; LBBP, left bundle branch pacing; LVEF, left ventricular ejection fraction; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association; PCI, percutaneous transluminal coronary intervention; and RBBB, right bundle branch block.

30.3±4.9 at baseline to 47.3±14.5 at 1 year, and the proportion of NYHA functional class III to IV decreased from 88.3% at baseline to 20% at 1 year in 60 patients with heart failure with reduced ejection fraction (HFrEF; both P<0.001). The mean LVEF increased from 56.3±12.1 to 62.3±9.1 at 1 year, and the proportion of NYHA functional class III-IV decreased from 69.4% to 2.8% (both P<0.001) in 36 patients with heart failure with preserved ejection fraction (Figure 3). After 1 year, no further significant improvement in NYHA functional class was observed in either group (all P>0.05). Similar dynamic changes in the proportions of moderate or severe tricuspid regurgitation and moderate or severe mitral regurgitation are shown in Figure 3. However, a further significant improvement in LVEF was observed at 2 years in the 2-year follow-up data of 53 patients with HFrEF and in the 3-year follow-up data of 29 patients with HFrEF (49±13.7 at 1 year and 52±14.7 at 2 years, N=53, P=0.005; 52±13 at 1 year and 55.1±12.6 at 2 years, N=29, P=0.027).
shown in Figure 4. Patients in both the PS-HBP and PS-LBBP groups exhibited similar improvements in LVEF, NYHA functional class, tricuspid regurgitation, and mitral regurgitation at the 1-, 2-, and 3-year follow-up examination, respectively (PS-LBBP versus PS-HBP, all P > 0.05).

Clinical Events and Late Lead-Related Complications

During a mean follow-up of 28.9±11.9 months, a total of 16 patients (18.6%) receiving HBP and 14 patients (16.3%) receiving LBBP had HFH or died from any cause. Details of the cause of death are provided in supplemental results (Results in Supplemental Material). The composite endpoint in the PS-LBBP group was similar to that in the PS-HBP group (hazard ratio: 0.94; P=0.872; Figure 5A). A total of 9 subjects (10.5%) experienced late lead-related complications, with 8 having a late threshold increase of ≥2 V at 0.5 ms (9.3%) and 1 with pocket infection (1.2%). The PS-LBBP group had a significantly lower risk of late lead-related complications than the PS-HBP group (1.2% versus 9.3%, respectively; hazard ratio: 0.19; P=0.012; Figure 5B). In the PS-HBP group, His leads failed to capture the His bundle as well as local cardiac tissue with an acceptable pacing output due to significant increase in His bundle capture threshold from 1.1±0.4 to 3.6±0.3 V at 0.5 ms at a mean follow-up of 6.7±3.3 months in 5 patients who also had high local ventricular myocardial capture threshold (all >3.5 V at 0.5 ms). In these 5 patients, right ventricular backup pacing was enabled, and hence ventricular pacing was maintained. However, most patients with LBBP...
have low and stable thresholds for capture left bundle branch (LBB) as well as local cardiac tissue. Only 1 patient in the PS-LBBP group lost LBB capture due to an increase in LBB capture threshold >2 V at 0.5ms, but the local myocardial capture threshold remained low at 0.75 V at 0.5ms.

### DISCUSSION

In this study, we prospectively examined the feasibility, long-term safety, and efficacy of LBBP in patients with AF and HF after AVJ ablation and provided a retrospective comparison of LBBP and HBP using PS matching analysis. Our main findings were as follows: (1) LBBP combined with AVJ ablation is feasible and safe, with an acute implantation success rate of 100%; (2) it can serve as a de novo implantation or useful alternative technique for failed HBP; (3) it delivered significant improvements in LVEF and NYHA functional class in patients with AF with both HFrEF and heart failure with preserved ejection fraction, which were sustained up to 3-year follow-up; (4) it has similar clinical benefits, higher success rates, better pacing parameters, and fewer late lead-related complications than HBP; and (5) it makes the ablation procedure technically easier and has less necessity for a safety backup lead compared with HBP.

### Implant Success Rates

This study found that LBBP and AVJ ablation had a high implant success rate (100%) in the setting of AF, which is consistent with previous studies.\(^{16,25}\) The high implantation success rate of LBBP is related to the following factors: wide target area covered with the LBB, deep lead fixation, and larger area for pacing distal to the site of conduction delay or block. In addition, failure of LBBP implantation mainly occurred in patients with nonspecific intraventricular conduction delay, and these patients were excluded from this study. An additional
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benefit to the LBBP location over the HBP location is that it provides adequate space between the pacing lead and AVJ ablation site, which means that ablation can be performed with minimal risk for disrupting pacing. Our previous study showed that the success rate of permanent physiological pacing using HBP or LBBP combined with AVJ ablation increases with the introduction of LBBP. Moreover, the high success rate of secondary LBBP in the present study indicated that LBBP could be a useful bailout technique for those who failed to achieve acceptable HBP.

Pacing Parameters and Complications

We observed that low capture thresholds and high sensed R-waves with LBBP in this patient population were sustained up to 3-year follow-up. It provides information regarding the feasibility and long-term safety of using LBBP at the time of AVJ ablation, and there are relatively few published data on the use of LBBP for this indication. Our data suggest that LBBP is a reliable method for delivering ventricular pacing in this clinical setting. During follow-up, only one patient had an increase in LBBP capture threshold of ≥2 V at 0.5 ms; however, the LV septal capture threshold remained low at 0.75 V at 0.5 ms. We provide further evidence of excellent lead performance with LBBP, which is consistent with previous studies. In contrast, the findings from our PS matching analysis showed that HBP was associated with a greater risk of lead-related complications during follow-up. Complications were observed in 9.3% of patients in the HBP group compared with 1.2% in the LBBP group during long-term follow-up. The higher rate of complications with HBP was mainly driven by a threshold increase (8.1%) and occurred in the early years. Increases in thresholds with HBP have previously been reported; Zanon et al27 reported a 6% incidence of significant threshold increase with HBP during a median follow-up of 3 years.

Echocardiographic and Clinical Outcome

Previous observational studies demonstrated that AVJ ablation combined with His–Purkinje conduction system pacing could improve LV function in patients with AF and reduce the incidence of inappropriate shocks with implantable cardioverter-defibrillator. However, there are limited data assessing conduction system

Figure 4. Echocardiographic data and New York Heart Association (NYHA) functional class between left bundle branch pacing (LBBP) and His bundle pacing (HBP).

Left ventricular ejection fraction (LVEF; A), NYHA functional class (B), mitral regurgitation (MR; C), and tricuspid regurgitation (TR; D) at 1-year follow-up; LVEF (E), NYHA functional class (F), MR (G), and TR (H) at 2-year follow-up; and LVEF (I), NYHA functional class (J), MR (K), and TR (L) at 3-year follow-up stratified according to propensity score matched His bundle pacing (PS-HBP) and propensity score–matched left bundle branch pacing (PS-LBBP) groups. N indicates number of patient; PS-HBP, propensity score–matched His bundle pacing group; PS-LBBP, propensity score–matched left bundle branch pacing group; and TR, tricuspid regurgitation.
pacing delivered using LBBP in this patient group. To the best of our knowledge, our study is the first to show that LBBP post-AVJ ablation provides significant improvement in LVEF and symptoms in patients with both HFrEF and heart failure with preserved ejection fraction. Moreover, this benefit was sustained for up to 3-year follow-up. Our study adds important data regarding the efficacy of LBBP in this indication. It provides prospectively rather than retrospectively collected data, which provides robust evidence of the long-term clinical benefit.

The magnitude of the improvement observed with LBBP was similar to that observed with HBP, and there was no significant difference in outcomes between LBBP and HBP in the PS matching analysis. This suggests that delayed right ventricular activation, which occurs with LBBP, does not appear to adversely affect outcomes. Hou et al. demonstrated that LBBP produces comparable LV electrical and mechanical synchrony measurements to those obtained with HBP. Our findings suggest that maintaining physiological LV activation is the key determinant of long-term outcomes. This concept is supported by the findings from studies evaluating LBBP in patients with left bundle branch block and HF, which found similar improvements in LVEF compared with those achieved with HBP (24±10.9 versus 23.9±11.7; \( P=0.977 \)). The APAF-CRT study, as a prospective, randomized, parallel, open-label study measuring morbidity and mortality, which showed AVJ ablation combined with BVP improved mortality and HF morbidity and demonstrated this approach was superior to rate control with pharmacological therapy in elderly HF patients with permanent AF. This trial showed the composite outcome of HFH and mortality occurred in 18 patients (29%) in the BVP+AVJ ablation group and 36 patients (51%) with medical management alone over a median follow-up of 29 months (\( P=0.002 \)). The morbidity endpoint showed the composite outcome of HFH and mortality occurred in 6 patients (12%) in the BVP+AVJ ablation group and 17 patients (33%) with medical management alone over a median follow-up of 16 months (\( P=0.013 \)). In the present study, the composite endpoint of HFH or all-cause mortality occurred in 14 (16.3%) HBP patients and 16 (18.6%) LBBP patients over a mean follow-up of 28.9 months. These findings are at least comparable with the findings of the APAF-CRT studies where this composite endpoint in pacing+AVJ ablation group occurred in 29% over a median of 29 months and in 12% over a median of 16 months. However, the outcomes cannot be directly compared, owing to major differences in baseline clinical characteristics. It is critical that further rigorous randomized studies between conduction system pacing and BVP with larger sample sizes be performed in this group of patients.

A potential concern with LBBP is that it may cause tricuspid regurgitation through its interaction with the septal leaflet. Surprisingly, we observed a reduction in the severity of tricuspid regurgitation in our study, which is likely to have occurred because of ventricular remodeling.

**LBBP Programming Considerations**

When LBBP is utilized in patients with intact intrinsic conduction, atrioventricular delays can be programmed to promote fusion with intrinsic right ventricular activation to eliminate the delay in right ventricular activation. This option is not available in the post-AVJ programming.
ablation population. A further option for shortening QRS duration in LBBP is to aim for anodal capture of the right ventricle. We observed a significantly shorter QRS duration with bipolar pacing than with unipolar pacing. However, RBBB morphology could only be eliminated in 23.2% of the patients in our study. Lead orientation within the septum and the thickness of the septum are likely factors that determine whether anodal septal capture can be achieved. In those areas where it can be achieved, this often comes at the cost of requiring higher pacing outputs. In present study, there are only 16 patients where the programming is bipolar mode and the anodal capture threshold is less than the programmed pacing output. Further work is required to assess whether programming the device with the aim of eliminating RBBB morphology produces any additional improvement in cardiac function.

Interestingly, we observed higher mean sensed-R waves in the bipolar tip-ring configuration than in the unipolar configuration. This may be because there is more myocardium near the ring electrode than that near the tip electrode in some patients. As is shown in a case, we observed a higher sensed R-wave at unipolar ring configuration than at unipolar tip configuration during the procedure (Figure S1). This finding supports programming sensing of bipolar configuration in most patients.

Backup Lead

There is a risk of ventricular capture loss during HBP. In the PS-HBP group, His leads lost capture for the His as well as for the local ventricular myocardium and required use of the ventricular backup lead in 5 (5.8%) patients during follow-up. The 2021 European Society of Cardiology pacing guidelines recommend that ventricular backup lead may be considered with HBP in patients post-AVJ ablation. In 84 patients with HBP, with additional ventricular leads, 36 were implanted specifically for safety backup, and 48 patients who underwent implantable cardioverter-defibrillator implantation had defibrillation leads with the ability to provide backup ventricular pacing. Two (2.3%) patients had a single ventricular lead implanted because they refused implantation of a backup lead for economic reasons, and both patients had nonselective HBP with reliable local ventricular capture. However, most patients with LBBP have low and stable thresholds for capturing LBB as well as local cardiac tissue. Only one LBB lead lost LBB capture, but no LBB lead lost local myocardial capture in any patient with LBBP. Three (3.5%) patients received safety backup leads because the safety of LBBP was uncertain at an early stage (before January 2018). There is no need for a backup lead for LBBP because LBBP can effectively capture nearby local myocardial tissue.

Choice for HBP or LBBP

The results of our study support the use of LBBP as first-line therapy for pacing in patients with AF, HF, and an indication for AVJ. However, HBP is the most physiological pacing modality, and its QRS duration was significantly shorter than that of LBBP. Although patients with HBP had a higher mean threshold than those with LBBP, most patients with permanent HBP had low and stable thresholds. Before we developed LBBP in 2017, our approach was to choose HBP (especially distal HBP that we utilized in 2015) over BVP if HBP could generate a relatively low capture threshold. Currently, LBBP and HBP both are our current approaches to AVJ ablation and pacing. The choice of HBP or LBBP should be a balance between safety and ventricular resynchronization. LBBP is often preferred over HBP which often requires the implantation of additional backup pacing safety lead. Moreover, HBP has more stringent requirements for a low pacing threshold at implant due to a higher risk of pacing threshold increase. We consider acceptable His bundle pacing threshold of <2 V at 0.5 ms, and a threshold of <1.5 V at 0.5 ms to be preferable. In patients who underwent implantable cardioverter-defibrillator implantation, right ventricular defibrillation leads can provide safety backup pacing. Hence, HBP with appropriate parameters and excellent resynchronization may be often suitable. On the other hand, HBP has a risk of failure to capture due to sudden threshold changes in patients without defibrillation lead or a ventricular backup safety lead, so the safer LBBP is preferred. Moreover, implantation of HBP and LBBP in some patients remains challenging. In patients with interventricular septal scar, LBBP could be switched to HBP if the lead was difficult to insert into the interventricular septum. Patients in whom we attempted HBP with the following conditions were crossed over to LBBP: (1) His bundle injury by ablation, (2) high His capture/corrective threshold, (3) failure to achieve His fixation, and (4) cost concerns as LBBP does not need a backup RVP lead.

Atrioventricular Junction Ablation

We observed a higher ablation success rate, shorter ablation time, and fewer AVJ ablation sites in the LBBP group than those in the HBP group. It is likely that the greater separation between the ablation site and the pacing lead made the ablation procedure technically easier. Moreover, in selected cases with unsuccessful AVJ ablation, a shift toward the proximal region of the His bundle could improve the ablation success rate. Previous studies have shown that insufficient distance between AVJ ablation and His pacing lead can lead to an increase in threshold after ablation. However, there is less risk of displacing the lead with the ablation catheter,
and a more distal conduction system can be targeted if required without the risk of interrupting pacing.

Limitations
This was a single-center, non-randomized study and, thus, is not without limitations. When comparing with the HBP group, we used PS matching to adjust for known confounders. As some patients with HBP were enrolled earlier than patients with LBBP, advances in medical therapy made during that time frame in the treatment of HF may have biased the results. Therefore, we captured medication use for HF in the PS matching analysis to mitigate the bias from more recent advances in heart failure treatment. Nevertheless, there is still a risk that unknown and/or unmeasured confounders may have affected our findings. Large-scale, multicenter, prospective randomized controlled trials with sufficient power for clinical prognostic endpoints are needed to further validate our findings. It is unclear whether there is a benefit to programming LBBP to achieve anodal capture with the aim of eliminating RBBB morphology and, therefore, minimizing right ventricular activation delay. Our study did not address this question, which should be addressed in future research. Given the high threshold for anodal capture with bipolar tip-ring configuration (tip cathode and ring anode) in most patients, dual-cathode pacing (both tip and ring electrodes as cathodes) may help eliminate RBBB and provide potential backup pacing in the future.

Conclusions
LBBP seems to be a feasible and safe method for delivering ventricular pacing in patients with HF and AF after AVJ ablation. The magnitude of improvement in clinical outcomes appears to be similar to that achieved with HBP. LBBP has the advantages of higher implant success rates, better pacing parameters, and fewer late lead-related complications than HBP.

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Disclosures
None.

Supplemental Material
Tables S1 and S2
Figure S1

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