ORIGINAL RESEARCH

Benefits of Permanent His Bundle Pacing Combined With Atrioventricular Node Ablation in Atrial Fibrillation Patients With Heart Failure With Both Preserved and Reduced Left Ventricular Ejection Fraction

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***Background*—**Clinical benefits from His bundle pacing (HBP) in heart failure patients with preserved and reduced left ventricular ejection fraction are still inconclusive. This study evaluated clinical outcomes of permanent HBP in atrial fibrillation patients with narrow QRS who underwent atrioventricular node ablation for heart failure symptoms despite rate control by medication.

***Methods and Results*—**The study enrolled 52 consecutive heart failure patients who underwent attempted atrioventricular node ablation and HBP for symptomatic atrial fibrillation. Echocardiographic left ventricular ejection fraction and left ventricular end-diastolic dimension, New York Heart Association classification and use of diuretics for heart failure were assessed during follow-up visits after permanent HBP. Of 52 patients, 42 patients (80.8%) received permanent HBP and atrioventricular node ablation with a median 20-month follow-up. There was no significant change between native and paced QRS duration (107.1±25.8 versus 105.3±23.9 milliseconds, P=0.07). Left ventricular end-diastolic dimension decreased from the baseline (P<0.001), and left ventricular ejection fraction increased from baseline (P<0.001) in patients with a greater improvement in heart failure with reduced ejection fraction patients (N=20) than in heart failure with preserved ejection fraction patients (N=22). New York Heart Association classification improved from a baseline 2.9±0.6 to 1.4±0.4 after HBP in heart failure with reduced ejection fraction patients and from a baseline 2.7±0.6 to 1.4±0.5 after HBP in heart failure with preserved ejection fraction patients. After 1 year of HBP, the numbers of patients who used diuretics for heart failure decreased significantly (P<0.001) when compared to the baseline diuretics use.

***Conclusions*—**Permanent HBP post–atrioventricular node ablation significantly improved echocardiographic measurements and New York Heart Association classification and reduced diuretics use for heart failure management in atrial fibrillation patients with narrow QRS who suffered from heart failure with preserved or reduced ejection fraction. **(*J Am Heart Assoc*. 2017;6:e005309. DOI: 10.1161/JAHA.116.005309.)**

Key Words: atrial fibrillation • atrioventricular node ablation • heart failure • His bundle pacing

Multiple clinical studies have demonstrated improved quality of life following atrioventricular node (AVN) ablation and permanent right ventricular (RV) pacing in patients with symptomatic atrial fibrillation (AF) refractory to optimal medical therapy.[1-4] However, several studies performed over the last decade have demonstrated that conventional long-term RV apical pacing can increase the risk of death and heart failure hospitalization.[4-6] It is well known that long-term RV apical pacing produces wide QRS duration (QRSd), left ventricular (LV) dyssynchrony, hemodynamic impairment, negative inotropy, and LV diastolic and systolic dysfunction in a subgroup of pacer-dependent patients.[4,7,8] Thus, other pacing sites as an alternative to RV apical pacing have been explored, although clinical benefits from alternative pacing sites are still inconclusive.[9,10]

The His-Purkinje conduction system allows the impulse generated by the sinoatrial node to rapidly propagate into both right and left ventricles and hence ensures synchronized ventricular contraction. An early study by El-Sherif

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et al demonstrated that distal His bundle pacing (HBP) could normalize bundle branch block and QRS morphology.[11] In 2000, Deshmukh et al first successfully implemented permanent direct HBP in a small number of patients with AF and dilated cardiomyopathy and found improvements in LV dimensions and cardiac function.[12] Since then, there have been multiple reports on HBP in patients who need pacemaker therapy including those with AVN ablation or heart failure or patients for conventional pacemaker therapy.[13-18]

Although cardiac resynchronization therapy (CRT) can be used in patients after AVN ablation, studies have shown no significant clinical benefits if patients have a narrow QRSd.[19,20] On the other hand, following AVN ablation, HBP can provide physiological activation and hence avoids ventricular dyssynchrony and preserves ventricular function in patients with a narrow QRSd. The objective of the present study was to evaluate clinical outcomes of permanent HBP in patients with heart failure who also underwent AVN ablation with AF and to compare the difference between patients with reduced LV ejection fraction (LVEF; HFrEF) versus those with preserved LVEF (HFpEF).

Methods

The present study was a single-center prospective registry in heart failure patients who underwent AVN ablation and had long-standing persistent AF with rate control and received a pacemaker or implanted cardioverter-defibrillator or CRT device. The study protocol was approved by the Institutional Review Board of The First Affiliated Hospital of Wenzhou Medical University. All patients completed written informed consent.

Study Patients

Consecutive patients who met the inclusion criteria were enrolled between August 2012 and August 2015. The inclusion criteria were the following: (1) patients had symptomatic heart failure and long-lasting persistent or permanent AF[21] even though their heart rate was controlled with pharmacological treatment during AF; (2) New York Heart Association (NYHA) classification was II or III; (3) patients had at least 1 heart failure–related hospitalization in the last 12 months despite optimal heart failure therapy; and (4) patients were at least 18 years old and not pregnant. The patients could present with either HFpEF or HFrEF. Patients with any of the following conditions were excluded: (1) intraventricular conduction block or delay on 12-lead ECG; (2) severe mitral or aortic valve regurgitation; (3) congenital heart disease requiring cardiac surgery; (4) chronic kidney disease with dialysis; and (5) severe chronic obstructive pulmonary disease.

Implantation Procedure

Lead Placement

Each patient underwent implantation procedures as described previously.[17,18,22] Briefly, the delivery sheath (model C304 or C315, Medtronic, Inc, Minneapolis, MN) was inserted via the left axillary vein into the His bundle region in the atrioventricular (AV) septum superior to the tricuspid valve. The Select Secure™ lead (model 3830, Medtronic, Inc, Minneapolis, MN) that was used for His bundle pacing was advanced through the sheath, and only the distal part of the lead was extended beyond the tip of the sheath for a unipolar HBP. In a few patients when the pacing lead could not achieve HBP, a multielectrode mapping catheter was used to identify the His bundle potential, and then the Select Secure™ lead was used for HBP. An electrogram from the lead tip electrode along with 12-lead surface ECG was displayed and recorded (GE CardioLab EP Recording System 2000, GE Inc, Waukesha, WI). Once pacing parameters were acceptable, the Select Secure™ pacing lead was fixed. If HBP parameters were not adequate, the first Select Secure™ lead was left in place as a marker while the second Select Secure™ lead was inserted to identify an optimal His bundle location where HBP parameters were accepted. If dual leads were used, one lead was placed in the His bundle region for HBP while the other lead was positioned in the right RV for backup pacing.

His Bundle Pacing Testing

Once the His bundle potential was recorded in an electrogram, an HBP test was performed to measure pacing parameters and compare the intrinsic ECG QRS with the ECG QRS during HBP, which was similar to the criteria defined by Deshmukh et al.[12] The morphology of ECG QRS-T waveform during HBP was similar to that during intrinsic rhythm, and the interval from the His-pacing artifact to the beginning of the paced ECG QRS was identical to the intrinsic His-QRS interval. A pacing output that was slightly higher than the HBP threshold that maintained 1:1 His-ventricular conduction at a rate of 140 beats/min was accepted. During HBP test, if direct His bundle pacing could not be obtained but para-Hisian pacing was obtained, para-Hisian pacing was accepted. Para-Hisian pacing was mainly characterized by the following: (1), the interval between the pacing artifact and ECG QRS at low pacing output was shorter than the intrinsic His-QRS interval, and (2) there was a similarity between the electrical axis of the paced QRS and that of the intrinsic QRS. In the present study, patients with direct HBP and para-Hisian pacing were pooled as 1 pacing group.

RV leads or LV leads were implanted in a standard fashion at the RV apex (or RV septum) or lateral cardiac vein, respectively. The HBP lead was connected to the device atrial port in 38 patients, in the LV port in 3 patients, and in the RV

port in 1 patient. After all leads were positioned, the device was buried in the pocket. The lower rate for permanent HBP was initially set at 80 beats/min, then programmed to 70 beats/min at 1 to 3 months while backup RV or LV pacing was programmed at long AV intervals.

Atrioventricular Node Ablation

After HBP was established, an 8.5-F sheath (SR0 or SL1, St. Jude Medical Inc, St. Paul, MN) was inserted via the femoral vein to the supra-His bundle region (including AVN and nearby proximal His bundle) with a more than 8 mm distance from the HBP site, where the HBP lead was served as a marker (Figure 1). Complete AV block was achieved by radiofrequency ablation using a conventional quadripolar 7-Fr 4-mm-tip ablation catheter (Celsius, Biosense Webster Inc, Diamond Bar, CA) (N=24), or a Thermocool™ (N=8) or Thermocool SF™ (N=10) mapping/ablation catheter (Biosense Webster Inc, Diamond Bar, CA). Desired success of AVN ablation was evidenced with complete AV block without change in HBP parameters. Based on our experience, we proposed the following criteria: (1) complete AV block, (2) no changes in HBP threshold and His-ventricular conduction, and (3) the same morphology of QRS complex during HBP before and after AVN ablation. Isoprenaline infusion (at 20-40 μg/min) over 10 minutes was given to ensure no recurrence of AV conduction.

Data Collection and Follow-Up

Demographic and medical history was collected at enrollment. Baseline mean HR was determined by either 24-hour Holter recording or ECG monitoring during hospitalization. Device electrical performance, including sensed R-wave amplitude, pacing threshold, and percentage of HBP, was assessed at outpatient visits at week 1, and 1, 3, 6, and 12 months up to 36 months postimplantation. Lead-related complications including infection, dislodgement, loss of capture, and early battery depletion were also tracked. Clinical outcomes including echocardiography, cardiac function assessment (NYHA classification), mortality, hospitalization, and medication for heart failure were assessed at 3-month and annual follow-up visits after permanent HBP. Echocardiographic images were obtained in the standard parasternal long- and short-axis and apical 4-chamber and 2-chamber views using commercially available ultrasound equipment (Philips, iE Elite, Amsterdam, Netherlands). LVEF was obtained using the modified Simpson rule. All echocardiograms were assessed by an experienced echocardiographer who was blinded to the study design. The LV end-diastolic dimension was measured in the parasternal long-axis view. Mitral jet area as a percentage of left atrial area was used to assess the severity of mitral valve regurgitation, and the severity of tricuspid valve regurgitation was graded by the proportion of jet area in right atrial area.[23] The severity of valve regurgitation was classified as 0, none; 1, mild; 2, moderate; 3, severe. Serum B-type natriuretic peptide (BNP) levels were measured before and after permanent HBP.

Statistical Analyses

Continuous variables were expressed with mean±SD if they met normal or similar to normal distribution, and paired t tests were performed to compare the differences between 2 time points, for example, the baseline and the specific time point

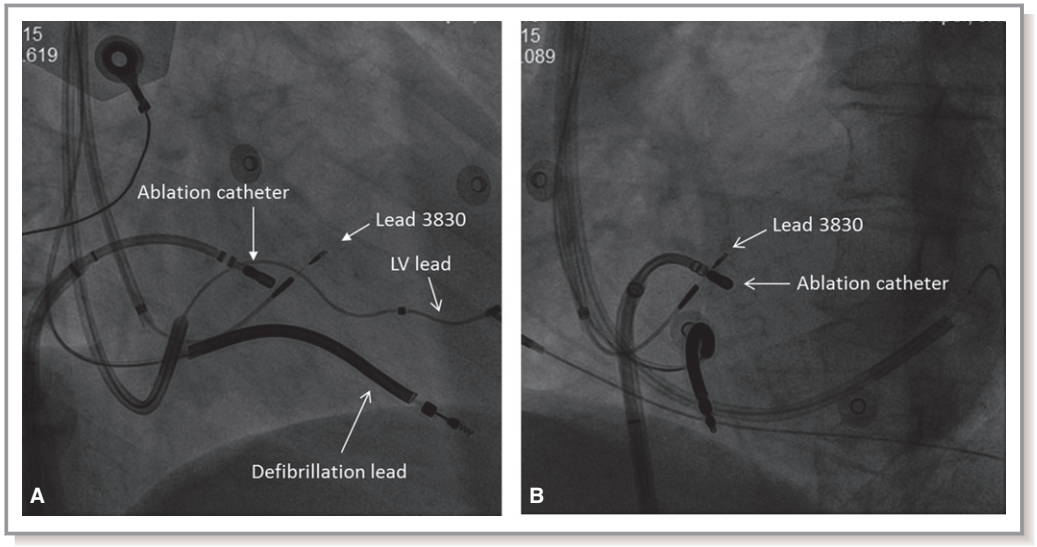

Figure 1. Right (A) and left (B) anterior oblique fluoroscopic projections showing location of His bundle pacing lead and ablation catheter.

during HBP. Otherwise, a signed rank-sum test would be applied for the comparison between the baseline and the specific time point during HBP for an ordinal variable such as NYHA class and valve regurgitations. For echocardiographic LV end-diastolic dimension (LVEDd) and LVEF and device interrogated parameters (HBP threshold, sensed R-wave amplitude, and the percentage of HBP) that were collected at baseline and later multiple different time points, univariate analysis of variance for repeated measures (generalized linear model) was used to assess the effects of HBP, and post hoc tests with least significant difference were performed for the variables that showed a statistically significant difference. Categorical data were described as number (%), and the McNemar test was used to determine whether the difference between a specific time point and baseline on the proportion of patients who received medications reached statistically significant level. Pearson product-moment correlation coefficient was selected to explore the association between echocardiographic changes in LVEDd and LVEF after HBP versus their related baseline values. Stratified analyses in echocardiographic measurements, clinical assessments, and medications were also performed for the subgroups of patients with either HFrEP (LVEF ≤40%) or HFpEF (LVEF >40%). All data management and analysis were finished with SPSS version 20.0 (SPSS, Chicago, IL). All hypothesis tests were 2-tailed, and *P* value of ≤0.05 was set as statistically significant.

Results

Implantation Results and Patient Characteristics

In all 52 enrolled patients HBP and AVN ablation were attempted (Figure 2). His bundle potential was not recorded in 2 of these patients (3.8%). Acute HBP was achieved in the remaining 50 patients (96.2%). Of the 50 patients with successful acute HBP, 42 patients (80.8% of all patients for HBP attempts) received permanent HBP (38 with direct HBP and 4 with para-Hisian pacing; Figure 2), and 8 patients (15.4%) did not receive permanent HBP because of His bundle injury by ablation (N=2), failed AVN ablation (N=2), or resumption of AVN conduction (N=4, heart rate at 83.8±15.6 beats/min at 16.8±19.8 days after successful acute AVN ablation). Permanent HBP was implemented by a dual-chamber pacemaker in 17 patients, by CRT-pacemaker/CRT-defibrillator in 17 patients, and by a dual-chamber implanted cardioverter-defibrillator in 8 patients, all for ventricular backup pacing.

Baseline characteristics of the patients with permanent HBP are summarized in Table 1. Baseline QRSd was 107.1±25.8 milliseconds, and averaged heart rate under AF rate control therapy was 83.9±14.1 beats/min. Baseline averaged heart rate was 83.4±15.2 beats/min in patients with HFrEF and 84.3±13.7 beats/min in patients with HFpEF. Prior to the HBP implantation, patients underwent heart failure pharmacological therapy including β-blockers, angiotensin-converting enzyme inhibitor, and diuretics for a median 28 months before HBP. The mean follow-up period after HBP was 21.1±9.3 months (median 20 months).

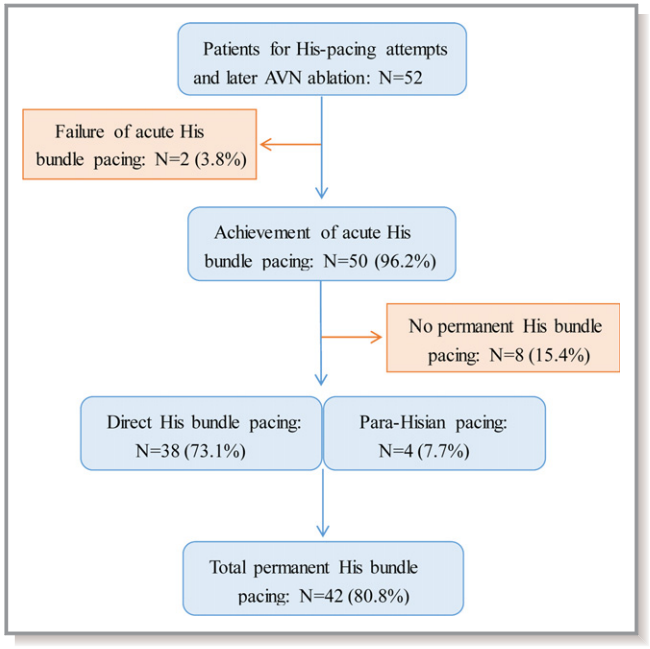

Figure 2. Schematic summary of study and patient flow.

Table 1. Patient Baseline Characteristics

Parameters	Mean±SD or Percentage (Number)
Age, y	72.8±8.3
Male	61.9% (26)
Height, cm	163.2±6.3
Weight, kg	66.6±11.9
Heart rate, beats/min	83.9±14.1
QRS duration, milliseconds	
Native QRS	107.1±25.8
Paced QRS	105.3±23.9
Hypertension	78.6% (33)
Coronary heart disease	28.6% (12)
PCI history	19.0% (8)
Myocardial infarction	9.5% (4)
Stroke history	38.1% (16)
Diabetes mellitus	23.8% (10)
Kidney dysfunction	11.9% (5)

PCI indicates percutaneous coronary intervention.

His Bundle Pacing at Implantation

Figure 3 shows an example of 12-lead surface ECG and 3830-lead recorded electrogram during implantation. The His-QRS interval during intrinsic AV conduction (Figure 3A and 3B) was identical to the HBP artifact-QRS interval (Figure 3C). The morphology of the ECG QRS complex during HBP was identical to that of the intrinsic ECG QRS complex (Figure 3), suggesting identical activation sequences during intrinsic rhythm and His bundle pacing.

Acute HBP threshold was 1.5±1.0 V at a pulse width of 0.5±0.1 millisecond. QRSd was 107.1±25.8 milliseconds during intrinsic rhythm and 105.3±23.9 milliseconds during HBP (P=0.07 versus intrinsic QRSd). The intrinsic His-QRS interval was 54.7±10.4 milliseconds and was not significantly different from the HBP artifact-QRS interval (54.0±7.5 milliseconds, P=0.499 versus the intrinsic His-QRS interval).

Temporary right bundle branch block occurred in 8 cases, and third-degree AV block occurred in 2 cases during the His bundle lead implantation procedure. Seven of 8 cases with right bundle branch block and 2 cases of third-degree AV block fully recovered during implantation. After implantation, there was no lead dislodgement.

Echocardiographic Changes After His Bundle Pacing

Compared to baseline echocardiographic values that were measured a median of 8 days before the HBP procedure, LVEDd significantly decreased while LVEF increased after permanent HBP (Table 2). The improvements in LVEDd and LVEF were present at 3 months of HBP, and more improvement was observed over 1 year of HBP (Table 2). The degree of mitral valve regurgitation at 1-year follow-up visit was significantly reduced (1.0±0.7) when compared to the baseline value (1.3±0.9, P=0.013). There was no significant change in tricuspid valve regurgitation between the degree at baseline (1.5±0.9) and that at 1-year follow-up (1.4±1.0, P=0.510 versus the baseline). The magnitude of the improvement in LVEF and LVEDd was significantly correlated to the baseline severity of ventricular function as shown in Figure 4 (eg, the lower LVEF and the larger LVEDd at baseline, the greater the improvement in LVEF and LVEDd after HBP). When the patients with HBP were divided into 2 subgroups based on an LVEF: the HFpEF group with LVEF >40% and HFrEF group with LVEF ≤40%, the percentage increase in LVEF (the ratio of LVEF at 1 year HBP over the baseline value) was 82.8±43.3% in HFrEF patients, which was significantly higher than that (14.0±24.4%) in HFpEF patients (P<0.001 versus the HFrEF group). In patients with HFrEF, both LVEDd and LVEF were improved at 3 months of HBP and further improved after 1 year of HBP (Table 2). In patients with HFpEF, there was no significant reduction in LVEDd after permanent HBP, whereas a significant improvement in LVEF was observed after 1 year of HBP (Table 2). Eleven patients with HFrEF received echocardiographic assessment ≈1 month (median 24 days) after the implementation of HBP. There was a moderate but significant improvement in LVEF during the acute phase of HBP, and the improvement continued further at 3 months and 1 year of HBP (Figure 5).

Clinical Outcomes After His Bundle Pacing

There was a significant overall reduction in the serum BNP concentration at the last follow-up (309.0±254.9 pg/mL) from the baseline concentration (531.9±468.5 pg/mL, P=0.019 versus the last follow-up). The BNP reduction after

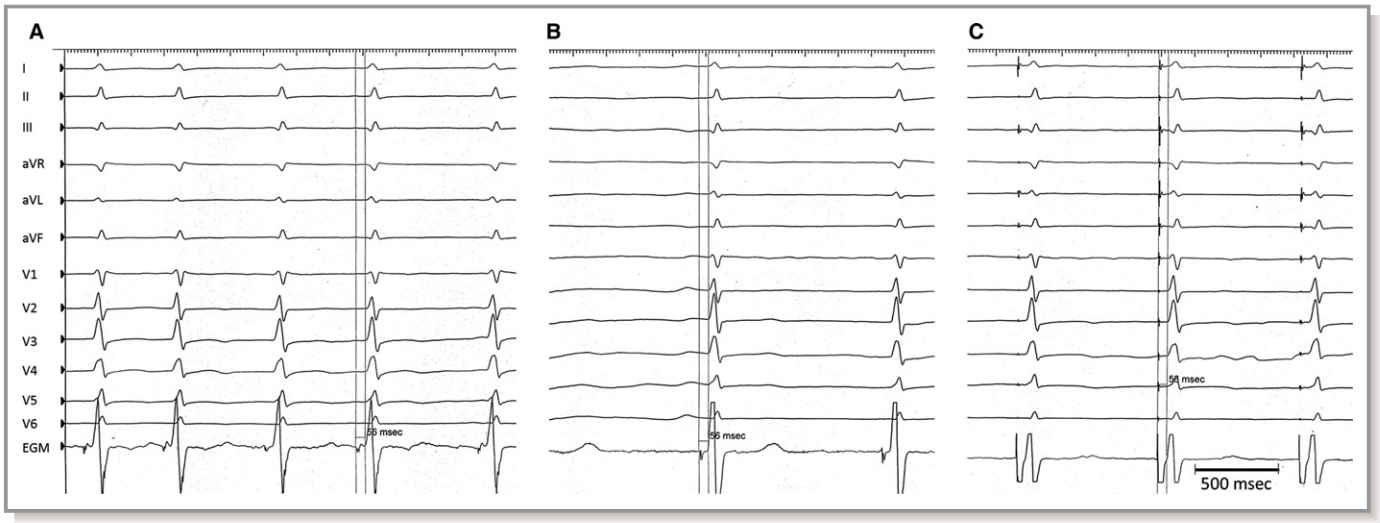

Figure 3. Twelve-lead body surface ECG (top 12 channels) and cardiac EGM with His bundle potential recording (bottom channel) in a patient. A, Recording of His bundle potential during atrial fibrillation. B, Recording of His bundle potential during escape rhythm after AVN ablation. C, His bundle pacing at 1.2 V and 0.5-millisecond pulse width after AVN ablation. AVN indicates atrioventricular node; EGM, electrogram.

Table 2. Comparison of the Echocardiographic Measurements at the Specific Time Points of HBP

	LVEDd (mm)	*P* Value	LVEF (%)	*P* Value
All patients (N=42)				
Baseline	55.8±8.1	Ref.	44.9±14.6	Ref.
3 months	52.7±5.3	0.031	56.5±8.7	<0.001
1 year	50.6±5.4	<0.001	59.7±9.8	<0.001
Last FU	51.0±5.1	<0.001	60.0±8.1	<0.001
HFpEF patients (N=22)				
Baseline	51.5±5.4	Ref.	56.6±9.9	Ref.
3 months	50.2±4.4	0.385	60.1±8.0	0.231
1 year	49.0±4.4	0.073	63.2±8.2	0.010
Last FU	49.6±3.9	0.159	62.6±6.9	0.019
HFrEF patients (N=20)				
Baseline	60.6±8.0	Ref.	32.2±4.8	Ref.
3 months	54.5±5.3	0.005	53.9±8.4	<0.001
1 year	52.3±6.0	<0.001	55.7±10.2	<0.001
Last FU	52.6±5.9	<0.001	57.2±8.7	<0.001

P value is of specific time points of His bundle pacing vs the baseline by post hoc tests with least-significant difference. FU indicates follow-up; LVEDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; Ref., reference.

HBP was different between HFrEF and HFpEF patients. At baseline, BNP concentration was significantly higher in HFrEF patients (726.0±730.7 pg/mL) than in HFpEF patients (298.2±212.2 pg/mL, *P*<0.001 versus HFrEF patients). After 1 year of HBP, BNP concentration reduced to 148.3±232.4 pg/mL in HFrEF patients (*P*<0.001 versus the baseline value), but there was no significant change in the HFpEF patients (308.5±254.1 pg/mL, *P*=0.831 versus the baseline value). NYHA classification improved to 1.4±0.4 after 1 year of HBP from the baseline 2.9±0.6 in HFrEF patients (*P*<0.001) and to 1.4±0.5 after HBP from the baseline 2.7±0.6 in HFpEF patients (*P*<0.001).

During the follow-up period, 2 patients died (1 due to end-stage renal disease and the other during sleep of unknown cause), 1 patient had ventricular tachycardia terminated by antitachycardia pacing, and 2 patients experienced implant-related hospitalizations (1 for device replacement and 1 for minor pocket infection). All patients had at least 1 hospitalization for heart failure (hospitalization frequency 1.4±0.7 per patient) within 1 year before HBP, but only 2 patients (4.8%) had heart failure-related hospitalization within 12 months of HBP. When compared to the baseline values, the number of patients taking diuretics, β-blockers, and digoxin significantly decreased at 12 months of HBP, although the number of patients taking an angiotensin-converting enzyme inhibitor did not significantly change (Table 3). Of the 23 patients still on diuretics, 18 took diuretics at lower doses compared to baseline doses. The number of HFrEF patients taking diuretics decreased from 20 (100%) at baseline to 14 (70%) after HBP (*P*=0.014 for reduction, Table 3), and the number of HFpEF patients taking diuretics decreased from 18 (81.8%) at baseline to 9 (40.9%) after HBP (*P*=0.003 for the reduction, Table 3).

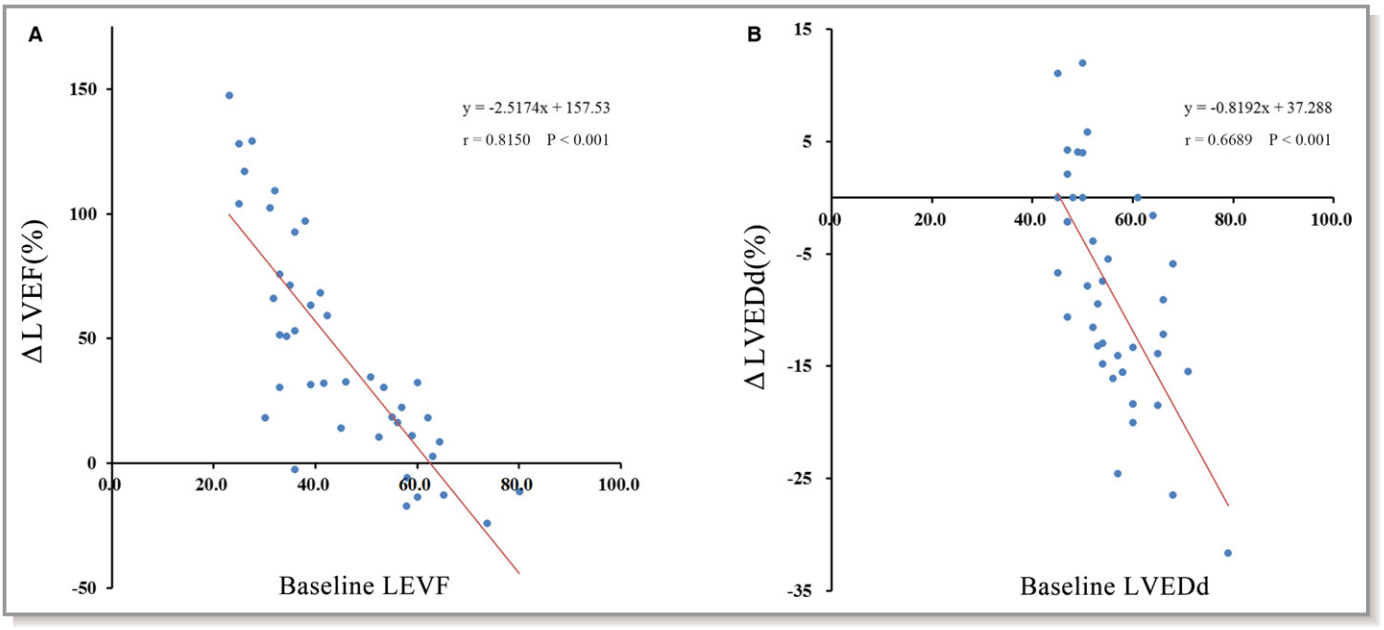

Figure 4. The Pearson product-moment correlation between echocardiographic changes in LVEDd and LVEF after HBP vs the baseline values. A, The correlation between the percentage change (ordinate, %) in LVEF after HBP over the baseline vs the baseline LVEF (abscissa). B, The percentage change (ordinate, %) in LVEDd after HBP over the baseline vs the baseline LVEDd (abscissa). HBP indicates His bundle pacing; LVEDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction.

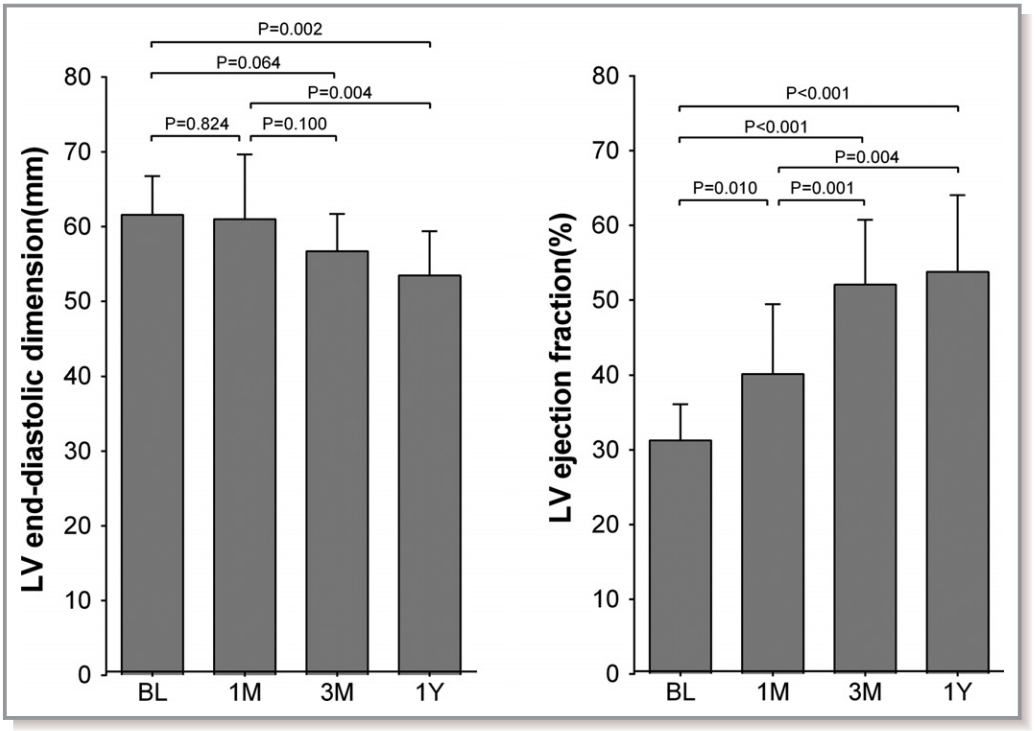

Figure 5. Acute and long-term improvement in LVEDd (left) and LVEF (right) after His bundle pacing in patients with HFrEF. BL, baseline; 1M, 1 month after HBP; 3M, 3 months after HBP; 1Y, 1 year after HBP. Inserted *P* values were obtained by post hoc tests with least-significant difference. HBP indicates His bundle pacing; HFrEF, heart failure with reduced left ventricular ejection fraction; LVEDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction.

Device Electrical Parameters During His Bundle Pacing at Follow-Up

Electrical data derived from implanted devices are summarized in a chronological order in Figure 6. Compared to the baseline, HBP thresholds did not significantly change during follow-up (Figure 6A). The percentage change in HBP thresholds at the last follow-up was 6.2±53.1% (median 0%) of baseline HBP thresholds. Five patients had an increase in HBP thresholds by at least 1 V over baseline thresholds (the range of the threshold increase was 1-1.35 V, and the range of baseline thresholds was 0.75-1.5 V). There was no statistically significant change in sensed R-wave amplitude (Figure 6B), and the percentage of HBP remained stable (Figure 6C). During the follow-up period, His-ventricular conduction remained intact without observation of exit block or progressive conduction delay.

Discussion

Major Findings

The present study utilized HBP after AVN ablation as a treatment for heart failure in AF patients with a narrow QRS complex and recent heart failure hospitalization despite heart rate control by medication. The study demonstrated that permanent HBP improved NYHA classification and reduced the use of diuretics for heart failure management in patients with either HFrEF or HFpEF. The echocardiographic measurements showed an improvement with a significant increase in LVEF and reduction in LVEDd, suggesting ventricular reverse remodeling, especially in HFrEF patients with lower baseline LVEFs. No serious adverse events, including lead dislodgement and exit block, were observed at implantation or during permanent HBP, demonstrating the safety and stability of HBP.

AVN ablation for AF requires permanent pacing. Options for pacing include pacing mode, such as RV pacing or biventricular pacing. Multiple clinical studies have demonstrated that long-term RV apical pacing can lead to cardiac dysfunction and heart failure deterioration.[4-6] A major mechanism of the detrimental effect of RV apical pacing is due to ventricular dyssynchrony caused by abnormal ventricular activation.[4,24] Cardiac resynchronization therapy is an option post–AVN ablation.[25] However, several trials have failed to show a benefit of cardiac resynchronization therapy in patients with narrow QRS.[19,20] Some degree of electrical dyssynchrony caused by biventricular pacing may be 1 potential mechanism.[20] The present study applied permanent

Table 3. Comparison of the Number of Patients Receiving Medications Before and 1 Year After HBP

	Baseline	After HBP	*P* Value
All patients (N=42)			
Diuretics	38 (90.5)	23 (54.8)	<0.001
β-Blockers	40 (95.2)	32 (76.2)	0.011
ACE inhibitors	36 (85.7)	38 (90.5)	0.480
Digoxin	20 (47.6)	2 (4.8)	<0.001
HFpEF patients (N=22)			
Diuretics	18 (81.8)	9 (40.9)	0.003
β-Blockers	21 (95.5)	14 (63.6)	0.020
ACE inhibitors	20 (90.9)	19 (86.4)	0.564
Digoxin	7 (31.8)	1 (4.5)	0.034
HFrEF patients (N=20)			
Diuretics	20 (100.0)	14 (70.0)	0.014
β-Blockers	19 (95.0)	18 (90.0)	0.317
ACE inhibitors	16 (80.0)	19 (95.0)	0.180
Digoxin	13 (65.0)	1 (5.0)	<0.001

Data were presented as N (%), and McNemar tests were performed to compare the differences between baseline and 1 year after HBP. ACE indicates angiotensin-converting enzyme; HBP, His bundle pacing; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

HBP in a subgroup of patients with heart failure who had recent heart failure hospitalizations even though medical therapy resulted in heart rate control during AF and patients had baseline narrow QRS complexes. HBP after AVN ablation in the present study not only provided heart rate control and rate regularization but also utilized the native His-Purkinje conduction system for synchronized ventricular activation.[26] Thus, HBP may be an additional pacing mode that could provide hemodynamic advantage to patients with a narrow QRS undergoing AVN ablation.

After a median follow-up period of 20 months, we observed a significant improvement in clinical outcomes of heart failure hospitalization and medication use, NYHA classification, plasma BNP concentration, and echocardiographic LVEF and LVEDd. Improved clinical outcomes were observed not only in HFpEF but also HFrEF patients, with a greater magnitude of the improvement in patients whose baseline ventricular remodeling was worse. Our findings of improved clinical outcomes in HFrEF patients are similar to the findings in the reports of His bundle pacing in heart failure patients with or without atrial fibrillation.[12,16,18] Previous studies demonstrated a significant improvement in echocardiographic LVEF or LV fractional shortening by 30% to 40% following AVN ablation and permanent RV pacing for refractory AF in HFrEF patients whose baseline heart rate was not controlled during AF.[27-29] The mechanism of the improvement we observed was likely multifactorial and included improved heart rate control by pacing post–AVN ablation. The magnitude of LV function improvement in HFrEF patients in the present study appeared greater when compared to previous studies,[27-29] likely due to synchronized ventricular contraction with HBP pacing post–AVN ablation. More importantly, the present study demonstrated that improvement after permanent HBP was inversely proportional to baseline ventricular function.

Previous studies in HFpEF patients who underwent AVN ablation and permanent RV pacing for refractory AF showed inconsistent results with respect to improvement in LV function.[1,2,28,29] Permanent RV pacing may not be an ideal option for patients with diastolic heart failure with preserved ejection fraction.[4,30] In the present study, the baseline LVEDd, LVEF, and BNP concentration in HFpEF patients were substantially different from those in HFrEF patients. However, significant improvements in all major clinical outcomes and echocardiographic measurements in HFpEF patients were measured after permanent HBP, suggesting that HBP should be an option for HFpEF patients with recent heart failure hospitalization and atrial fibrillation.[31,32]

Connecting the lead for HBP to the right atrial port of a pacemaker in the present study is consistent with practices at other centers.[12,15,17] When that is done, the RV pacing lead is left for backup pacing in case of loss of HBP. However, no backup pacing was present during permanent HBP in our study. Furthermore, we did not observe a significant change in HBP threshold and exit block. Thus, permanent HBP in the present study is safe and reliable.

The present study adopted the concept of HBP with backup RV or biventricular pacing in patients who received a CRT-pacemaker or CRT-defibrillator device. Near 100% HBP during the follow-up period (Figure 6) is consistent with no CRT or biventricular pacing in our patients. However, use of 1 (CRT) device can potentially provide 2 pacing strategies: the strategy of HBP with backup biventricular pacing and the biventricular pacing strategy. If a patient does not respond to biventricular pacing or has failure of LV lead implantation,[16,33] HBP can be an option. If clinical outcomes provided by HBP are equal to or better than those of biventricular pacing, HBP can be considered,[18,33] especially in patients with narrow QRS complexes who are less likely to benefit from CRT. Thus, HBP, once shown to have long-term safety and stability, can be a choice for patients with a narrow QRS complex and needing permanent pacing.

The present study demonstrated that performing AVN ablation and HBP implantation was safe and feasible. The AVN ablation site should be at least 8 mm away from the HBP site to avoid potential injury to the distal His bundle. The success of AVN ablation and HBP was evidenced by a complete AV block without change in HBP parameters, including (1) no changes in HBP threshold and His-ventricular conduction time

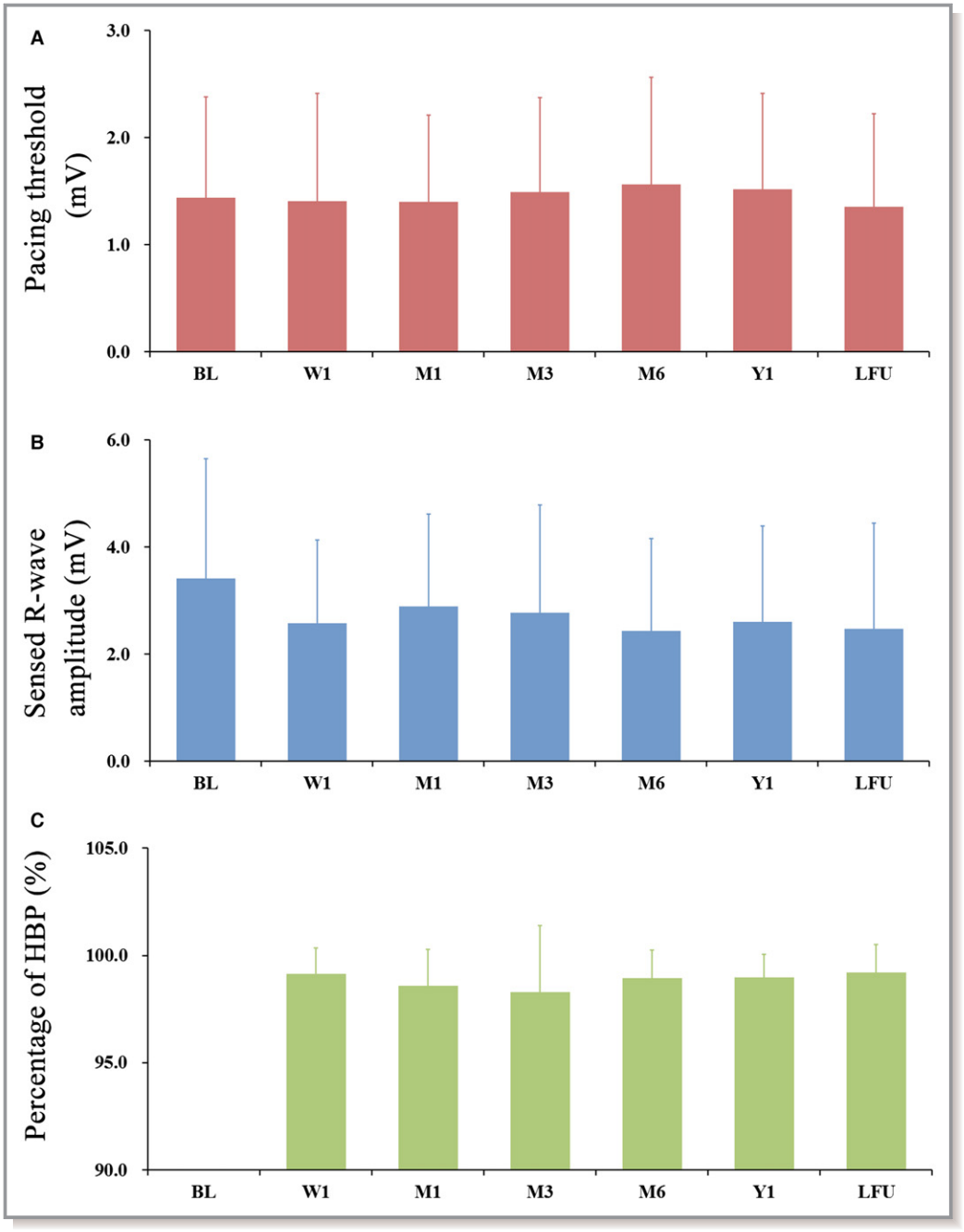

Figure 6. Electrical parameters of HBP and the percentage of HBP during the follow-up period. A, HBP threshold; (B) sensed R-wave amplitude; and (C) the percentage of HBP. BL indicates baseline value; W1, 1-week follow-up visit; M1, 1-month follow-up visit; M3, 3-month follow-up visit; M6, 6-month follow-up visit; Y1, 1-year follow-up visit; LFU, last follow-up visit. No significance (P>0.05) among different time points was detected by repeated-measures analysis of variance. HBP indicates His bundle pacing.

and (2) the same morphology of QRS complex during HBP before and after AVN ablation. The present study demonstrated successful permanent HBP in 80.8% of all enrolled patients (96.2% patients had successful acute HBP), which was comparable to the success rate of HBP in previous investigations.[12,15,17,18] During the median follow-up of 20 months in the present study, the overall HBP threshold remained relatively stable, and there was no observation of progressive His-ventricular conduction delay and exit block. Moreover, the present study did not observe serious adverse events related to implantation procedures, AVN ablation, or late lead dislodgement. Thus, our findings demonstrated that implantation procedures in conjunction with AVN ablation and permanent HBP are safe and stable.[12-18]

Limitations

First, the present study did not have a control group of heart failure patients who had heart rate control and heart rate irregularity controlled by methods other than HBP after AVN ablation. Permanent pacing is required after AVN ablation. Biventricular pacing is recommended for patients who have heart failure and need permanent pacing.[25] There is no investigation on whether beneficial clinical outcomes by HBP in patients with heart failure and narrow QRS complex would be better than that from biventricular pacing. The recent study by Lustgarten et al found that HBP provides equivalent clinical benefits to CRT using biventricular pacing.[18] A randomized controlled study is needed to compare clinical outcomes between permanent HBP and biventricular pacing. Second, the improvement in the echocardiographically measured ejection fraction is likely related to long-term HBP and not solely related to the acute correction of ventricular rate and rhythm irregularity during AF. Our results (Figure 5) showed a moderate improvement in LVEF during the acute phase of HBP and a significantly greater improvement at 3 months and 1 year after HBP, suggesting that a long-term beneficial effect of HBP is present in addition to acute effects via ventricular rate and regularity control by HBP. Furthermore, the present study is limited by the small patient population studied. Thus, clinical benefits generated by permanent HBP in the present study should be confirmed in future large-scale clinical trials of diverse groups of heart failure patients with longer follow-up. Moreover, permanent HBP could not be achieved in some patients, and implantation procedures were longer and more complicated than RV apical lead implantation. Thus, strategies to prescreen patients for HBP and improvement in techniques to identify the His bundle region with a low and stable HBP threshold are needed.

Conclusion

The present study demonstrated that the permanent HBP is safe and stable in a population of heart failure patients who had narrow QRS and underwent AVN ablation for AF. We observed a significant improvement in NYHA classification and echocardiographic LVEF and LVEDd and reduction in use of diuretics for heart failure treatment without an exit block and the development of progressive abnormality of His-ventricular conduction during a median 20-month follow-up of permanent HBP. Although the improvement after permanent HBP was present in patient groups with either HFrEF or HFpEF, randomized, controlled clinical trials with a larger sample size are needed to further confirm these findings before permanent HBP can be adopted as a standard practice for these patients.

Disclosures

None.

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