Future Developments in His Bundle Pacing

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KEYWORDS

- His bundle pacing • Clinical trials • Future developments

KEY POINTS

- Because there has been a significant push toward His bundle pacing (HBP), multiple studies and advancements are underway to provide new and improved delivery tools and lead designs, allowing one to apply this technology in daily practice.
- A better understanding of the pacing configurations and ultimately development of dedicated algorithms will alleviate some of these aforementioned challenges.
- Ultimately, with such technological advances and mounting clinical evidence, one can surely anticipate HBP to revolutionize the field of cardiac pacing.

INTRODUCTION

The past few decades have seen significant advances in cardiac implantable electronic device therapies. A continually increasing emphasis on the study of electrophysiological mechanisms has driven the field of cardiac electrophysiology. Recently, there has been resurgence in the concept of physiologic pacing using the His Purkinje system, which has emerged as an alternative solution to traditional right ventricular (RV) pacing as well as resynchronization therapy.

The observations by Purkinje and His and the seminal work of Sunao Tawara established the framework and paved the way for the future investigations into the cardiac conduction system. In 1919, Kaufman and Rothberger first conceptualized the functional longitudinal dissociation of His bundle. They were the first to propose that normal conduction in the His Purkinje system was mediated by pathways originating in the atrioventricular (AV) junction that connected to predesignated right or left ventricular Purkinje fibers. In 1977, Narula[1] demonstrated in a series on 27 patients with left bundle branch block (LBBB) and prolonged His-ventricular (HV) intervals, the ability to normalize the QRS complex with His-bundle pacing (HBP). Then, in 1978, El-Sherif and colleagues[2] showed that in patients with acute right bundle branch block (RBBB) after a myocardial infarction and those with chronic LBBB, His bundle-pacing resulted in normalization of the QRS complex with a shorter stimulus to ventricular interval compared with the intrinsic HV interval, likely because of the site of pacing being distal to the location of block.[3] Deshmukh and colleagues[4] were the first to study the immediate and long-term effects of HBP in patients who had heart failure, atrial fibrillation (AF), and AV nodal ablation; they showed an improvement in the left ventricular ejection fraction (LVEF), decreased left ventricular (LV) dimensions, and improved clinical outcomes.

This article provides a summary of the recent studies in the field of HBP as well as ongoing clinical trials and future developments.

HIS BUNDLE PACING: A PHYSIOLOGIC WAY OF PACING THE HEART

HBP can be advantageous in patients with conduction disease without heart failure. As demonstrated by DAVID I and DAVID II trials, a high

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percentage of RV pacing induces a similar level of dyssynchrony and shares similar outcomes to patients with heart failure and LBBB, including an increased risk of AF and death.[5,6] Biventricular (Biv) pacing mitigates such detrimental effects of RV-only pacing. The BLOCK-HF study demonstrated superiority of Biv to RV-only pacing and showed a significant mortality benefit and improved clinical outcomes with improved New York Heart Association (NYHA) class as well as quality of life. Furthermore, Biv pacing resulted in reverse remodeling as demonstrated by improved echocardiographic indices.[7]

HBP similarly mitigates the adverse effects of RV-only pacing and was shown to be associated with significantly lower heart failure hospitalizations.[8] In a long-term follow-up study, despite high pacing burden, patients with a His bundle pacemaker had a stable LVEF, suggesting long-lasting benefits of HBP.[9] A recent study by Huang and colleagues[10] studied 52 patients with heart failure and narrow QRS, who underwent AV node ablation for AF and received His bundle pacemakers. In the postablation period, patients with HBP had significantly improved LVEF, LV end diastolic pressure, and NYHA functional status as well as decreased diuretic use. These clinical benefits were of greater magnitude in patients with reduced LVEF.

Heart failure with impaired left ventricular function with conduction abnormalities is an ominous combination that results in ventricular dyssynchrony, further decline of heart function, and an increased risk of death.[11] Cardiac resynchronization therapy (CRT) is established as a treatment of systolic HF with ventricular dyssynchrony as described by the presence of an LBBB with QRS greater than 140 milliseconds.[12–15] To date, multiple studies have demonstrated improved mortality, left ventricular function, and quality of life in patients with reduced LVEF and LBBB who undergo CRT.[15,16] As such, CRT has become a guideline-recommended therapy. However, CRT achieved with Biv pacing can be mired with multiple challenges. Occasionally, natural anatomic vein variations preclude feasibility of delivering the CS lead successfully, and even when the lead is delivered successfully, the nonresponse rate for CRT can be as high as 30%.[17,18] In addition, the site of latest activation in the left ventricle might not be accessible for lead delivery. Moreover, functional lines of block occur in patients with underlying heart block and RV pacing. Currently, the only way to identify the latest site of activation in this situation is via activation mapping and 3-dimensional electroanatomical mapping. Furthermore, the added risks of CS dissection/perforation during implantation and reversed depolarization and repolarization sequence due to epicardial pacing pose additional risks to patients. Although challenges exist with HBP also, even in its early stages, it appears to be an attractive and safe alternative. Since the early works by Deshmukh and colleagues,[4] several studies have provided sufficient evidence in support of using HBP in the treatment of conduction abnormalities as well as in patients with heart failure.

HIS BUNDLE PACING AS AN ALTERNATIVE TO BIVENTRICULAR CARDIAC RESYNCHRONIZATION THERAPY

Sharma and colleagues[19] recently reported that the HBP in 2 CRT nonresponders significantly narrowed the QRS interval (165 $\pm$ 31 to 115 $\pm$ 13 milliseconds) and improved the LVEF (30 $\pm$ 10 to 47 $\pm$ 11%) and NYHA functional class. A study by Shan and colleagues[20] demonstrated similar results in a CRT nonresponder patient. Several studies have reported the use of HBP for CRT with success rates ranging from 56% to 92%. Barba-Pichardo and colleagues[21] reported a 56% success rate in HBP among cardiomyopathy patients with failed CRT with improvements in NYHA class and LVEF. Lustgarten and colleagues[22] performed a randomized crossover patient-blinded study comparing CRT and HBP in patients meeting CRT indications. After an initial assignment to either group, patients were crossed over to the other group after 6 months and followed for another 6 months. The study reported a 72% success rate with HBP for CRT, with clinical improvements in 6-minute walk, NYHA functional class, quality of life, and LVEF in both CRT and HBP arms. HBP in lieu of an LV lead is also feasible. Ajijola and colleagues[23] recently reported significant QRS narrowing, improved NYHA functional class, and LV dimensions in 21 patients with an indication for CRT. HBP is a possible alternative to CRT for systolic HF and conduction delay. A recent study published by Sharma and colleagues[19] assessing HBP for CRT in CRT-eligible patients and CRT nonresponders further showed the feasibility of HBP for CRT. The study reported a 90% success rate with significant QRS narrowing (157 $\pm$ 33 to 117 $\pm$ 18 milliseconds), increase in LVEF, and improvement in NYHA class after 14-month follow-up. Furthermore, HBP may also provide an opportunity for patients with RBBB or nonspecific interventricular conduction delay.[19] Vijayaraman and colleagues[8] demonstrated QRS narrowing in 94% of patients (29 of 31) with