Electrophysiologic Insights Into Site of Atrioventricular Block
Lessons From Permanent His Bundle Pacing

Pugazhendhi Vijayaraman, MD,* Angela Naperkowski, RN, CCDS, CEPS,* Kenneth A. Ellenbogen, MD,† Gopi Dandamudi, MD*

ABSTRACT

OBJECTIVES This study sought to report the feasibility of permanent His bundle pacing (HBP) in patients with advanced atrioventricular block (AVB) and electrophysiological observations into site of block in patients with infranodal AVB.

BACKGROUND HBP is a physiological alternative to right ventricular pacing. Historic studies have reported a low incidence of intra-His AVB. Recent studies of permanent HBP reported limited success in patients with infranodal AVB.

METHODS Consecutive patients with advanced AVB underwent permanent HBP using Medtronic 3830 lead (Minneapolis, Minnesota) and a fixed-shaped catheter (C315 His). The HB was mapped using unipolar recording from the lead tip or by pace mapping. Success of HBP, type of AVB, and pacing outcomes were documented. Patients were followed at 2 weeks, 2 months, and then yearly.

RESULTS A total of 100 patients with advanced AVB (age 75±12 years; male 62%; AV nodal 46%; infranodal 54%) underwent permanent HBP. HBP was successful in 84 patients (84%; AV nodal 93%, infranodal 76%). Mean procedure time was 71±21 min, mean fluoroscopy time was 11±6 min. Baseline QRS duration was 122±27 ms; paced QRSd was 124±22 ms. The HB pacing threshold at implant, 2 weeks, 2 months, and last follow-up (19±12 months; range: 6 to 46 months) was 1.3±0.9 V, 1.6±1.0 V, 1.6±1.1 V, and 1.7±1.0 V at 0.5 ms, respectively. Five patients required lead revision.

CONCLUSIONS Permanent HBP was successful in 84% of unselected patients with AVB. His-Purkinje conduction could be normalized in 76% of patients with infranodal block, suggesting intra-His block. Incidence of infra-His AVB was low (24%) in this series. Routine HBP in patients with AVB is feasible and safe for at least up to 18 months. (J Am Coll Cardiol EP 2015;1:571–81) © 2015 by the American College of Cardiology Foundation.

The right ventricular (RV) apex is the most commonly used site for ventricular pacing in patients with atrioventricular (AV) conduction disease and bradycardia. RV apical pacing has been associated with ventricular dyssynchrony, reduction in left ventricular (LV) ejection fraction, and adverse clinical outcomes (1-5). RV outflow tract and septum have been used as alternative sites without proven clinical benefit (6-8). Cardiac resynchronization therapy has been proposed as an alternative to RV pacing in patients with heart block and heart failure (9).

After the original description of permanent His bundle pacing (HBP) by Deshmukh et al. (10) in 2000, there have been multiple reports on permanent HBP demonstrating its feasibility (11-16). Permanent HBP has been successfully performed in patients with AV block (AVB) and preserved His-Purkinje conduction, but the success rates have varied from 52% to 84% (10,15-18). Interestingly, HBP can also correct...
infranodal conduction disturbances (17). However, the success rates of permanent HBP in patients with infranodal AVB have been reported to be very low (19,20). Early studies using His bundle (HB) recordings have suggested that intra-His block contributes only 15% to 20% of patients with infranodal AVB (20–23). More than 70% of infranodal AVB has been attributed to infra-His (distal to the HB) block. We recently reported the feasibility and clinical outcomes of permanent HBP compared with RV pacing (16). During this study, we unexpectedly observed a higher degree of success in patients with infranodal AVB than previously reported. The aim of our single-center, observational study was to report the success rates and outcomes of permanent HBP in consecutive patients with advanced AVB, especially in patients with infranodal block.

METHODS

PATIENT SELECTION. From January 2011 to June 2014, all patients referred for pacemaker implantation routinely underwent an attempt at permanent HBP at Geisinger Wyoming Valley Medical Center by 2 experienced operators (P.V., G.D.). Patients undergoing device implantation for cardiac resynchronization therapy, pulse generator changes, sinus node dysfunction, and first- or second-degree AVB were excluded from the study. Patients who met the following criteria were included in the study: 1) complete AVB; 2) advanced AVB with 2:1 or greater (3:1) AV conduction ratio; and 3) AV node ablation. This retrospective study was approved by our institutional review board.

HB PACING. HBP was performed using the Select Secure (Model number 3830, 69 cm, Medtronic Inc., Minneapolis, Minnesota) pacing lead delivered through a fixed-curve sheath (C315 His, Medtronic Inc.), as previously described (15,16). The delivery sheath was inserted into the RV, just beyond the tricuspid annulus. Subsequently, the pacing lead was advanced through the sheath such that only the distal electrode/screw was beyond the tip of the catheter. A unipolar electrogram was recorded from the lead tip at a gain setting of 0.05 mV/mm and displayed on Medtronic Pacing System Analyzer (model number 2290) at a sweep speed of 50 mm/s. HB electrogram was identified by mapping the AV septum. The lead was then screwed into position with 4 or 5 clockwise rotations. HB capture threshold was assessed and accepted if found to be <2.5 V at 1.0 ms and only if 1:1 His-ventricular conduction at a minimum of 120 bpm was demonstrable during pacing. If acceptable HB capture could not be achieved after 5 attempts at lead positioning or fluoroscopy duration of <20 min, the lead was then placed in the mid-RV septum. When the HB electrogram was not recordable during mapping, pacing was performed in unipolar fashion to identify the successful site. During implantation, attempts were made to obtain selective His bundle pacing (S-HBP) in patients with AV nodal block, but if HBP with fusion (nonselective His bundle pacing [NS-HBP]) was obtained, this position was accepted. If the patient had infranodal AVB, NS-HBP was preferred to ensure local RV myocardial capture in addition to HB capture. A mapping catheter to locate the HB and a backup RV pacing lead was not routinely used in these implants. In patients undergoing AV node ablation, biventricular pacing using a LV lead in addition to the HB lead was performed in patients with reduced LV ejection fraction.

DEFINITIONS. S-HBP was defined based on the criteria published by Williams et al. (24) as evidenced by ventricular activation occurring solely over the His-Purkinje system. These included: 1) His-Purkinje-mediated cardiac activation and repolarization as evidenced by electrocardiographic concordance of QRS and T wave complexes; and 2) the paced ventricular interval was almost identical to the His-ventricular interval (Figure 1).

NS-HBP was defined based on capture of basal ventricular septum in addition to HB capture as: 1) no isoelectric interval between pacing stimulus and QRS; 2) the electrical axis of the paced QRS must be concordant with the electrical axis of the spontaneous QRS (if known); and 3) narrowing of QRS with higher output. Paced QRS complexes may be narrower than the escape rhythm or the conducted beats (Figure 2).

HB and ventricular (myocardial) pacing thresholds, R-wave amplitudes, intracardiac electrograms, and pacing lead impedances were measured at implantation. Total fluoroscopy time and procedure duration for each patient were recorded. A 12-lead electrocardiogram at baseline and during HBP, along with baseline and paced QRS duration, were also recorded for each patient.

FOLLOW-UP. Patients were followed in the device clinic at 2 weeks, 2 months, 1 year, and yearly thereafter. R-wave amplitudes, pacing thresholds, and lead impedances were recorded at each visit. Patients were also followed by remote monitoring every 3 months. Any significant increases in pacing

ABBREVIATIONS AND ACRONYMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AV</td>
<td>atrioventricular</td>
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<td>AVB</td>
<td>atrioventricular block</td>
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<td>HB</td>
<td>His bundle</td>
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<td>HBP</td>
<td>His bundle pacing</td>
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<td>NS-HBP</td>
<td>nonselective His bundle pacing</td>
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<td>RV</td>
<td>right ventricle</td>
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<td>S-HBP</td>
<td>selective His bundle pacing</td>
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JACC: CLINICAL ELECTROPHYSIOLOGY VOL. 1, NO. 6, 2015 DECEMBER 2015:571–81
threshold, lead dislodgement, or loss of capture were tracked routinely.

**STATISTICAL ANALYSIS.** Normally distributed data are reported as mean \( \pm \) SD. Absolute frequencies and percentages are reported for categorical data. Differences between groups were evaluated with Student t tests. All statistical tests were 2-tailed; \( p < 0.05 \) was considered to indicate statistical significance. The electrical characteristics of the 2 groups in follow-up were analyzed using repeated-measures analysis of variance with a group by time interaction.

**RESULTS**

Between January 2011 and June 2014, 260 patients underwent permanent pacemaker implantation at our institution (HBP was not performed in 2012 due to nonavailability of Medtronic 3830 pacing lead in the United States). All patients underwent an attempt at permanent HBP. Indications for pacemaker implantation were sinus node dysfunction in 104 patients (40%) and AV conduction disease in 156 patients (60%). Complete heart block or advanced AVB was present in 100 patients (38%; mean age, 75 \( \pm \) 12 years; 62 men [62%]) and comprised the study group. AV nodal block was present in 46 patients (46%), and 54 patients (54%) had infranodal His–Purkinje disease.

At baseline, narrow QRS was seen in 40 patients (40%), and wide QRS was present in 60 (60%). Baseline characteristics are shown in Table 1.

**IMPLANT OUTCOMES.** Permanent HBP was successful in 84 of the 100 patients (84%) with advanced AVB (Figure 3). Single-chamber pacer was implanted in 12 (12%) patients, dual-chamber device in 82 (82%) patients, and biventricular pacer in 6 (6%) patients. Backup RV lead was placed in only 2 of these patients. Mean procedure time was 71 \( \pm \) 21 min (range: 36 to 132 min), and mean fluoroscopy duration was 11 \( \pm \) 6 min (range: 4 to 46 min).
S-HBP was achieved in 22 (22%) patients, NS-HBP in 62 (62%) patients, and RV septal pacing in 16 (16%) patients. In patients with AV nodal block (n = 46), HBP could not be achieved in 3 (7%) patients (high threshold, n = 2; failure to map HB, n = 1). In patients with infranodal AVB (n = 54), HBP was unsuccessful in 13 (24%) patients (failure to capture and recruit HB, n = 9; failure to map HB, n = 4).

Permanent HBP was successfully achieved in significantly more patients with AV nodal block compared with patients with infranodal AVB (93% vs. 76%; p < 0.05). S-HBP was achieved in 44% of patients with AV nodal block and 7% of patients with infranodal AVB, and NS-HBP was achieved in 56% of patients with AV nodal block and 93% of patients with infranodal AVB. There were no differences in procedure or fluoroscopy duration between the 2 groups (Table 2). Baseline QRS duration was 103 ± 20 ms (range: 72 to 145 ms) in AV nodal block patients compared with QRS duration of 143 ± 18 ms (range: 120 to 186 ms) in patients with infranodal AVB. The paced QRS duration of 114 ± 21 ms (range: 82 to 150 ms) and 134 ± 17 ms (range: 100 to 162 ms), respectively, in the 2 groups were significantly narrower compared with paced QRS duration of 167 ± 14 ms (n = 16; range: 150 to 198 ms; p < 0.05) in patients with RV septal pacing (unsuccessful HBP).

HB pacing threshold at implantation, 2 weeks, 2 months, and last follow-up (19 ± 12 months; range: 6 to 46 months) was 1.4 ± 1.0 V, 1.5 ± 1.2 V, 1.7 ± 1.0 V, and 1.6 ± 1.0 V at 0.5 ms, respectively. The HBP threshold at last follow-up ranged from 0.5 to 3.75 V at 0.5 ms. At implantation, pacing thresholds and lead impedances were similar between the 2 groups (1.3 ± 0.7 ms vs. 1.4 ± 1.2 V at 0.5 ms and 577 ± 132 Ohms vs. 565 ± 153 Ohms, respectively). Sensed R-wave amplitudes were smaller (5.3 ± 3.9 mV vs. 6.9 ± 5.8 mV; p < 0.05) in the AV nodal block group compared with infranodal AVB group. HB pacing thresholds, sensing, and lead impedances remained

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**FIGURE 2** Nonselective His Bundle Pacing

(Top) Baseline 12-lead electrocardiogram of a patient with 2:1 atrioventricular block with right bundle branch block, QRS duration of 120 ms. (Middle) Intracardiac electrogram from the permanent His bundle pacing lead at the time of implantation. Atrial electrogram (A) is followed by His (H) and then ventricular (V) electrogram in a 2:1 fashion. (Arrow) His bundle injury current, which resolved in 20 min. (Bottom) atrioventricular sequential pacing. The pacing spike is immediately followed by QRS complexes with evidence for fusion from ventricular and His bundle capture. Note that the right bundle branch block has also resolved with His bundle pacing, suggesting both the atrioventricular block and right bundle branch block are at the level of the proximal His bundle.
In our series, 84% of patients with complete or advanced AVB, regardless of the location of block, underwent successful permanent HBP. In patients with AV nodal block, 93% had a successful outcome.
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increased operator experience. The success rate in the present study is attributable to high His-bundle pacing thresholds during mapping. These patients after excluding 32% of patients due to QRS. They attempted permanent HBP in only 68% of compared with 76% of patients with infranodal AVB. Deshmukh et al. (11), reported success rates of 72% (39/54) in patients with atrial fibrillation undergoing AV node ablation. In a recent series by Kronborg et al. (18), permanent HBP was successful in 85% of patients with high-grade AVB and a narrow QRS complex. They achieved S-HBP in 11% (4 of 38) and NS-HBP in 74% (28 of 38). In our series, S-HBP was achieved in about one-half of patients with AV nodal block. We reported a success rate of 75% (15 of 20) in our earlier study consisting of a smaller number of patients with complete heart block (16). A higher success rate in the present study is attributable to increased operator experience.

**INFRANODAL AVB.** HBP can correct chronic bundle branch block and complete AVB due to infranodal disease (17,19-28). Longitudinal dissociation of the HB has been suggested to explain this observation (27). Fibers destined to be right and left bundle branches are differentiated histologically and separated in the main His trunk (28). Disease in the fibers in the central trunk can cause bundle branch block or complete heart block. Pacing adjacent or distal to these fibers can correct these conduction abnormalities. Barba-Picharda et al. (17) studied 182 patients with AVB (84 with narrow QRS and 98 with wide QRS) and were able to recruit the HB by temporary pacing in 98% (82 of 84) of patients with narrow QRS compared with 52% (51 of 98) of patients with wide QRS. They attempted permanent HBP in only 68% of these patients after excluding 32% of patients due to high His-bundle pacing thresholds during mapping. Of these 133 patients, permanent HBP was successful in 59 patients (44%). Considering all patients with heart block, permanent HBP was achieved successfully in only 32% (44 of 84 in narrow QRS and 15 of 98 in wide QRS) of patients. Differences in methodology and tools used could explain the higher success rates in our study. Compared with a traditional pacing lead with a retractable screw (Tendril 1488 or 1788, St. Jude Medical, Irvine, California) used by Barba-Picharda et al. (17), we used a dedicated pacing lead with exposed screw (Medtronic, 3830) delivered through a specially designed sheath with an orthogonal secondary curve (Medtronic, C315 His).

**INTRA-HIS AVB.** In 29 of 54 patients (54%) with infranodal disease, HB could be recruited successfully by pacing at the site with evidence for HV block on a local electrogram recorded from the pacing lead suggesting that the disease may be discrete (intra-His AVB) at this level (Figures 2 and 4). In 12 patients (22%), the capture threshold was high, and by positioning the lead slightly more distally, we were able to recruit the distal HB at lower output (Figure 5). It is likely that the remaining 13 patients (24%) had heart block due to distal Purkinje system disease (infra-His AVB), and permanent HBP was unsuccessful. Early studies using HB recordings have suggested that intra-His block contribute to only 15% to 25% of patients with infranodal AVB (21–23). More than 70% was attributed to distal, infra-His AVB. In these studies, the diagnosis of intra-His block depended on identifying split His potentials and/or distal HB potential or HV block in the setting of narrow QRS, and hence intra-His block could have been significantly underestimated. In our study, split His potentials (Figure 6) were recorded in only 2 patients and narrow QRS was seen in 2 patients. However, our study demonstrates that in the majority of patients with infranodal AVB (41 of 54; 76%), the site of conduction block is localized to the main HB. The postulated mechanisms for this recruitment of distal His and bundle branches in patients with intra-His block are: 1) longitudinal dissociation in the HB with pacing adjacent or distal to the site of delay/block; and/or 2) differential source-sink relationships during pacing versus intrinsic impulse propagation; and/or 3) virtual electrode polarization effect (29,30). Virtual electrode polarization is an electrical phenomenon by which a stimulus of any polarity creates regions of

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**TABLE 3 Electrical Parameters**

<table>
<thead>
<tr>
<th>Visit</th>
<th>AV Nodal Block</th>
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<th>Infra nodal Block</th>
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<tbody>
<tr>
<td></td>
<td>HBP Threshold, V</td>
<td>R-Wave, mV</td>
<td>Impedance, Ohms</td>
<td></td>
<td>HBP</td>
<td>R-Wave, mV</td>
<td>Impedance, Ohms</td>
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<td>Implant</td>
<td>1.3 ± 0.7</td>
<td>5.3 ± 3.9</td>
<td>577 ± 132</td>
<td>1.4 ± 1.2</td>
<td>6.9 ± 5.8*</td>
<td>565 ± 153</td>
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<tr>
<td>2 weeks</td>
<td>1.5 ± 0.8</td>
<td>6.7 ± 4.6</td>
<td>475 ± 111</td>
<td>1.7 ± 1.2</td>
<td>9.7 ± 7.9*</td>
<td>476 ± 121</td>
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<tr>
<td>2 months</td>
<td>1.5 ± 0.9</td>
<td>7.2 ± 5.5</td>
<td>442 ± 109</td>
<td>1.7 ± 1.3</td>
<td>9.9 ± 8.3*</td>
<td>469 ± 81</td>
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<tr>
<td>Last follow-up (19 ± 12 months)</td>
<td>1.6 ± 0.9</td>
<td>6.4 ± 4.4</td>
<td>437 ± 75</td>
<td>1.7 ± 1.1</td>
<td>9.6 ± 9.1*</td>
<td>463 ± 78</td>
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Values are mean ± SD. Pacing threshold tested at 0.5-ms pulse duration. *p < 0.05 versus atrioventricular nodal block. HBP = His bundle pacing.
depolarization and hyperpolarization in the vicinity of the pacing electrode tip, which can result in de-excitation of previously refractory tissue and so provide a pathway for propagation. Virtual electrode polarization induced by HB pacing may play a role in promoting propagation in diseased HB tissue.

PROCEDURAL OUTCOMES. Despite not using a mapping electrophysiology catheter to locate the HB we were able to locate the HB using the pacing lead in 95 patients (95%). By not using a mapping catheter, we could avoid femoral venous access, as well as the associated costs and potential risks, without increasing the procedural duration or fluoroscopy times. Kronborg et al. (18) reported mean total procedural duration and fluoroscopy times of 85 ± 31 min and 23 ± 13 min, respectively, in their patients with AV nodal block and narrow QRS complexes, compared with 71 ± 21 min and 11 ± 6 min, respectively, in our study. Zanon et al. (14) reported a fluoroscopy duration of 15 ± 9 min and 18 ± 13 min for S-HBP and NS-HBP lead placement, respectively, in a series of 307 patients. Both studies used the Medtronic 3830 pacing lead delivered via a deflectable sheath (Medtronic C304) and a mapping catheter placed through the femoral vein.

QRS DURATION. In patients with AV nodal block, paced QRS duration was only slightly prolonged compared with baseline (103 ± 20 ms vs. 114 ± 21 ms). Most patients with NS-HBP had minimal ventricular pre-excitation due to capture of adjacent septal myocardium in the setting of normal HV intervals. In patients with infranodal AVB, baseline QRS was
significantly wider ($143 \pm 18$ ms; $p < 0.05$) than patients with AV nodal block, and paced QRS duration was slightly narrower ($134 \pm 17$ ms) compared with baseline ($p = $ NS). In a subgroup of patients ($n = 7$), there was 60 to 80 ms of pre-excitation leading to QRS duration >150 ms, suggesting slow conduction in the His-Purkinje system despite HB recruitment, allowing for greater degree of RV pre-excitation. It is unclear if these patients would lose HB capture during long-term follow-up. However, it is important to note that patients with NS-HBP pacing have significantly lower RV capture threshold ($1.3 \pm 0.6$ V at 0.5 ms in our series) through the same lead serving as RV backup. Baseline QRS duration or morphology was not predictive of successful HBP in patients with infranodal block. RV septal pacing is associated with narrower QRS than apical pacing but has not been shown to improve clinical outcomes (8). In a recent crossover, randomized study of 38 patients, NS-HBP (para-Hisian pacing) was shown to preserve LV function and ventricular synchrony compared with RV septal pacing (31). Larger, randomized trials would be necessary to prove clinical benefits of permanent HBP.
PACING THRESHOLDS. Another important finding in this study was that the HB pacing thresholds were within acceptable range in the majority of patients. The mean HB pacing threshold at implant was $1.4 \pm 0.8$ V at 0.5 ms in patients with S-HBP compared with $1.3 \pm 1.0$ V at 0.5 ms in NS-HBP. Kronborg et al. (18) reported pacing thresholds of $2.3 \pm 1.0$ V and $1.7 \pm 1.5$ V in AV nodal block patients with S-HBP and NS-HBP, respectively. Barba-Picharda et al. (17) reported acute pacing thresholds of $1.4 \pm 0.6$ V at 1.0 ms and $1.9 \pm 1.2$ V at 1.0 ms in patients with AV nodal and infranodal block, respectively. We believe that the main reason for better pacing thresholds in our series was due to the use of C315 His sheath (28). Because of the secondary septal curve, this sheath delivers the lead perpendicular to the septal tissue allowing better contact. We recently demonstrated that HB injury current, similar to myocardial injury current, can be recorded in 37% of patients undergoing successful permanent HBP and were associated with significantly lower thresholds (15).

AV NODAL VERSUS INFRANODAL BLOCK. We did not notice significant differences between the 2 groups in the procedural outcomes. However, due to the unstable nature of the escape rhythm in the infranodal group, we often placed the atrial lead in the right ventricle to provide temporary backup pacing during HB mapping. Despite advanced AVB, the HB could be located easily in patients with infranodal block. In patients with AV nodal block, intravenous isuprel may be necessary to increase junctional escape rates to identify the His electrograms. In patients with AV nodal block and S-HBP, R waves
may be <2 mV, requiring adjustment of sensitivity threshold. Occasionally atrial oversensing may be an issue in this group.

**LEAD FAILURE.** During a mean follow-up of 19 ± 12 months, 5 patients required lead revision: 2 had lead dislodgements with intermittent loss of capture, and 3 had significant increase in thresholds from 1 to 1.5 V at implant to 4 to 4.5 V and underwent elective lead revision (nodal block, 3; infranodal, 2; NS-HBP, 3; S-HBP, 2). Previous studies had described similar or higher incidence of lead dislodgement in permanent HBP compared with RV pacing.

**STUDY LIMITATIONS.** The present study describes the implant success of permanent HBP in patients with advanced heart block without comparisons of clinical outcomes with RV pacing. Although HBP may be superior physiologically to RV pacing and several small studies have shown improvement in LV function and clinical outcomes compared with RV pacing (12,16,31), a randomized trial assessing clinical outcomes (functional status, heart failure hospitalization, LV function, and echocardiographic parameters) would be necessary to prove superior clinical outcomes. In addition, this study was conducted in a high-volume center with extensive experience in HB pacing. Although many of our patients had follow-up of 2 to 3 years, longer term follow-up is necessary to assess the efficacy and safety of HBP, especially in patients with infranodal disease. Because pacing thresholds with permanent HBP are still higher than with a standard RV lead, improvement in lead designs (longer helix), delivery sheaths, and new devices with longer battery life may be necessary.

**CONCLUSIONS**

This study demonstrates that permanent HBP pacing can be performed safely and successfully in 84% of unselected patients with advanced or complete AVB. Contrary to previous reports, the majority of infranodal AVB occurs in the main HB (intra-His) and can be corrected by permanent HBP. The procedure and fluoroscopy duration are less than previously reported and within an acceptable range. A mapping electrophysiology catheter to locate the HB or routine placement of a backup RV lead may not be necessary.

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KEY WORDS complete heart block, His bundle pacing, His Purkinje system, intra-His block