REVIEW

His Bundle Pacing: Rebirth of an Important Technique for Pacing the Intrinsic Conduction System

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Abstract

Permanent pacemaker implant is a commonly performed cardiac procedure for treatment of bradycardia or conduction system abnormality. With conventional right ventricular (RV) pacing a lead is implanted at the RV apex or on the RV septum. However, RV apical or RV septal pacing causes iatrogenic left bundle-branch block and ventricular dyssynchrony and can lead to adverse cardiac remodeling, a pacing-mediated cardiomyopathy, and congestive heart failure. Alternatively, permanent His-bundle pacing uses the intrinsic rapidly-conducting His-Purkinje system to activate the ventricle, thereby maintaining (or sometimes even restoring) ventricular synchrony. Many patients may derive benefit from permanent His-bundle pacing.

Keywords: His-bundle pacing; ventricular dyssynchrony; cardiac resynchronization therapy; permanent pacing

Introduction

The cardiac conduction system consists of cells specialized for conduction of electrical impulses. Cardiac electrical activity arises via automaticity of cells within the sinoatrial node, usually generating an action potential at a rate of 60–100 bpm. That action potential is then conducted through atrial myocardium to the AV node, through the bundle of His, and down the right and left bundle branches to activate the ventricular myocardium via arborization of Purkinje fibers. Importantly, the bundle of His and bundle branches contain fibers specialized for rapid conduction of electrical impulses. Ventricular activation via the bundle of His and bundle branches not only ensures rapid and synchronous ventricular activation, but also activates the myocardium in such a way that papillary muscle contraction precedes that of the ventricles, thereby preventing AV valve regurgitation.

Permanent pacemaker implantation is most commonly indicated for sinus node dysfunction and atrioventricular (AV) block [1]. The percentage of dual-chamber (atrial-ventricular) permanent pacemaker implantation is increasing [1, 2]. Most commonly, the ventricular lead in a dual-chamber pacemaker system is implanted via trans-venous access to an endocardial location at the right

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ventricular (RV) apex or RV septum. However, pacing the RV results in non-physiologic electrical activation of the ventricular myocardium and causes electrical and mechanical dyssynchrony, and strong evidence now exists showing deleterious effects of chronic RV pacing. Chronic RV pacing is associated with altered cardiac histology with myofiber size variation and fibrosis on endomyocardial biopsy [3]. In addition, clinical outcome studies show that higher cumulative percentage of RV pacing increases the risk of atrial fibrillation, heart failure hospitalization, and mortality [4, 5].

Role of Cardiac Resynchronization Therapy

Cardiac resynchronization therapy (CRT) is currently the most common approach to reduce ventricular dyssynchrony in cardiac pacing. CRT involves placement of two ventricular leads, one at the RV apex or septum, and one on the left ventricular (LV) lateral wall. Most commonly the LV lead is implanted via a trans-venous approach utilizing specialized delivery sheaths to place the lead in a lateral branch of the coronary sinus (CS); however, surgical epicardial LV lead placement can also be performed. Both ventricles are then paced simultaneously in an effort to treat (or prevent) ventricular dyssynchrony. In patients with preserved LVEF, CRT with "biventricular pacing" has been shown to result in higher LVEF at follow-up evaluation compared to RV apical pacing alone [6]. In addition, patients with NYHA class I, II or III congestive heart failure and LVEF ≤50% randomized to CRT were found to have a lower risk of a combined endpoint of heart failure exacerbation requiring IV therapy, increase in LV end-systolic volume index, or all cause-mortality compared with patients randomized to RV pacing alone [7].

Limitations of CRT with Biventricular Pacing

Cardiac resynchronization therapy with biventricular pacing has several limitations. First, not all patients have suitable anatomy for trans-coronary-sinus LV lead placement, with overall failure rate for CS lead placement estimated at 3–4% [8]. Inability

to cannulate the CS, poor CS branch anatomy, myocardial scar resulting in elevated LV pacing thresholds, and phrenic nerve stimulation are all anatomic barriers that can prevent successful CRT device implant. Moreover, even in patients in whom an LV lead is successfully implanted, some patients will not respond favorably to CRT. Although agreement amongst criteria to define CRT response is poor [9], estimates of non-response has been reported from 16% [10] to 48% [11]. Finally, there are likely many more patients presenting for pacemaker implant that would benefit from having RV and LV synchrony than currently recommended by published CRT guidelines [12, 13] or appropriate use criteria [14] documents. Published guidelines and appropriate use criteria documents are published infrequently, and are slow to adapt as new studies are published. Third party payers, too, are slow to expand payment coverage for expensive CRT devices.

Permanent His-Bundle Pacing

Permanent His-bundle pacing represents a unique alternative to RV apical or RV septal pacing, and in some instances to LV-lead cardiac resynchronization. The His-Purkinje system is a longitudinally-oriented collection of cells specialized for rapid conduction of electrical signals. The His bundle cells are insulated from the surrounding ventricular myocardium and are normally activated by the electrical output from the compact AV node. Thus, in patients without significant infra-His conduction delay or block, His-bundle pacing allows synchronous activation of the ventricles, avoiding the deleterious effects of traditional RV-pacing induced dyssynchrony.

His-Bundle Pacing: Early Days

While His-bundle pacing has re-emerged as an important technique in cardiac pacing, the concept is not new. Benjamin Sherlag and Anthony Damato first reported catheter recording of a His-bundle potential in humans in 1969 [15]. While catheter studies of transient His-bundle pacing were reported in the interim [16], the first report of His-bundle pacing with a permanent pacing lead was not reported until 2000 [17]. In this initial cohort

permanent His-bundle pacing was successful in 12 of 18 assessed patients.

His-Bundle Pacing: A Re-Birth

More recently an observational, retrospective, case-control study compared 94 consecutive patients undergoing permanent pacemaker implant with attempt at His-bundle pacing at one hospital with 98 consecutive patients undergoing permanent pacemaker implant with conventional RV lead implantation at a separate hospital [18]. In this study His-bundle pacing was successful in 80% of attempted cases and while procedure time was higher in the His-bundle pacing group, fluoroscopy time was similar between the two groups. Stability and reliability of a permanent pacing lead in the His-bundle location appears adequate with ventricular lead revision required in only three patients in the His-bundle pacing group and ventricular lead revision necessary in two patients in the conventional RV pacing group. Importantly, His-bundle pacing was associated with fewer heart failure hospitalizations in patients with >40% ventricular pacing burden.

Personal Experience with His-Bundle Pacing: Procedure Technique

In our lab we use a technique for direct His bundle pacing that has been described previously by Sharma and colleagues [18]. A fixed curve sheath (C315 HIS, Medtronic, Inc. Minneapolis, MN, USA) is used to direct a bipolar fixed helix screw pacing lead (model 3830, 69 cm, Medtronic, Inc.,) to a location on the AV septum. Left axillary or subclavian vein access is obtained via the Seldinger technique and a short 7 French peel-away sheath is inserted into the vein. The His can be targeted either by advancing the sheath and lead directly from the right atrium (RA), or by advancing the sheath and lead into the RV and withdrawing until a His bundle potential is mapped. A 150 cm j-tipped guidewire is advanced into the RA and the C315 HIS fixed curve sheath is inserted through the short 7Fr sheath and into the RA over the j-tipped guidewire. The guidewire is then removed and the 3830 pacing lead is advanced through the C315HIS sheath until only

the very tip of the lead protrudes from the end of the sheath. Unipolar mapping is then performed from the tip of the lead and the unipolar electrograms are displayed on both the pacing analyzer (gain setting of 0.05 mV/mm and sweep speed of 50 mm/s) and the electrophysiology lab recording system (displayed at a sweep speed of 100 mm/s). Once the tip of the lead is through the delivery sheath and in the RA, the sheath is advanced to a low RA/high RV septal location and the tip of the lead is manipulated (and the AV septum mapped) by advancing (and later withdrawing, if necessary) the sheath, as well as placing clockwise or counterclockwise torque on the sheath. With the RV approach oftentimes a right bundle branch potential can be seen initially and then a His potential seen as the sheath and lead are withdrawn further across the septal leaflet of the tricuspid valve. When a septal site with a His potential on the lead tip (Figure 1) is identified, the lead is secured into place by clockwise rotation of 4–6 turns on the lead. The sheath is then withdrawn slightly, adequate slack added to the lead system (Figure 2), and testing of sensing and pacing thresholds performed in both unipolar and bipolar sensing and pacing configurations. Once the lead is secured in a position with His bundle capture, adequate ventricular sensing measurements, and an acceptable pacing threshold, the C315HIS delivery sheath is slit away from the lead, the short 7Fr sheath peeled away from the lead, and the lead is secured to the pocket floor. The atrial lead (if indicated) is then placed, and the leads are connected to the pacemaker generator (Figure 3).

While we have successfully implanted permanent His bundle pacing leads with either the RA or RV septal approach, we have occasionally had difficulty with the lead tip getting caught on the septal leaflet of the tricuspid valve when withdrawing the sheath and lead from the RV. Additionally, care should be given to not let more than just the tip of the 3830 lead extend beyond the C315 HIS sheath, because further extension can risk the lead getting entrapped in the tricuspid valve chordae.

Our early experience with eight cases (Table 1) demonstrates that utilizing the above recently described techniques, successful permanent His-bundle pacing can be achieved with a short learning curve in the majority of candidates. While His-bundle pacing lead implant was initially successful

Table 1 HBP Outcomes.

Age (years)	Gender	Pacing indication	Intrinsic (pre-pacing) QRS	Initial result- (selective vs. non-selective His-bundle pacing)	RV sensing (mV)	Fluoroscopy time (min:s)	Threshold
77	Male	Sinus node dysfunction	102 ms	Selective HBP	2.0	29:03	1.1 V at 0.5 ms
53	Female	Sinus node dysfunction	94 ms	Selective HBP	3.3	22:00	1.4 V at 1.0 ms
73	Male	Persistent AF with symptomatic pauses	94 ms	Selective HBP	1.5	18:04	2.5 V at 1.0 ms
53	Male	Complete AV block after MI	79 ms	Selective HBP	2.0	15:04	1.6 V at 0.5 ms
82	Male	Sinus node dysfunction	85 ms	Non-selective HBP	2.8	23:00	2.3 V at 1.0 ms (RV) and 3.2 V at 1.0 ms (His)
79	Male	Sinus node dysfunction	LBBB with QRS duration 158 ms	Selective HBP with narrowing QRS to 101 ms	2.2	55:50	0.8 V at 1.0 ms
73	Male	Chronic RV pacing, multiple prior transcoronary sinus LV lead dislodgements – attempted HBP for resynchronization	RV paced QRS 124 ms	Failure to place HBP lead due to infra-His AV block without junctional escape rhythm	–	21:00	–
35	Female	Chronic RV pacing with new-onset cardiomyopathy and CHF	RV paced QRS158 ms, junctional escape QRS 111 ms	Selective HBP with narrowing QRS to 111 ms	3.3	02:54	1.5 V at 1.0 ms
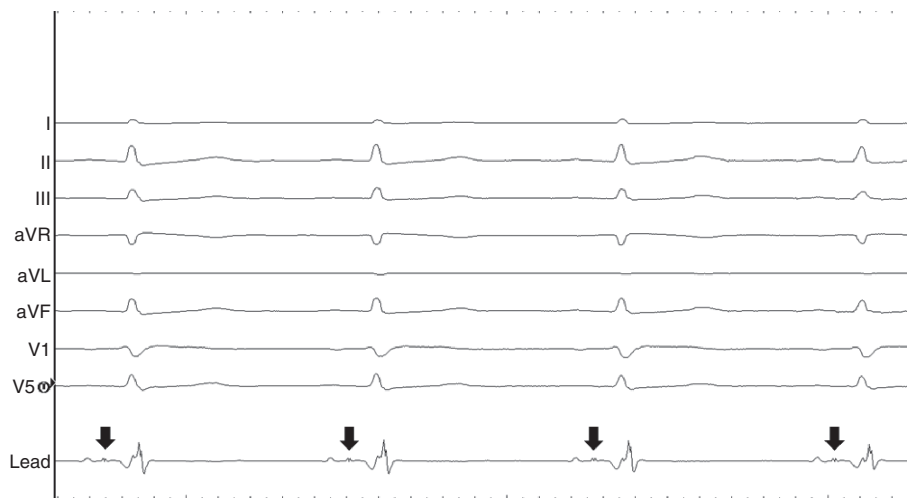
Figure 1   Display of Surface ECG Leads and Unipolar Electrogram from Lead Tip (Bottom Tracing) Showing His Electrogram Potentials (Solid Black Arrows).
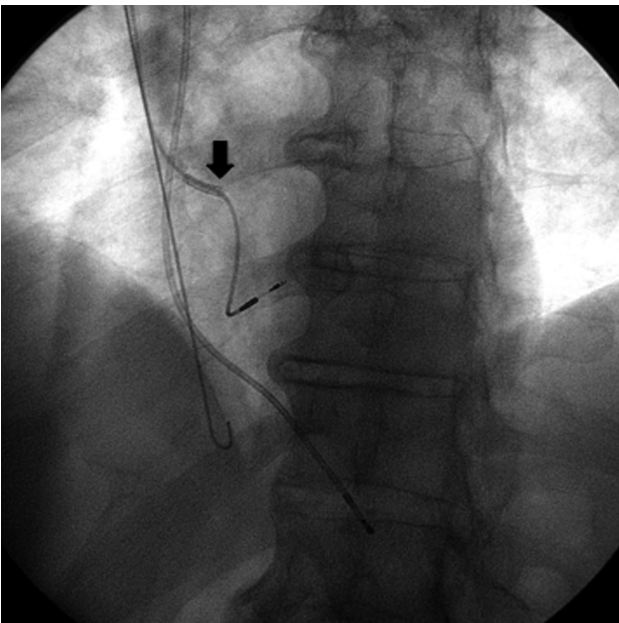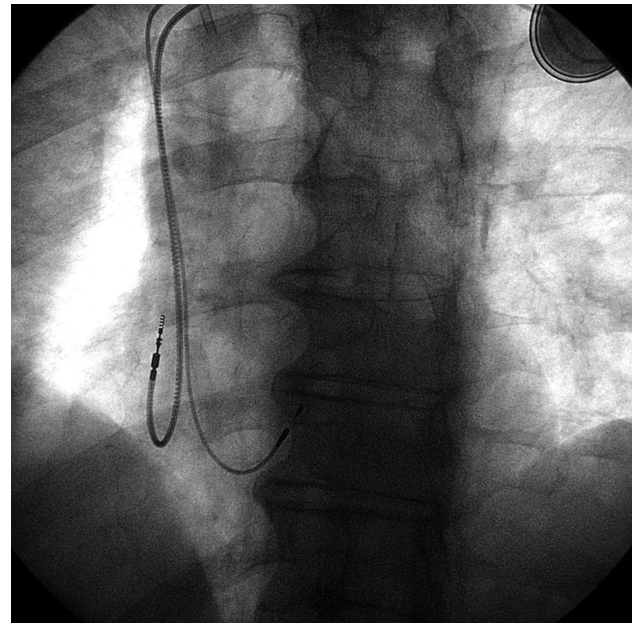

Figure 2   C315 His Delivery Sheath is Withdrawn and Slack Added to Lead to Test Unipolar and Bipolar Sensing and Pacing Thresholds.
Solid black arrow indicates tip of delivery sheath.

Figure 3   Final LAO Cine of Dual-Chamber Permanent Pacemaker with Permanent His Bundle Pacing Lead and Right Atrial Appendage Lead.

in seven of our eight attempted cases, long-term follow-up data are needed to assign long-term success.

Responses to His-Bundle Pacing

Two different responses to His bundle-pacing are possible, depending on the precise location of lead tip fixation and pacing capture. When the tip of the lead is fixed directly into His bundle fibers, direct (selective) His-bundle pacing results (Figure 4). In direct His-bundle pacing lower pacing outputs capture only His-bundle fibers resulting in a paced QRS with the same morphology as the native (non-paced) QRS, and a pacing stimulus to QRS interval equal to the HV interval in sinus rhythm. With direct (selective) His bundle pacing at higher energy outputs, both the His bundle fibers and the "paraHis" ventricle are stimulated resulting in
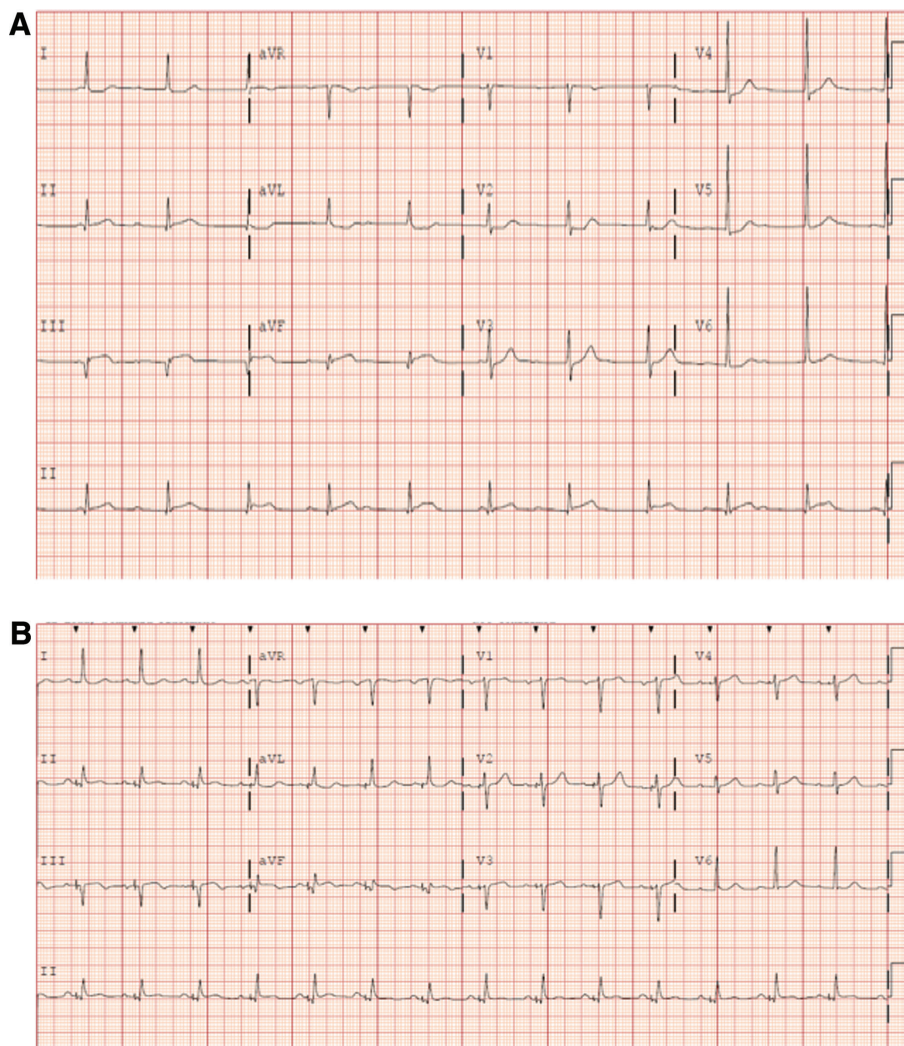
Figure 4 Direct (Selective) His-Bundle Pacing, All Images from Same Patient.
(A) Baseline ECG with complete AV block and junctional escape rhythm. (B) ECG with direct (selective) His bundle pacing at pacing output of 2.0 V at 1.0 ms with paced QRS duration and morphology identical to non-paced QRS duration and morphology. (C) Decreasing pacing output to loss of capture. In direct (selective) His bundle pacing the pacing stimulus to V interval equals the HV interval. RBBB is iatrogenic from sheath manipulation trauma and was transient. (D) Increasing pacing output above "paraHis" pacing threshold with direct (selective) His bundle pacing results in capture of the "paraHis" ventricle and ventricular pre-excitation. Pacing stimulus to QRS interval shortens as the ventricle is "pre-excited." Again, RBBB morphology during selective His bundle capture (first two beats) is iatrogenic, and later resolved. (E) Pacing from His bundle lead at an output of 6.0 V at 1.0 ms demonstrates both His bundle and "para His" ventricular capture with a delta-wave appearance and slight widening of the QRS compared to baseline.

pre-excitation of the ventricle; this is characterized by a delta-wave appearance of the QRS complex, a QRS morphology that is slightly wider than the native (non-paced) QRS morphology, and a pacing stimulus to QRS interval shorter than the HV interval in sinus rhythm.

The second type of response seen with His bundle pacing is called indirect (non-selective) His bundle pacing and occurs when the tip of the lead is fixed into the ventricular myocytes immediately adjacent to the His bundle ("para-His" ventricle) (Figure 5). With indirect (non-selective) His bundle pacing, pacing at lower pacing outputs results in only septal RV capture, whereas pacing at higher pacing outputs narrows the QRS duration as both the His bundle and the para-His ventricle are activated. Either direct or indirect His bundle pacing is considered acceptable.
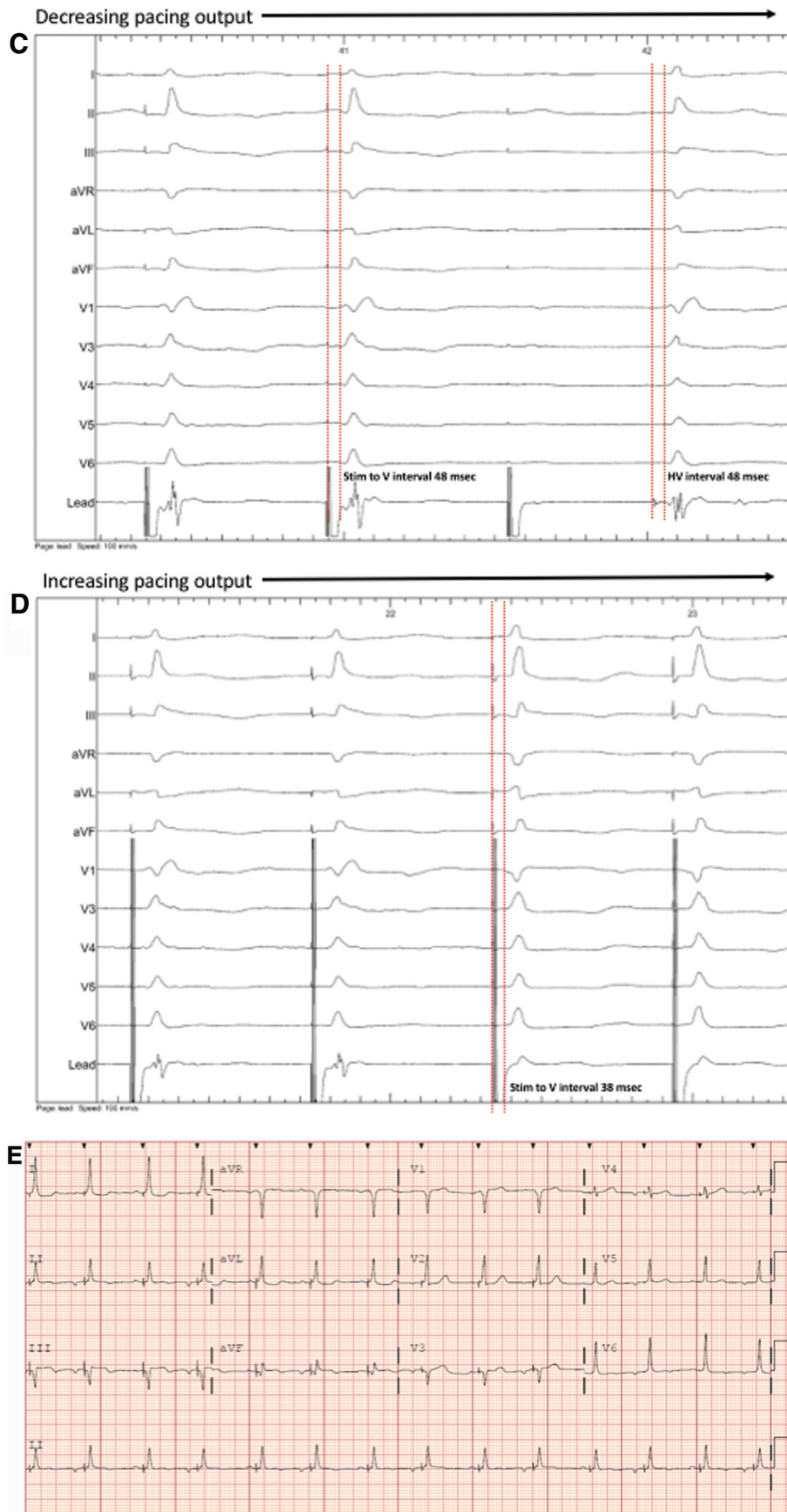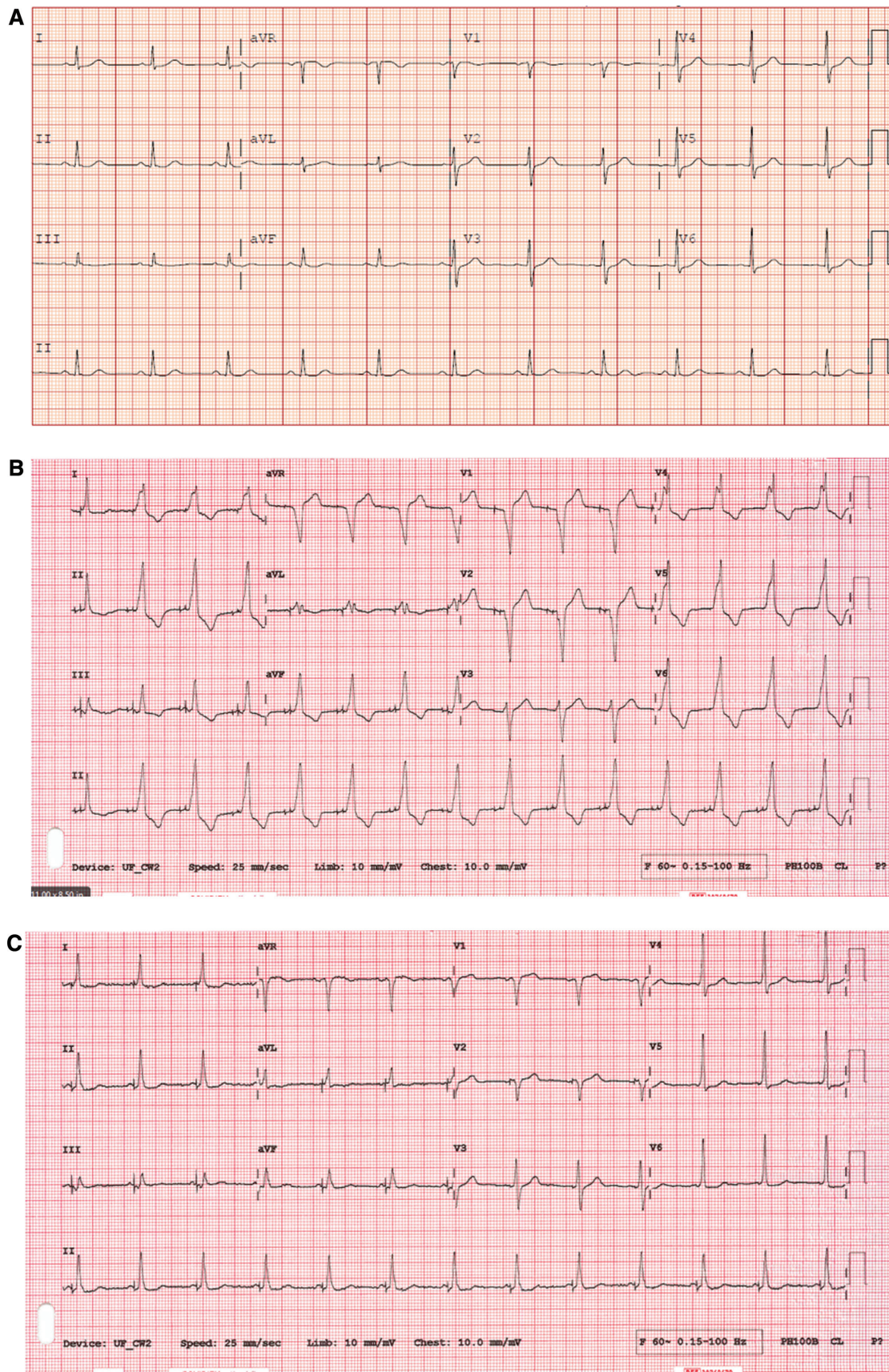
Figure 4 (Continued)

Figure 5 Indirect (Non-Selective) His-Bundle Pacing.
(A) Baseline ECG. (B) Pacing at lower pacing outputs results in only septal RV ("paraHis" ventricle) capture. (C) Pacing at higher pacing outputs captures both the His-bundle and the "paraHis" ventricle, narrowing the QRS complex.

Advantages of His-Bundle Pacing

There are multiple advantages to placement of the ventricular lead at the His-bundle location instead of the conventional RV location. First, pacing the ventricle via the intrinsic conduction system preserves ventricular synchrony and can prevent the aforementioned deleterious effects of chronic RV pacing. Secondly, tricuspid valve dysfunction is a reported complication of trans-venous lead placement across the tricuspid valve [19]. Autopsy analysis of direct (selective) His-bundle pacing lead placement has shown lead tip location on the atrial side of the tricuspid valve [20]. As such, direct (selective) His-bundle pacing lead location may prevent lead-related tricuspid valve dysfunction associated with conventional RV apical or RV septal lead placement.

Moreover, in some patients with bundle branch block His bundle pacing can actually narrow the QRS and restore ventricular synchrony [21] (Figure 6). In 1977 Narula first described the phenomenon
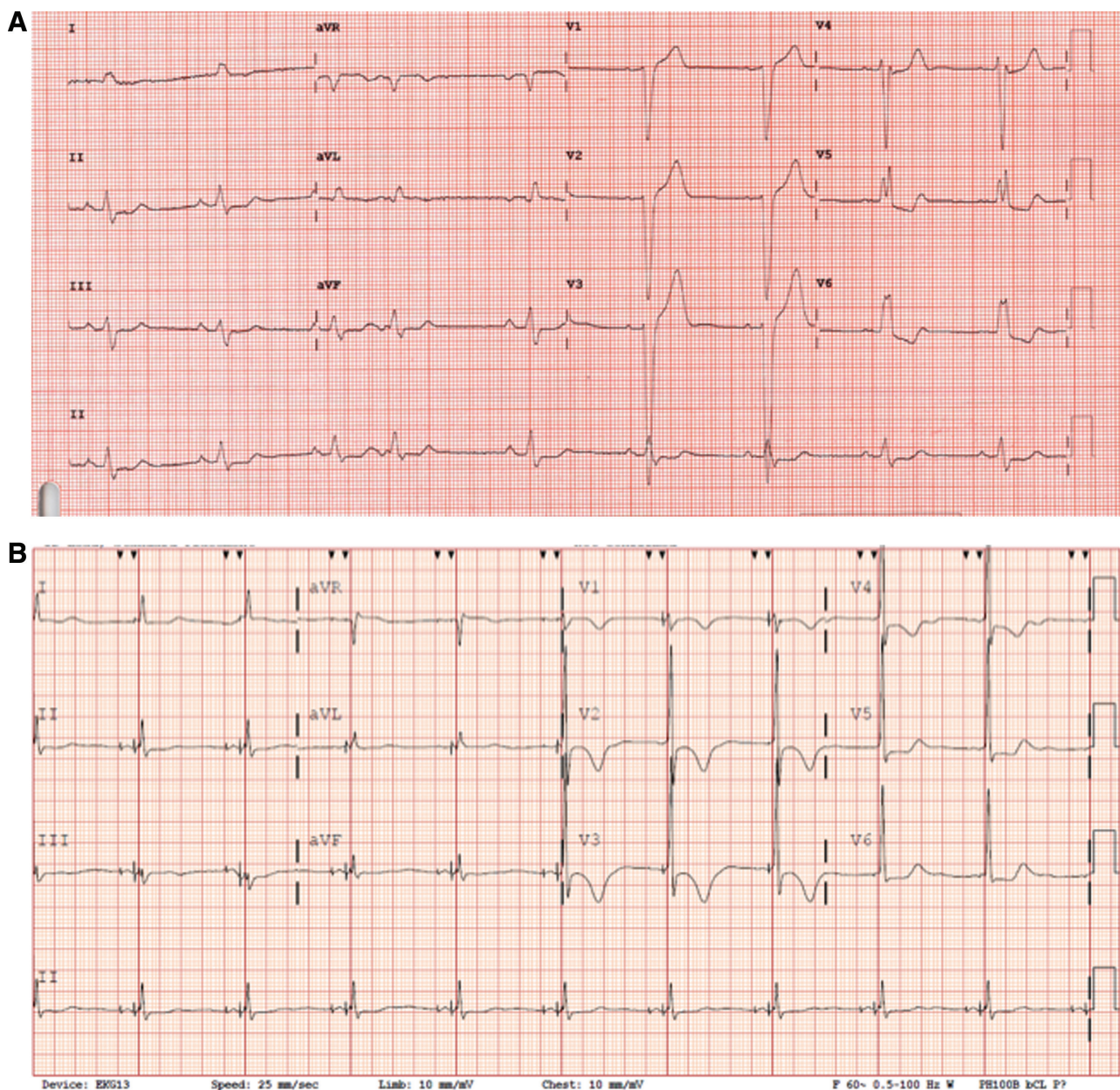
Figure 6 His-Bundle Pacing Narrows Lbbb.
(A) Baseline ECG with LBBB with QRS duration of 159 ms. (B) ECG with permanent His-bundle pacing with narrowing of the QRS to 101 ms. T-wave inversions are likely due to t-wave memory from prior longstanding LBBB.

of "longitudinal dissociation in the His bundle" whereby bundle branch block was identified in some individuals as a discrete conduction slowing or block within the His bundle (and not block more distally in the bundle branches, which is what many conceptualize). He demonstrated that in 25 patients with LBBB pacing the distal His bundle (presumably distal to a focal lesion in the fibers of the proximal His) abolished the left bundle branch block and narrowed the QRS [16]. The potential to abolish bundle branch block and narrow the QRS with His-bundle pacing represents an alternative to conventional biventricular pacing in patients with bundle branch block who do not meet guideline criteria for CRT, in patients in whom attempted CS lead implant is unsuccessful, or in patients who do not respond to CRT. There is theoretical reason to believe that normal His-Purkinje conduction provides better synchrony than even the best biventricular pacing.

Limitations to Permanent His-Bundle Pacing

Limitations to permanent His bundle pacing exist. In the largest published study of His bundle pacing to date, implantation of a permanent His bundle pacing lead was unsuccessful in 20% of patients, and the lead instead had to be placed in a RV septal location [18]. Challenges to successful His bundle pacing include variation in patient anatomy and limited equipment at present designed for His bundle lead placement. As His bundle pacing becomes more widely accepted, hopefully medical device companies will invest in developing new sheaths and leads that will increase success rates in difficult cases.

Summary

Emerging literature suggests that His bundle pacing can be reliably performed in a majority of patients, and in some instances may be superior to conventional RV pacing. While not appropriate for all patients, many patients in need of permanent pacing may benefit from maintaining synchronous activation of the ventricle via the rapidly conducting His-Purkinje system. Short-term follow-up is good, but long-term follow-up is necessary to assess the value of His-bundle pacing in preventing or treating ventricular dyssynchrony. Permanent His-bundle pacing should be considered in patients with indication for cardiac pacing, and procedure technique and outcomes should continue to improve as new tools become available to assist with the implant procedure.

Conflict of Interest

The authors declare no conflict of interest.

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