CLINICAL REVIEW

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Permanent His Bundle Pacing: The Past, Present, and Future

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Permanent His Bundle Pacing. Long-term right ventricular (RV) apical pacing has been associated with an increased risk of death, heart failure, and atrial fibrillation (AF). Alternative sites for RV pacing have not proven to be superior to RV apical pacing. Cardiac resynchronization therapy (CRT) using a biventricular (BiV) lead system is indicated for patients with a low left ventricular ejection fraction and QRS prolongation, but there remains about a 25–30% nonresponse rate. CRT has been less effective for nonleft bundle branch block conduction delay and with normal/low normal left ventricular function. Over the past decade, there have been more data on the feasibility and advantages of pacing at the His Bundle (HB) region. We review the anatomy and physiology of the HB, the available data on permanent HB pacing, its current and potential future applications. *(J Cardiovasc Electrophysiol, Vol. 28, pp. 458-465, April 2017)*

cardiac resynchronization, clinical outcomes, bundle branch block (BBB), permanent His bundle pacing (HBP)

Introduction

Long-term right ventricular (RV) apical pacing has been associated with cellular and structural changes in the ventricles, thereby resulting in an increased risk of death, heart failure (HF), and atrial fibrillation (AF).[1-3] The pursuit of a more optimal site of ventricular pacing site to minimize these potential adverse outcomes has been ongoing for the past decade. There have been conflicting data on the potential advantages of alternative site pacing such as the RV outflow tract and RV septal pacing.[4,5] Cardiac resynchronization therapy (CRT) using a biventricular (BiV) lead system has been demonstrated to be useful in patients with reduced left ventricular (LV) function and interventricular conduction delay, particularly left bundle branch block (LBBB).[6,7] However, CRT with BiV pacing is not always feasible and the percentage of nonresponders remains high. There is no evidence of significant benefit among patients with right bundle branch block (RBBB).[7] BiV pacing has recently been evaluated in patients with normal/low normal LV function and the need for significant ventricular pacing. These trials have demonstrated mixed results.[8,9] Over the past decade, there has been growing interest in permanent pacing at the His Bundle (HB) region. In this paper, we hope to review some of the history, current data on permanent HB pacing and discuss its potential future implications.

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Original Descriptions of Pacing the His Bundle

Temporary His Bundle Pacing (HBP) was described for the first time in 1967 by Scherlag *et al.*, using an epimyocardial approach in dogs undergoing open chest surgery, through the positioning of a catheter pacing the His bundle.[10] Subsequently, the same group published their experience on temporary recordings of the HB in humans using intravascular endocardial catheters.[11] In 1970, Narula *et al.*[12] demonstrated how it was possible to obtain HBP in man, using a multipolar catheter positioned at the atrioventricular junction, above the septal leaflet of the tricuspid valve.

Permanent HBP was first described in clinical practice in 2000 by Deshmukh *et al.*[13] They demonstrated successful HBP in 12 of 18 patients (67%) with chronic AF, left ventricular ejection fraction (LVEF) <40%, and a QRS duration <120 milliseconds after ablation of the AV junction. Subsequently, a few European groups described the success of permanent HBP.[14,15] Barba-Pichardo *et al.* reported a success rate of 65% in patients with AV block using standard pacing leads with retractable screws and manually shaped stylets.[16] These studies routinely used a mapping catheter to localize the HB.

The Anatomy of the His Bundle

The bundle of His is a chord-like structure that traverses from the compact AV node through the membranous interventricular septum and measures an average of 20 mm in length by 4 mm in diameter. Kawashima *et al.*[17] studied the macroscopic anatomy of the HB and described its variability in location relative to the membranous interventricular septum in 105 elderly human hearts. They described 3 different anatomical variations: (1) The most common anatomical pattern (Type I) was where the AV bundle ran along the lower border of the membranous septum and was usually covered with a thin layer of myocardial fibers. This accounted for 47% of the specimens; (2) Type II where the AV bundle was discretely separated from the membranous septum and insulated by thick myocardial fibers (seen in 32% of the specimens); and (3) Type III (21% of the specimens) where the AV bundle was "naked" and ran beneath the endocardium with no insulation from the surrounding myocardial fibers.[17]

The location of the implanted HBP lead and its relationship to the triscuspid annulus has been reported in a few reports. Correa de Sa *et al.* demonstrated in the autopsy study of an 81-year-old woman with a previously implanted HBP lead that the lead tip was unequivocally implanted on the trial side of the tricuspid annulus.[18] Vijayaraman *et al.* performed an imaging evaluation of a 42-year-old man with an HBP lead and demonstrated similarly that the tip of the lead was on the atrial aspect of the tricuspid valve plane.[19] Whether this is always the case, particularly when the lead is implanted distal in the HB region, remains unclear.

The Physiology of the His Bundle

An important concept/theory pertaining to the physiology of the HB is the concept of "longitudinal dissociation of the HB." Narula *et al.* first described the concept of longitudinal dissociation in the HB back in 1977.[20] They postulated that bundle branch block could be due to delay within fibers in the HB that are predestined to become either the RBB or LBB. They elegantly demonstrated that pacing distal to the site of conduction delay could recruit fibers predestined to be the bundle branches and thereby narrow the QRS duration. El-Sherif *et al.* demonstrated similar findings in an experimental model.[21] As noted below, various studies on permanent HB pacing have validated this concept by recruiting diseased portions of the conduction system and narrowing the QRS in patients with BBB.

Potential Indications and Relative Contraindications

Based on the data presented below, most patients with an anticipated high burden of ventricular pacing are ideal candidates. These include patients with: (1) AV conduction disease with narrow QRS; (2) permanent AF (with narrow native QRS) that might require substantial pacing given need for AV nodal blocking agents or anticipated AV node ablation; (3) AF with wide QRS that require ventricular pacing; (4) failed BiV CRT implants (with the HB lead in the LV port).

Patients with SND undergoing dual chamber pacemaker implants with the potential need for ventricular pacing in the future might also be potential candidates. Patients with prosthetic valves and AV conduction disease are also good candidates.[22]

Patients with concern for distal/parietal conduction system disease and need for ventricular pacing or need for resynchronization might be candidates who do not benefit from HBP. Even if HBP is attempted in these cases, one might consider implantation of a back-up RV lead given unclear data on the progression of disease in such cases. Patients needing pacemaker implants following a TAVR with Medtronic Core valve might be another group that might warrant caution since the large profile of this valve might result in a more parietal block/delay in conduction.[22]

Implant Technique and Programming

Since the original implantation of pacing leads at the HB region over a decade ago, techniques have evolved as implantation tools specifically designed for selective site pacing, consisting of a steerable sheaths and newer leads have become available. These tools have made it feasible to map the HB region and achieve permanent HBP without the need for an additional mapping catheter to localize the HB.

We have previously described details on our technique of performing permanent HBP.[23,24] Permanent HBP is typically performed using the SelectSecure (model 3830, 69 cm, Medtronic Inc., Minneapolis, MN, USA) pacing lead delivered through a fixed curve sheath (C315 HIS, Medtronic Inc.) or a steerable sheath (C304, Medtronic Inc.). Unipolar electrogram recordings from the lead tip are displayed either on the mapping system in the electrophysiology lab using alligator cables or directly on a Medtronic pacing system analyzer (model 2290) at a sweep speed of 50 mm/s. After identifying an HB electrogram by mapping the HB region, pacing is performed to confirm HB capture. The lead is then screwed into position by means of 4–5 clockwise rotations.

Subsequently, the sheath is pulled back and pacing is performed in both unipolar and bipolar configurations (typically at a pulse width of 1 millisecond) to define capture thresholds and identify different QRS morphologies as noted below.

Given that the HB is surrounded by fibrous tissue, the average capture thresholds tend to be higher than routine RV pacing (1.35 V @ 0.5 millisecond vs. 0.6 V @ 0.5 millisecond, $P < 0.001$) and mean R-wave amplitudes are lower (6.8 mV vs. 13.7 mV, $P < 0.05$).[23] It must be noted that the presence of a HB injury current, when present (37% cases in 1 report), has been associated with a lower capture threshold.[25] On average, capture thresholds above 2.5 V @ 1 millisecond would result in shorter battery longevity and must make the operator consider implantation a different site of the HB or accept lead implant in the RV septum. This would also need to be individualized to the patient and the indication for pacing. It would also be advisable to ensure R-wave sensing above 1 mV to avoid far-field atrial over sensing. Checking R-wave sensing in both unipolar and bipolar configurations might allow for more programming options when it comes to sensing.

With more data available on lead stability and stable pacing thresholds as noted below, it has made the decreased the need for implantation of a back-up RV lead. Patients with concern for distal/parietal conduction system disease and need for ventricular pacing would benefit from a back-up lead. This would also be a consideration for a patient with permanent AF and planned for an AVJ ablation (HB lead in the RA port and RV lead in RV port for back-up pacing), especially during one's early implant experience.

In a case of an HBP lead implant for a failed LV lead implant, the HB lead is usually hooked up to the LV port with one of 3 options for pacing: (1) program VV delays to LV→ RV 80 milliseconds such that ventricular capture occurs via pacing from the HB lead; (2) program RV pacing output to subthreshold value; (3) use a combination of His Tip to RV ring (might have lower capture thresholds).[26]

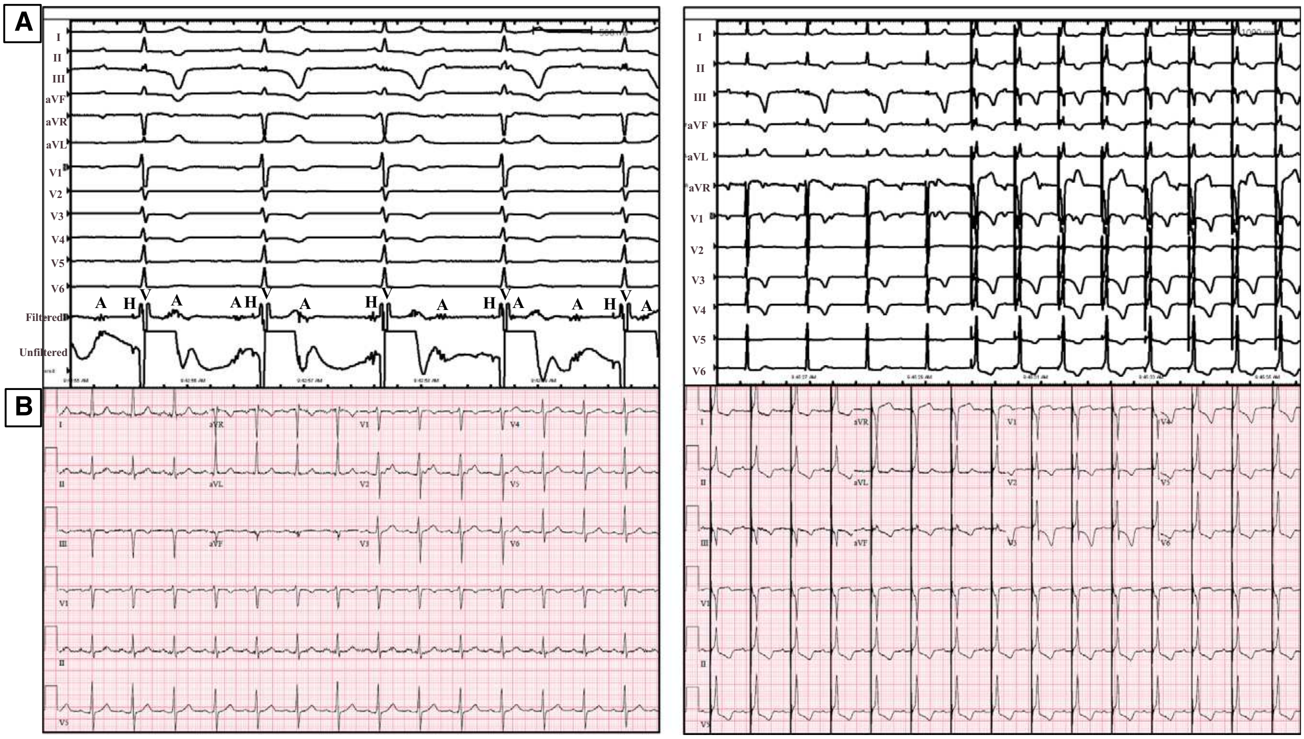

Figure 1. *A: Top panel: Represents the unipolar recordings from the tip of the 3830 (Medtronic, Inc) His lead demonstrating block at the level of the AV node. B: Baseline electrocardiogram (ECG) and postimplant paced ECG. The paced morphology is consistent with nonselective HBP and a QRS duration of 110 milliseconds. [Color figure can be viewed at wileyonlinelibrary.com]*

HBP Morphologies and Terminology

Permanent HBP can result in different paced QRS morphologies.[23] The QRS morphology is dependent on: (1) the output of pacing; (2) position of the His lead; and (3) the anatomy of the HB region in each individual patient.

Selective HBP is the term used when there is fusion and para-Hisian morphology (His +RV capture) with high output pacing and pure His-bundle pacing at lower outputs. If the lead tip is anchored to the His bundle, at high output the surrounding myocardial fibers are also recruited along with the His bundle resulting in fusion. At low outputs, the current density is low enough that the His bundle is preferentially recruited resulting in pure His-bundle pacing. This is also the morphology that is seen in patients with Type I HB anatomy. In about 10–15% of cases, pure His-bundle pacing is seen no matter what the output is and this is possibly suggestive of Type III anatomy.

Nonselective HBP is the term used when para-Hisian morphology (His +RV capture) is present (regardless of pacing output) and there is always fusion between local myocardium and the His bundle. This is more suggestive of Type II anatomy.

Case Examples

(1) Case 1:
A 49-year-old male with *Enterococcus faecalis* endocarditis post a bioprosthetic aortic and mitral valve developed complete heart block without an escape rhythm postoperatively. He continued to have complete AV block with an unstable ventricular escape rhythm on postoperative day #5 and was sent for permanent pacemaker implant. Given the potential need for a significant burden of ventricular pacing, permanent HBP was attempted. Figure 1A represents the unipolar recordings from the tip of the 3830 (Medtronic Inc.) His lead demonstrating block at the level of the AV node. Figure 1B represents the baseline electrocardiogram (ECG) and postimplant paced ECG. The paced morphology is consistent with nonselective HBP with a QRS duration of 108 milliseconds.

(2) Case 2:
A 78-year-old male with sinus node dysfunction, RBBB, and syncope was referred for a dual-chamber pacemaker implant with an attempt at PHBP. Figure 2A represents the unipolar recordings from the tip of the 3830 (Medtronic Inc.) His lead. Figure 2B represents the baseline ECG and postimplant paced ECG. The paced morphology is consistent with para-Hisian pacing and nonselective HBP with recruitment of the baseline RBBB and a QRS duration of 100 milliseconds. Figure 3 demonstrates the fluoroscopic location of the HBP lead in right anterior oblique and left anterior oblique projections.

(3) Case 3:
An 81-year-old man with known history of coronary disease, ischemic cardiomyopathy (CMP) with LVEF of 30%, NYHA class III symptoms, and an LBBB of 168 milliseconds was referred for a BiV ICD implant. The patient underwent an unsuccessful attempt at coronary sinus lead placement due to limited targets, high LV capture thresholds in available targets with phrenic nerve stimulation from all poles of a quadripolar lead.

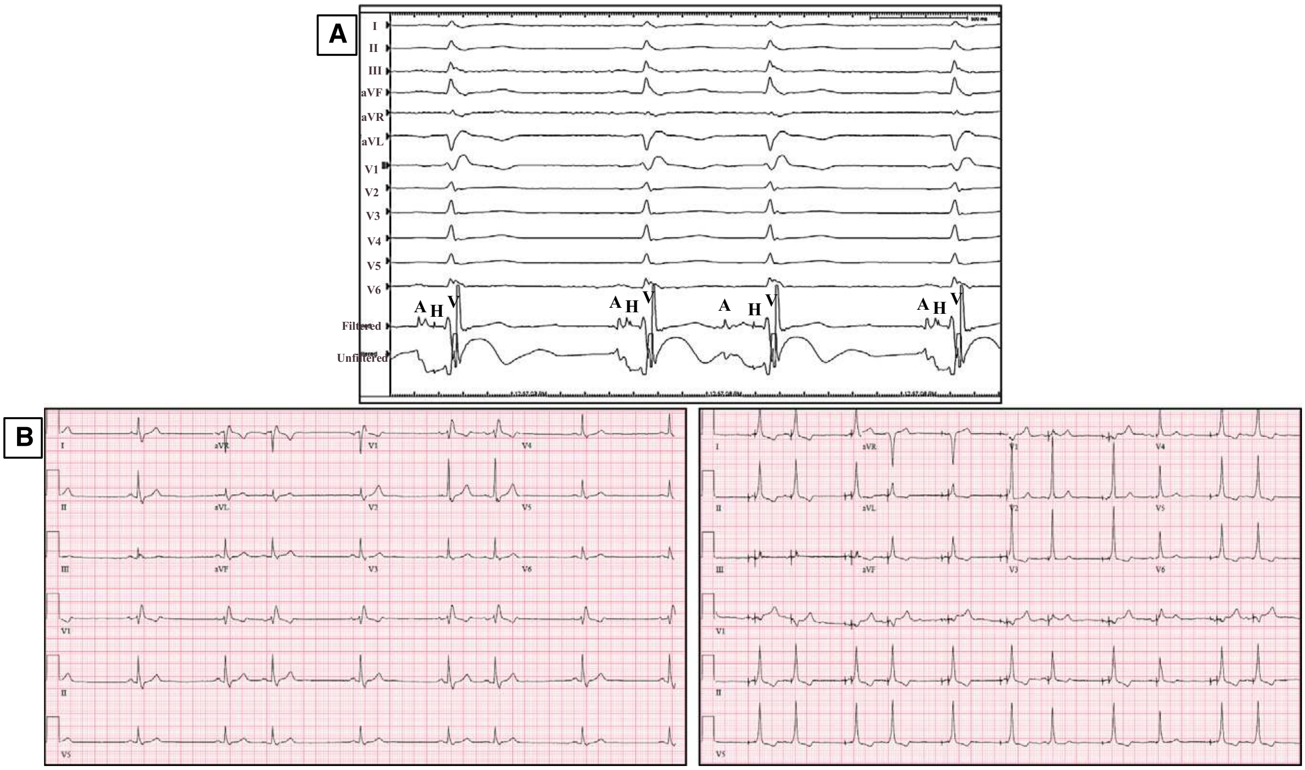

Figure 2. *A: Represents the unipolar recordings from the tip of the 3830 (Medtronic, Inc) His lead. B: Represents the baseline ECG and postimplant paced ECG demonstrating nonselective HBP with recruitment of the baseline RBBB and a QRS duration of 100 milliseconds. [Color figure can be viewed at wileyonlinelibrary.com]*

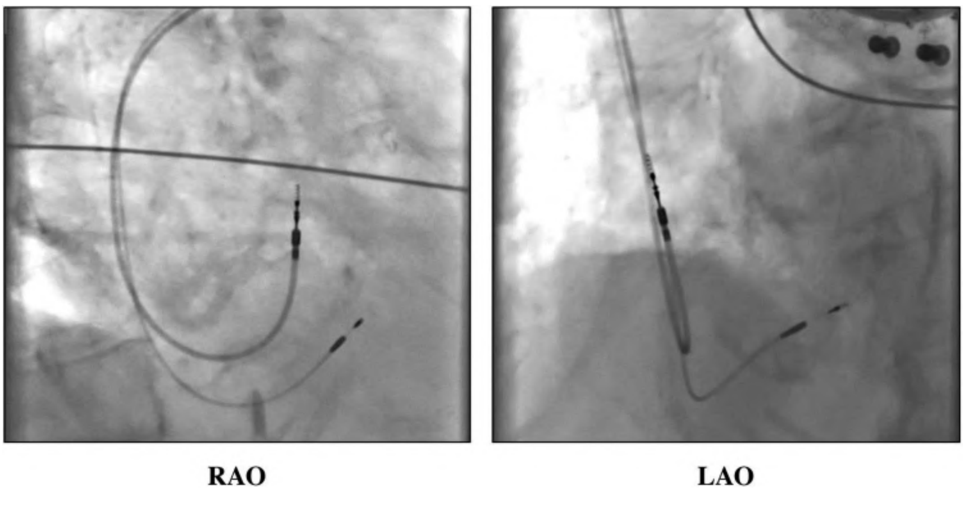

Figure 3. *Fluoroscopic position of the HB lead in right anterior oblique (RAO) and left anterior oblique (LAO) projections.*

Hence, a decision was made to attempt to overcome the LBBB with HBP. Figure 4A represents unipolar recordings (prescrew and postscrew) from the tip of the 3830 (Medtronic Inc.) His lead during mapping as recorded on a Medtronic PSA. This demonstrates a "His current of Injury" postscrew placement. The baseline ECG (LBBB 168 milliseconds) and paced ECG are shown in Figure 4B and demonstrate selective HB capture with a paced QRSd of 88 milliseconds and a stimulus to QRS onset duration of 44 milliseconds consistent with the HV interval.

Available Outcomes Data on PHBP

Table 1 provides a summary of available data on permanent HBP. Available procedural and clinical outcomes on permanent HBP as listed below.

Procedural Outcomes: (Acute and Long Term)

Acute procedural success

The procedural success of HBP has varied from 65% in the early experiences (without the use of a guiding sheath

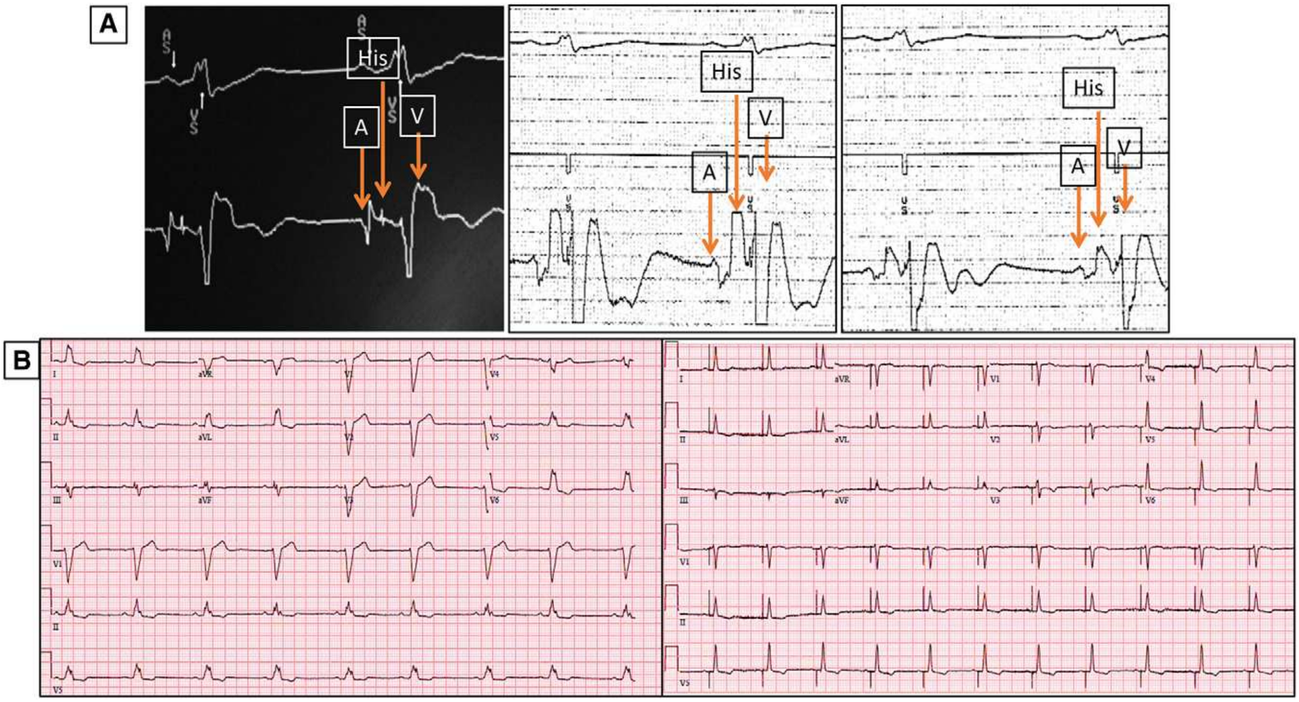

Figure 4. *A: HB recordings from the Medtronic programmer revealing an A-H-V with evidence of a His injury current postscrew-in. Pacing from this position lead revealed selective HB capture with successful recruitment of LBBB. B: Baseline ECG and postimplant paced ECG. The paced morphology is consistent with selective HBP with recruitment of the baseline LBBB and a QRS duration of 88 milliseconds. [Color figure can be viewed at wileyonlinelibrary.com]*

and using a HB mapping catheter) to as high as 85–90% in the new era with the availability of newer tools.

Barba-Pichardo *et al.*[16] described their experience with HBP among 182 patients with AV conduction abnormalities. An electrophysiologic mapping catheter was used to mark the HB. They used an active fixation lead (Tendril model 1488T and 1788TC, St. Jude, Sylmar, CA, USA). They were successful achieving permanent HBP in 65% of all patients. Zanon *et al.* reported their experience using the Select Secure Medtronic delivery system in 307 successful cases of HBP (28% selective HBP and 72% nonselective HBP).[27]

We described our experience in a large series of 192 patients undergoing dual chamber pacemaker implants comparing permanent HBP (75 of 94 patients) to RV pacing (98 patients).[23] Mapping of the HB region was performed using the pacing lead. Permanent HBP was feasible in 75 of 94 patients (80%).

The ability to recruit and narrow BBB with HBP has been systematically reported by our group. We reported success rates of 90% among 58 patients undergoing permanent HBP with underlying BBB.[28] Studies have looked at the ability of recruiting LBBB among patients with failed BiV CRT cases and success rates have been reported to be as high as 90%.[22,29]

Long-term pacing thresholds

Even though pacing thresholds are generally higher and R-wave sensing is low in this region, multiple studies have reported an overall stable pacing threshold on long-term follow-up.

In our original description,[23] we reported a higher pacing threshold in the HBP group than in the RVP group (1.35 V @ 0.5 millisecond vs. 0.6 V @ 0.5 millisecond; $P < 0.001$). There was a small but nonsignificant increase in pacing thresholds (1.35 V to 1.5 V @ 0.5 millisecond) and remained stable over a 2-year follow-up period. Zanon *et al.* reported similar findings in a 307 patient series. Selective HBP with pure HB capture resulted in a significantly higher threshold (2.5 V vs. 1.3 V @ 0.5 millisecond), lower sensed-wave amplitude (3.4 mV vs. 11.3 mV; both $P < 0.001$), and higher impedance ($P = 0.008$) when compared to nonselective HBP.[27] Over a 2-year follow-up, no changes were observed on intragroup pacing thresholds and R-wave sensing.

Lead stability/dislodgement rates

Based on available data, the dislodgement rates of HBP leads is not significantly higher than conventional RV leads. Zanon *et al.* reported a lead-related complication rate of 2.6% during a follow-up of 20 ± 10 months.[27] Specifically, 5 (5.7%) patients with selective HBP and 7 (3.2%) patients with nonselective HBP developed either an increased threshold above 5 V @ 0.5 millisecond, lead dislodgement or decrease in sensed R-waves. Overall, 3 patients required lead replacement and no complications due to lead extraction were reported. In our series, we reported a lead-related complication among 3 of the 75 successful cases, 2 with loss of capture, and 1 with increased capture threshold above 5 V @ 0.5 millisecond as compared to 2 lead dislodgements in the RV pacing group.[23]

Clinical Outcomes

As noted below, various small and larger studies have demonstrated a clinical benefit of HBP versus conventional RV pacing with preservation of LVEF, decreased HF hospitalization, improvement in quality-of-life and NYHA functional class.

TABLE 1

Available Outcomes Data on HBP

Study Name	Design	Study Population	Total Attempted Cases	Success Rates Using HBP	Outcomes
PHBP in All Comers					
Deshmukh *et al.*[13]	Prospective	Chronic AF, LVEF <40%, QRS duration <120 milliseconds, AV junction ablation	18	12 (66%)	Improvement in LV dimensions, functional status, cardiothoracic ratio, and LVEF
Orchetta *et al.*[15]	Prospective, crossover, randomized	Chronic AF, AV junction ablation randomized to 6-months of RV pacing versus para-Hisian HBP	18	17 (94%)	Improvement in NYHA functional class, 6-minute walk test, QoL, and hemodynamic parameters
Barba-Pichardo *et al.*[16]	Prospective	All patients with AV block as the pacing indication	91 of 182 selected cases	59 (65% of attempted cases)	No long-term clinical outcomes reported
Zanon *et al.*[27]	Prospective, multicenter	All patients with indication for pacing, feasibility of select secure delivery system		307 cases successful (28% selective HBP and 72% nonselective HBP)	Mean follow-up of 20 ± 10 months; 5 (5.7%) patients with DHB lead and 7 (3.2%) patients with a lead in the PH region had events (increased thresholds, 2 with dislodgements)
Kronborg *et al.*[30]	Prospective, crossover, randomized	AV block, narrow QRS, and left ventricular ejection fraction >40%, 12 months of HBP versus RV pacing	38	32 (84%)	Improvement in LVEF, no significant improvement in NYHA functional class, 6-minute walk test or QoL
Sharma *et al.*[23]	Prospective	All patients with indication for PPM implant, comparing PHBP versus RV pacing	94	75 (80%)	Improvement in HFH outcomes, no significant improvement in mortality or AF
PHBP for Cardiac Resynchronization					
Barba-Pichardo *et al.*[33]	Prospective	HBP attempted in patients with failed BiV	16	9 (56%)	Improvement in NYHA class; improvement in LVEF and LV dimensions
Lustgarten *et al.*[34]	Crossover	HBP and LV leads in all patients undergoing CRT	29	21 (72%)	Significant improvements in LVEF, functional status, 6-minute walk distance with both HBP and BiV in 12 patients who completed the crossover
Ajijola *et al.*[29]	Prospective	HBP attempted in patients with failed BiV	13	12 (92%)	Improvement in LVEF and LV dimensions; improvement in longitudinal strain
Vijayaraman *et al.*[35]	Prospective	Failed LV lead placement; HBP with LV leads; HBP alone in patients with indication for CR	32	29 (91%)	Improvement in NYHA functional class; improvement in LVEF

AF = atrial fibrillation; BiV = biventricular; HBP = His Bundle pacing; LV = left ventricular; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PHBP = permanent HBP.

Orchetta *et al.*[15] performed a randomized, crossover study in 16 of 18 patients with chronic AF undergoing AV junction ablation and randomized them to 6 months of RV pacing versus para-Hisian HBP. Mean QRS duration was 88.3 ± 7.1 milliseconds at baseline, 121.1 ± 9.9 milliseconds during para-Hisian pacing, 179.4 ± 17.8 milliseconds during apical pacing ($P < 0.001$ QRS width during para-Hisian vs. apical stimulation). Para-Hisian pacing resulted in improvement in New York Heart Association functional class, in quality-of-life score and in the 6-minute walk test.

Kronborg *et al.*[30] compared HBP to RV septal pacing in a prospective, randomized, double-blinded crossover trial of 38 patients with AV block, narrow QRS, and LVEF >40%. All patients were treated with 12 months of PHBP and 12 months of RVSP. The primary endpoint was LVEF, which was significantly lower after a 12 months RVSP (0.50 ± 0.11) than after 12 months of HP (0.55 ± 0.10), $P = 0.005$. There was no difference in New York Heart Association class, 6-minute hall walk test, quality-of-life assessments, or device-related complications.

In our series comparing permanent HBP to conventional RV pacing, over a 2-year follow-up period, among patients with significant ventricular pacing there was a significantly lower incidence of HF hospitalizations the HBP group (2% vs. 15%, $P = 0.02$).[23] There was also a trend toward an improved mortality outcome; however, the study was not powered for this analysis.

Permanent HBP for Cardiac Resynchronization in BBB Disease

Permanent HBP has been demonstrated to normalize ventricular activation presumably by recruiting distal conduction fibers in patients with LBBB and RBBB and has been evaluated as an alternative to BiV pacing for cardiac resynchronization.[31-34] We reported success rates of 90% among 58 patients undergoing permanent HBP with underlying BBB.[28]

Postulated mechanisms for recruitment of the specialized conduction system in patients with bundle branch block/delay have been reported.[31] These include: (1) longitudinal dissociation in the HB with pacing 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.

The available data on HBP as an alternative to BiV pacing for CRT are limited (Table 1). Only a few studies with small numbers of participants and limited experience have been reported.

Barba-Pichardo *et al.*[33] described their experience with HBP in 16 patients with cardiomyopathy and failed CRT (ischemic CMP in 7, idiopathic in 9) and attempted HBP in 13 patients. Successful CRT by permanent HBP was then obtained in 9 patients, corresponding to 69% of the selected patients (ischemic 4, idiopathic 5). The mean QRSd decreased from 166 ± 8 milliseconds to 97 ± 9 milliseconds. The HBP threshold at implant was 3.09 ± 0.44 V @ 1 millisecond. NYHA functional class improved from class III to class II and there was an improvement in left LVEF and LV dimensions.[33]

Lustgarten *et al.*[34] compared HBP versus BiV pacing in a crossover design among patients with indications for CRT defibrillator implants. They were successful in demonstrating electrical resynchronization in 21 (72%) cases. Patients were randomized in single patient-blinded fashion to either HBP or BiV pacing. After 6 months, patients were crossed over and followed for another 6 months. Twelve patients completed the crossover analysis at 1 year. Both groups of patients demonstrated significant improvements in ejection fraction, functional status, and 6-minute walk distance.[34]

Vijayaraman *et al.* presented data on 29 patients with successful HBP for CRT (of 32 attempted cases).[35] Fourteen of these were for failed coronary sinus LV leads, 9 with primary HBP (AV nodal block), 7 patients with HBP and LV leads, and 2 patients with HBP leads due to conventional CRT nonresponse. There was improvement in mean QRSd from 165 ± 31 milliseconds to 115 ± 19 milliseconds ($P < 0.001$), LVEF improved from a mean value of 30 ± 10 to 47 ± 11% ($P < 0.05$), and NYHA functional status improved by one class.

Limitations of PHBP

The biggest limitation of permanent HBP is the inability to map the HB and perform implantation of the lead at the HB in 10–20% of cases. This is particularly true in patients with dilated and remodeled atria or other structural heart disease where the preformed sheath is unable to steer high up on the septum to map the HB and makes delivery of the lead difficult. Another limitation is the true lack of available randomized large scale data to justify the use of HBP in all cases needing a high percentage of ventricular pacing.

Battery longevity would be dependent on: pacing output programmed, lead impedance and the burden of ventricular pacing. The potential need for higher pacing output with permanent HBP might result in shorter battery longevity of devices, which is also a concern in some cases. However, when comparing a dual chamber device with an HB lead to a BiV CRT device, longevity might be comparable.

Future Directions

Permanent HBP has emerged as a more physiological form of ventricular pacing over the past few years. There is enough data to suggest that permanent HBP is a feasible and safe and the risks associated with this procedure are not greater than conventional RV pacing.[23,36] However, there are no large scale randomized controlled trial data published on the benefit of HBP compared with conventional dual chamber pacing and/or CRT in patients with either LBBB or RBBB. The cost effectiveness of PHBP in comparison to other forms of ventricular pacing is also an unanswered question. The HIS-SYNC study[37] (HBP vs. Coronary Sinus Pacing for Cardiac Synchronization Therapy) is an ongoing study comparing PHBP to BiV pacing in a randomized systematic manner, and should provide important answers to these pivotal questions.

As more clinical outcome data become available on the benefits of permanent HBP, there also needs to be technical advances with better delivery systems to allow for HB mapping and delivery of the pace/sense lead in patients with challenging cardiac anatomy.

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