

Can His bundle pacing prevent right ventricular pacing-induced cardiomyopathy, heart failure, or death?

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Right ventricular (RV) pacing (RVP) with the lead positioned in the apex is the current standard when ventricular pacing is indicated for bradycardia. However, frequent RV apical pacing is associated with an increased risk of atrial fibrillation, heart failure hospitalization (HFH), or death (1,2). RV apical pacing causes non-physiologic propagation of electrical wave fronts through the ventricles outside of the His-Purkinje conduction system and a wide QRS complex pattern. This abnormal electrical activation pattern as well as the resulting inter and intra-ventricular mechanical dyssynchrony may underlie the observed adverse clinical outcomes associated with RV apical pacing such as the development of RVP induced cardiomyopathy or heart failure (3).

Minimizing the ventricular pacing burden is currently the main strategy used to reduce adverse clinical outcomes associated with RV apical pacing. However, this approach is not feasible in many patients, especially those with significant atrioventricular (AV) nodal diseases. Thus, alternate pacing strategies have been sought to minimize the deleterious effects of RVP. Among these strategies is His bundle pacing (HBP), which simulates normal electrical conduction through stimulation and capture of the His-Purkinje system in the ventricles, and produces a "normal" or narrow QRS complex. Several studies have shown that HBP is associated with an improvement in surrogate markers of inter- and intra-ventricular synchrony, physiologic distribution of myocardial blood flow, left

ventricular systolic and diastolic function, and left atrial function when compared to RV apical pacing (4-7). Although the difference in clinical outcomes between HBP and RVP is not as well investigated, the result of a small retrospective cohort study suggested that HBP may reduce HFH compared to RVP in patients with >40% ventricular pacing burden (8).

In the *Journal of American College of Cardiology* published in May 2018, Abdelrahman *et al.* presented the data from a large observational cohort study evaluating permanent HBP compared to conventional RVP (9). This study included patients aged >18 years from two hospitals in the same health system who needed permanent pacemaker implantation based on standard bradycardia indications. Patients were excluded if they underwent cardiac resynchronization therapy or had existing cardiac implantable electronic devices. Permanent HBP was attempted in 332 consecutive patients at one hospital and was successful in 304 patients (91.6%) while 433 consecutive patients at the other hospital underwent standard RVP (40.6% apical and 59.4% non-apical). After the mean follow-up of 725 days, the primary endpoint of death, HFH, or upgrade to biventricular pacing (BiVP) was significantly reduced in the HBP group (25%) compared to RVP (32%) ($P=0.02$); hazard ratio 0.71. The primary endpoint was mainly driven by HFH (12.4% *vs.* 17.6%), and a trend towards reduced mortality was observed but it did not reach statistical significance. In subgroup analyses,

the benefit of HBP was primarily seen in patients with ventricular pacing >20%.

To date, this is the largest study evaluating permanent HBP compared to conventional RVP. Other strengths of this study include selection of relevant clinical outcomes and excellent rate of follow-up. The results of this study are consistent with the findings from a previous smaller study and further substantiates the potential clinical benefits associated with HBP in patients with frequent ventricular pacing. However, this positive result should be interpreted with caution and considered as exploratory due to several limitations. First, the intervention allocation in this study is not randomized. Although the baseline clinical characteristics between the two groups are quite similar and the result remained statistically significant after adjusting for baseline clinical characteristics, other confounders that were not evaluated may contribute to the observed clinical benefit in HBP group. In addition, as the mean follow-up of 725 days in this study is relatively short, long-term longevity of HBP and potential late complications were not evaluated. Lastly, HBP was performed by highly experience operators in this study. Less experienced operators may not be able to achieve the same result.

Certain disadvantages of HBP observed in this study were noted. HBP was associated with persistent higher pacing threshold and, more importantly, higher rate of ventricular lead revision (4.2% *vs.* 0.5%) compared to RVP (0.5%). Lead revision can be associated with serious complications such as major bleeding, vascular complications, and infection. Although these complications were not observed or were similar in both groups in this study, a larger study with longer follow-up is likely required to evaluate for these complications. Also, the mean procedure time and the mean fluoroscopy duration in HBP group were approximately 15 and 3 minutes longer than in RVP group, respectively.

No pericardial effusion requiring pericardiocentesis occurred in the HBP group; however, possible ventricular lead perforation occurred in three patients (0.7%) in the RVP group. Although the numerical difference is too small to draw a definite conclusion, it is conceivable that HBP lead placement may avoid the risk of ventricular lead perforation or pericardial effusion since the procedure positions and places the lead on the septum and does not involve lead fixation in the proximity of the RV free wall.

HBP is a novel therapy which allows ventricular stimulation to occur through the natural conduction system. The authors of this study should be commended for showing that permanent HBP is feasible and safe in patients

requiring permanent pacemakers for bradycardia when there is no indication for biventricular pacing or cardiac resynchronization therapy. Based on results from their non-randomized observational cohort study, patients who received HBP had a lower combined incidence of death, heart failure hospitalization, or upgrade to BiVP compared to those treated with standard RVP. In particular, patients requiring frequent ventricular pacing >20% burden or significant AV block appear to receive the most benefit from HBP compared to RVP. A large randomized controlled trial is now needed to confirm if permanent HBP is superior to RVP before it can become the new standard for treatment of bradycardia.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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