Evolution of Conduction System Pacing

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Cardiac pacing has evolved with time since the first pacemaker implantation in 1958.[1] Right ventricular (RV) apical pacing has been the standard site for pacing. However, RV apical pacing is non-physiological in nature due to the conduction of electrical wavefronts through the myocardium rather than through the His-Purkinje conduction system, leading to abnormal electrical and mechanical activation of the ventricles. In some patients, this abnormal activation of the ventricles can result in heart failure (HF), mitral regurgitation, atrial fibrillation (AF), and increased morbidity and mortality due to inter, intra, and atrioventricular (AV) asynchrony.[2,3] Pacing at alternative RV sites, such as the RV septum and outflow tract, have not been shown to be superior to RV apical pacing.[4,5] Even though biventricular pacing (BiVP) has been shown to improve morbidity and mortality in advanced HF patients with left bundle branch block, it is also non-physiological in nature with the activation spreading between the RV endocardium and the left ventricular (LV) epicardium. Over the past 20 years, conduction system pacing (CSP) has evolved in the field of cardiac pacing as it has the possibility of mitigating the deleterious effects of right ventricular pacing (RVP). In this review, we summarize the evolution of CSP focusing on His bundle pacing (HBP) and left bundle branch area pacing (LBBAP).

His Bundle Pacing (HBP)

HBP was first described in humans in 1970 by Narula et al.[6] It was first reported as an alternative to RVP in 2000 by Deshmukh et al in patients with AF and atrioventricular node ablation (AVNA)[7] and as an alternative to cardiac resynchronization therapy (CRT) in 2006 by Barba-Pichardo et al.[8] HBP can be either selective or non-selective depending on whether the His bundle (HB) is captured alone or with surrounding myocardium, respectively (Figure 1). In selective HBP, there is an isoelectric segment between the pacing spike and the paced QRS complex which is identical to the His-ventricular (H-V) interval of the intrinsic rhythm in most cases. In non-selective HBP, there is no isoelectric segment between the pacing spike and the paced QRS onset. Instead, there is a pseudo-delta wave due to local myocardial capture (fusion). When compared to selective HBP, non-selective HBP was associated with similar clinical outcomes.[9] Depending on the anatomical location of the HB, various responses can be seen with HBP at varying pacing outputs.[10] The HB is most commonly located in the membranous septum between the septal and anterior leaflets of the tricuspid valve on the right side and between the right and non-coronary sinuses of Valsalva on the left side. Three types of anatomy of the HB have been described by Kawashima et al based on macroscopic studies.[11] In patients with type I anatomy, pure HB recruitment is seen at low output and fusion with myocardial fibers is seen at high output. In type II anatomy, the HB runs intramyocardially in the interventricular septum.[11] In patients with type II anatomy, HB activation is fused with local myocardial activation regardless of the pacing outputs. Lastly, in type III anatomy, the HB is subendocardial.[11] In this case, pure HB recruitment can be seen regardless of the pacing outputs.

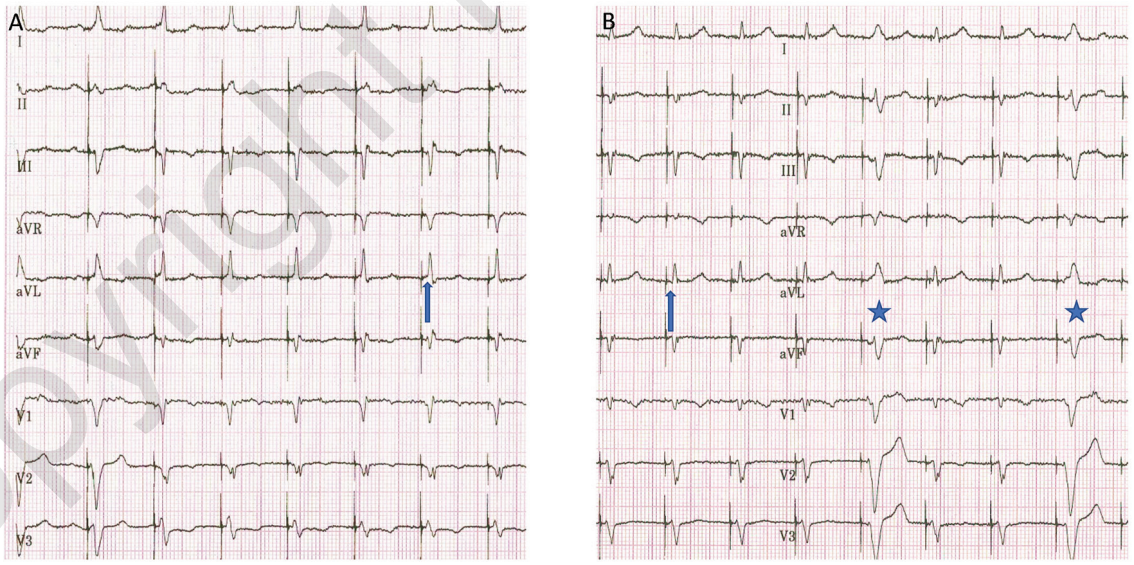

Figure 1. His bundle pacing demonstrating non-selective capture (A). The arrow indicates fusion between local RV myocardial capture and His bundle capture. (B) There is selective His bundle capture with no local myocardial recruitment (arrow). Also, at very low pacing output, there is selective recruitment of right bundle branch fibers only, resulting in a left bundle branch block pattern (asterisk).

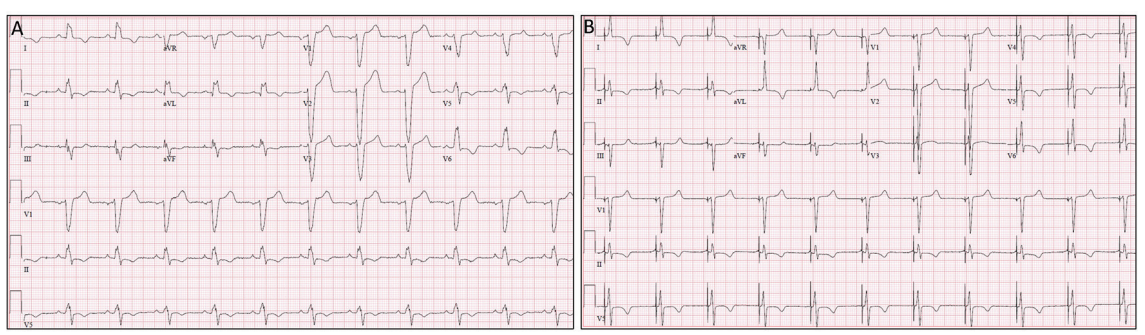

Figure 2. A 58-year-old male with non-ischemic cardiomyopathy, EF 20%, and NYHA class II HF symptoms with LBBB was referred for CRT (A). The patient underwent successful selective His bundle pacing with recruitment of the underlying left bundle branch block (B). Notice the T wave changes related to cardiac memory that normalize over time.

Clinical Benefits

HBP activates the ventricles in a synchronous way by using the native conduction system. Echocardiographically, the synchronous ventricular activation provided by HBP is supported by the lack of paradoxical septal motion which is usually seen in patients with RVP or intrinsic LBBB.[12] HBP was shown to be clinically feasible and safe in patients with bradycardia pacing indications due to AV nodal block as well as infranodal block, in patients with AF prior to AVNA, and in patients with CRT indications. When compared to patients with RVP, patients with HBP had fewer HF hospitalizations and lower mortality.[13] In patients with bundle branch blocks, HBP can result in bundle branch recruitment and narrowing of the QRS interval (Figure 2). This was first reported by Narula et al in 1977 and was explained by the longitudinal dissociation of the HB fibers which are already predestined to become right and left bundle branches (LBB), respectively.[14] In patients who are candidates for CRT, HBP was shown to improve left ventricular function and reverse cardiac remodeling in observational studies.[15-19]

These beneficial effects were even seen in patients with RBBB[20] and in those who did not respond to conventional CRT with a CS lead.[21] His-SYNC, the first randomized controlled trial comparing HBP to coronary sinus pacing, showed that His-CRT resulted in greater reduction in QRS duration with a similar improvement in left ventricular ejection fraction as compared to conventional BiVP.[22] There was significant crossover between the groups and the study was not powered to detect significant differences. His-Alternative was another randomized trial comparing His-CRT to BiVP. This trial showed that His-CRT resulted in significant improvement in LV function, QRS width, and HF symptoms, similar to BiVP at the expense of higher pacing thresholds.[23]

Procedural Success Rates

The success rates of His lead implantation have improved with time and with increasing operator experience, ranging from 60% to 95% based on several observational studies.[24-26] Most common implantation tools to perform HBP at the present time include the SelectSecure 3830 lead (Medtronic), the SelectSite C304-HIS deflectable catheter (Medtronic), and the C315HIS non-deflectable delivery catheter (Medtronic). Recently, other manufacturers such as Abbott, Boston Scientific, and BIOTRONIK have also developed specific delivery tools to improve the success of the procedure. Unlike RV lead placement, His lead implantation relies on precise electrical mapping. The HB is usually mapped using the pacing lead in a unipolar configuration. Following lead fixation, a HB injury current was recorded in around 37% of patients undergoing HBP.[27] The presence of injury current was associated with favorable acute and chronic pacing capture thresholds.[27]

Challenges

His lead implantation may be challenging in the case of anatomical variations such as right atrial and/or right ventricular enlargement. Other situations include congenital disorders in which the HB is displaced (AV septal defects, double inlet LV, and congenitally corrected transposition of the great arteries [ccTGA]) or in which twin HB may be present (ccTGA and right atrial isomerism). Furthermore, owing to the fibrous structure of the HB, lead fixation may be problematic. Pacing thresholds in HBP are usually higher than those in RVP, which results in higher energy consumption and faster battery depletion. An increase in pacing thresholds was reported in 10% of patients with HBP.[28] A higher rate of lead revision (6.7%) was also observed due to increased pacing threshold or loss of capture.[29] Another problem pertaining to HBP is the lack of device-based algorithms designed for HBP, which may make device programming challenging in some cases.[30] For example, in pacing-dependent patients receiving HBP CRT devices with the His lead in the LV port, capture management algorithms should be turned off to avoid unintended consequences such as ventricular asystole.[30] In patients with the His lead in the atrial port, the lowest possible sensitivity should be programmed to avoid oversensing atrial and His potentials.[30]

Left Bundle Branch Area Pacing (LBBAP)

LBBAP has emerged as an extension of CSP due to concerns with HBP related to challenging lead fixation, higher pacing thresholds, lower sensed R wave amplitudes, and potential to develop distal conduction disease. LBBAP was first reported in 2017 by Huang et al after failure of LV and His leads implantation in a CRT-eligible patient.[31] LBBAP can be either selective or non-selective depending on whether the LBB is captured alone or with surrounding myocardium. In selective LBBAP, there is a discrete local signal separate from the stimulus artifact on the unipolar electrogram from the pacing lead, whereas in non-selective LBBAP, there is no discrete local signal (Figure 3). Selective LBBAP is characterized by a change in the paced QRS morphology from qR to rSR in lead v1 with fixed peak left ventricular activation time (pLVAT) while doing unipolar threshold measurement. In non-selective LBBAP, the QRS duration increases with prolongation of pLVAT without a change in the paced QRS morphology in lead v1 (qR).[32] Deep septal pacing is another variation of LBBAP and recent data have shown that screwing the lead in close proximity to the LBB fascicles can also result in physiological pacing.[33] Uniform criteria to confirm LBB capture are still lacking. Recently, Vijayaraman et al published a new criterion for LBB capture confirmation which relies on the R-wave peak times (RWPTs) measured in lateral precordial leads. RWPTs are shorter in LBBAP compared to HBP because LBBAP is distal to the site of HBP. An absolute value of 8 ms for ΔRWPT (difference in RWPTs during HBP and non-selective LBBAP/LV septal pacing) has a 100% sensitivity and 93% specificity to confirm LBB capture in patients with LBBB.[34]

Clinical Benefits

As compared to HBP, LBBAP has the potential to bypass distal conduction disease in the majority of patients. In patients with bradycardia pacing indications, LBBAP was shown to be safe and clinically feasible. A significant reduction in QRS duration was noted as compared to patients with RVP.[35-37] LBBAP has also been an attractive alternative pacing modality in patients who are eligible for CRT. It resulted in significant QRS narrowing with improvement in clinical and echocardiographic outcomes in several observational studies.[38-41] More data are emerging touting the benefits of LBBAP as a routine form of CSP.

Procedural Success Rates

Due to the anatomy of the left bundle which forms a wider target for pacing, LBBAP has higher implant success rates, better pacing thresholds and sensed R wave amplitudes, and lower lead-related complications as compared to HBP. Success rates have ranged from 80.5% to 97%.[32] Left bundle potentials were recorded in 30% to 80% of patients undergoing LBBAP.[35-37] In a large multicenter retrospective study, lead revision was needed in only 1.04% of patients.[38]

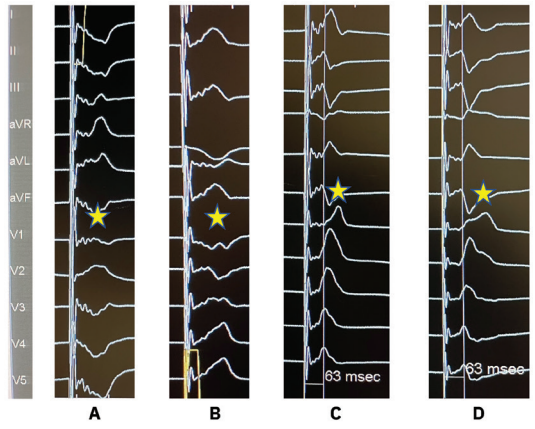

Figure 3. A 52-year-old female underwent left bundle branch area pacing (LBBAP). (A) Shows initial morphology of V1 (asterisk) with initial notching with pacing on the RV septum. As the lead is screwed further deep into the septum, the notching in V1 moves further into the QRS (B). Eventually, when the lead reaches close to the LBB, there is non-selective LBBAP with a right bundle branch block morphology (C). In its final position, there is selective LBBAP (D). Notice that the R-wave peak time (RWPT) shortens significantly to 63 ms in V5 with both non-selective and selective LBBAP.

Challenges

Septal scarring or fibrosis may make the transeptal lead implantation challenging. With manipulation of the sheath at the basal septum, there is a risk of right bundle branch injury. There is also a risk of septal artery injury that can be avoided by ensuring lead placement at least 1 cm below the HB area.[42] Lastly, a significant portion of the pacing lead behind the helix is usually inserted into the septum to achieve successful LBBAP. With this degree of penetration, there may be long-term adverse effects on lead integrity due to myocardial contractility which have yet to be clinically manifested.

Conclusion

Both HBP and LBBAP have rapidly evolved in the past few years to become alternative forms of permanent pacing on a global scale. Evidence is mounting showing the physiological and clinical benefits of CSP. Recent bradycardia guidelines by the ACC/AHA/HRS have given a class IIa recommendation for HBP in patients with a LV ejection fraction between 36%-50% who require >40% ventricular pacing.[43] Larger randomized trials are needed to elucidate the benefits of CSP in various cohorts. Further advances in the design of dedicated tools, leads, and devices for HBP and LBBAP are welcomed to move the field of CSP forward. ■

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