

## EDITORIAL COMMENT

# His Bundle Pacing

## A New Promise in Heart Failure Therapy?\*

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A prolonged PR interval results in reduced left ventricular filling, abnormal filling pattern, loss of atrioventricular (AV) synchrony, and presystolic mitral regurgitation due to delayed and ineffective closure of the mitral valve. Prolongation of the PR interval results from cardiac conduction disease but may also be a marker of advanced structural heart disease associated with atrial electrical and structural remodeling. A prolonged PR interval is independently associated with an increased risk of atrial fibrillation, increased mortality, and heart failure hospitalization in the general population, in patients with coronary artery disease, and in patients with left ventricular (LV) dysfunction (1-3).

Cardiac resynchronization therapy (CRT) is clearly effective in patients with a wide QRS interval, LV systolic dysfunction, left bundle branch block (LBBB), and heart failure. In patients with a non-LBBB, CRT has not been effective (4). However, in a subgroup of patients with prolonged PR intervals (>230 ms), CRT was associated with a 73% reduction in the cumulative risk of heart failure/death (5). However, in patients with a PR interval <230 ms, CRT was associated with a trend toward an increased risk of heart failure/death. It was noted in this study that patients with PR intervals >230 ms had the highest risk of HF/death, whereas the clinical benefit of CRT was greater. In patients with narrow QRS interval (<130 ms) and cardiomyopathy, CRT did not show improvement in exercise capacity,

quality of life, New York Heart Association functional class, or LV indexes (6). Subgroup analysis in this study suggested a possible benefit in patients with a PR interval >180 ms (7). Similarly in the COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) trial, a PR interval >200 ms was associated with 41% increased risk of all-cause mortality or heart failure hospitalization (8).

A prolonged PR interval is a potentially modifiable risk factor in patients with LV dysfunction and AV asynchrony, but without ventricular dyssynchrony. Modifying the long PR interval by AV synchronous right ventricular pacing introduces ventricular dyssynchrony, offsetting any potential benefits. In this issue of *JACC: Clinical Electrophysiology*, Sohaib et al. (9) present acute hemodynamic data for 16 patients with LV dysfunction (narrow QRS interval in 13 patients and right bundle branch block [RBBB] in 3 patients) and a prolonged PR interval (>200 ms) during

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AV synchronous His bundle pacing (HBP). They demonstrated a mean increment of  $4.1 \pm 3.8$  mm Hg in systolic blood pressure (BP) with HBP, comparable to a  $4.3 \pm 4.2$  mm Hg increment in systolic BP with biventricular pacing. There was no change in systolic BP during right ventricular (RV) pacing. The authors postulate that the acute hemodynamic improvement seen in this study was directly related to AV delay optimization. His bundle pacing, by virtue of normal electrical activation through the native conduction system, does not induce deleterious ventricular dyssynchrony caused by right ventricular or biventricular pacing in patients without pre-existing ventricular dyssynchrony. It is not clear in this study whether both selective and nonselective HBP (6 patients in each group) resulted in similar acute systolic BP changes. Judging from previous evaluations of HBP, both are likely to result in similar hemodynamic benefit (10,11).

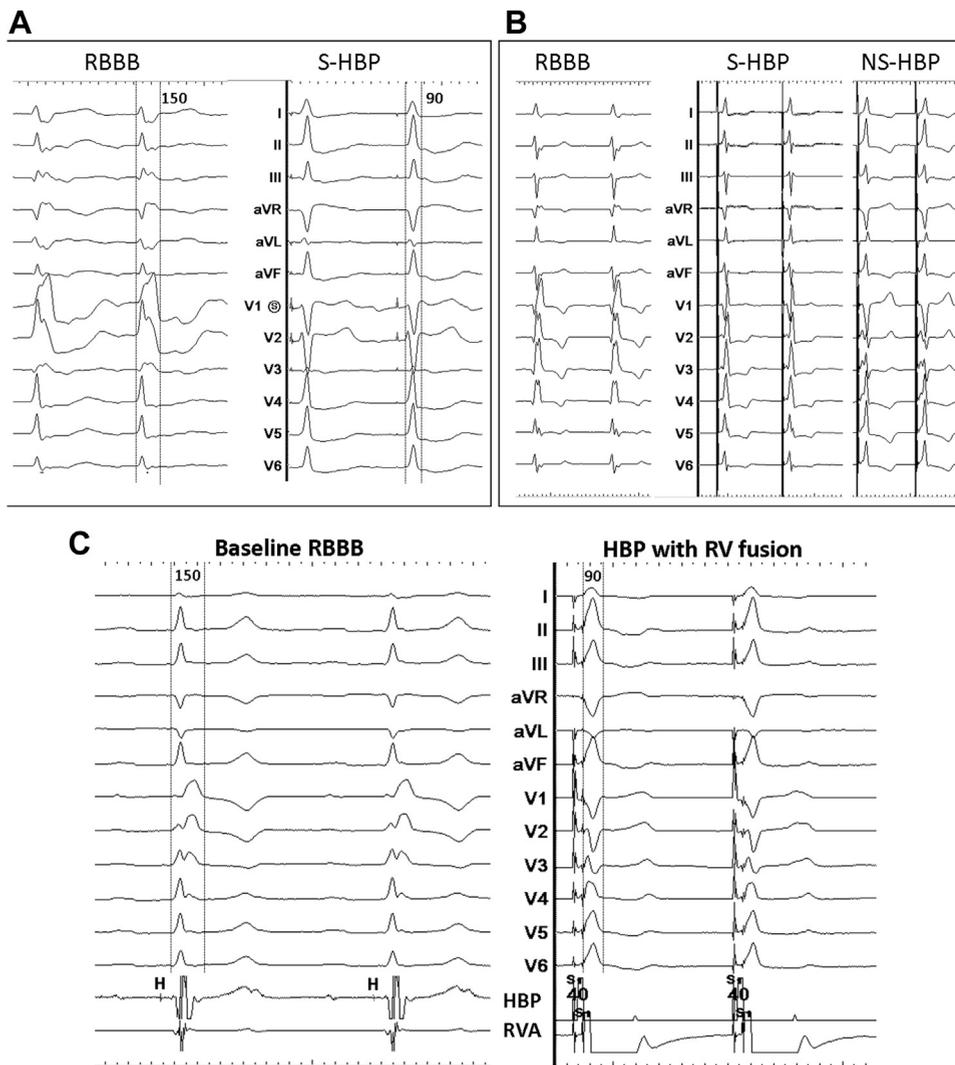
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Several questions remain.

1. Is the prolonged PR interval a modifiable risk factor or a marker of advanced heart disease? Several observations suggested that the prolonged PR interval is an independent predictor of a worse clinical outcome, irrespective of treatment (CRT vs. optimal medical treatment) (12,13).
2. What should be the cutoff for the PR interval? PR intervals >180 ms, >200 ms, and >230 ms have been variably suggested to influence clinical outcomes in several studies mentioned (5-8).
3. Will the acute hemodynamic improvement seen in AV synchronous HBP translate to meaningful clinical outcomes during long-term randomized studies? Several hemodynamic studies in patients with LV dysfunction, heart failure, and LBBB

**FIGURE 1** Correction of RBBB by His Bundle Pacing



**(A)** Surface 12-lead electrocardiogram (ECG) of a patient with chronic right bundle branch block (RBBB) and a QRS duration of 150 ms at a sweep speed of 100 mm/s. With permanent selective His bundle pacing (S-HBP), QRS duration has completely normalized with a duration of 90 ms. **(B)** Surface 12-lead ECG of a patient with chronic RBBB at a sweep speed of 50 mm/s. With S-HBP, QRS is partially corrected but still shows terminal R-wave in V<sub>1</sub>. With nonselective His bundle pacing (NS-HBP) at a slightly higher output, the terminal R-wave in V<sub>1</sub> is resolved with fusion (basal septal right ventricular [RV] capture in addition to His capture). **(C)** Surface 12-lead ECG of a patient with chronic RBBB and a QRS duration of 150 ms is shown at a sweep speed of 100 mm/s. Pacing from His and RV apex (RVA) with a His-RV delay of 40 ms completely normalized the RBBB with a QRS duration of 90 ms with fusion from the RV apex. H = His.

acutely demonstrated remarkable improvements in systolic BP, pulmonary capillary wedge pressure, and LV dP/dt with biventricular pacing. The heart failure and mortality benefits of CRT have contributed to a paradigm shift in heart failure management. Long-term randomized studies would be necessary to assess the long-term clinical benefits of AV optimization with HBP.

4. How feasible is long-term His bundle pacing in this population? With significant improvements in lead design and delivery system, permanent HBP has recently been demonstrated to be feasible and safe in many patients requiring permanent pacemakers with acceptable short- and intermediate-term pacemaker function (14-16). Success of permanent HBP in patients with advanced heart failure and conduction disease has been variable and is likely to require additional modifications in lead and delivery system.
5. How do we optimize the AV delay? There are significant differences in the sensed and paced AV delay as atrial pacing leads to significant intra-atrial and interatrial conduction delay. Right and left AV synchrony may vary significantly in sinus-versus atrial-paced rhythm. The site of the atrial lead may also affect the AV intervals determined by the device compared with surface PR intervals. Additionally, optimal AV delays as determined by echocardiographic or electrocardiographic parameters have been shown to be different during follow-up, as seen in CRT studies.
6. Would AV synchrony benefit patients with RBBB and prolonged PR intervals? Most CRT trials have shown minimal or no benefit in patients with RBBB. In patients with RBBB, LV dyssynchrony is minimal because the left ventricle is predominantly activated through the normal His-Purkinje system. Biventricular pacing may create new deleterious LV dyssynchrony in this subset. Recently, adaptive CRT pacing (synchronized, fusion LV pacing with

conduction via the right bundle) in patients with intrinsic AV conduction and LBBB has been shown to be associated with superior clinical outcomes compared with traditional biventricular pacing (17). HBP may offer a unique opportunity to improve outcomes in patients with RBBB. Vijayaraman et al. (18) recently demonstrated that RBBB can be normalized by HBP in the majority (>90%) of patients with indications for permanent pacing (Figure 1A). The incidence of proximal His disease amenable to correction by HBP in patients with advanced cardiomyopathy is unknown. Unlike adaptive CRT pacing in patients with LBBB, His bundle pacing can provide AV synchrony in patients with long AV intervals in addition to synchronized RV fusion pacing with conduction via the native left bundle. This fusion pacing can be achieved by nonselective HBP through the His pacing lead (Figure 1B) or additional pacing from the defibrillator lead in the RV apex (Figure 1C).

The benefits of CRT in patients with cardiomyopathy and narrow QRS interval or RBBB have been minimal regardless of PR interval prolongation. HBP has the potential to offer additional opportunities to improve clinical outcomes in this subset of patients. Sohaib et al. (9) should be commended for their initial study demonstrating the acute hemodynamic benefits of HBP in this subset of patients. A randomized study addressing all of these questions would be a logical next step in evaluating the clinical benefits of HBP in systolic heart failure patients with AV dyssynchrony and/or RBBB.

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**KEY WORDS** first degree AV block, heart failure, His bundle pacing, right bundle branch block