Letter to the Editor: His Bundle Pacing: A New Frontier in the Treatment of Heart Failure

Theodoros Zografos

Dear Sir,

I read with great interest the elegant article by Ali et al.1 on His bundle pacing in issue 17.2 of AER. I do concur with the authors’ view and conclusions. However, there are two issues that may merit further attention.

First, specific His-bundle pacing is indeed the reasonable option that mimics the natural ventricular excitation. However, no benefit of mid-septal over apical pacing has been shown in randomised comparisons.2,3 Is this because of the relatively short-term follow-up that did not allow apical pacing to expose its deleterious effects on the ventricle or just reflects the fact that mid-septal is not equivalent to specific His pacing?

Second, acute results of His-bundle pacing are comparable to those of cardiac resynchronisation therapy (CRT).4,5 Do the authors believe that we have enough data to implement this principle in clinical practice, even before a randomised trial confirms this notion? That should have a tremendous impact on cost and efficacy of pacing in the setting of intractable heart failure, especially in view of the cost and complications of CRT, as demonstrated in the BLOCK-HF trial.6

Dear Sir,

We read Dr Zografos’ response to our article1 with interest. He agrees with the findings of our review but highlights two important issues for further discussion, which we address below.

Right ventricular lead position

Dr Zografos points out that randomised comparisons of different right ventricular lead positions have not shown superiority of septal pacing over apical pacing.7 This is important because right ventricular (RV) septal pacing is considered to be “more...
physiological” than apical pacing due to its closer proximity to the bundle of His. It is therefore postulated that the activation of the ventricular myocardium has a pattern and duration closer to that of native conduction through the His–Purkinje system. If more physiological pacing is not more beneficial, this might lead some to cast doubt on the efficacy of His bundle pacing. Dr Zografos speculates on two explanations for this: insufficient follow-up duration to detect differences between septal and apical pacing or important differences between His bundle pacing and septal pacing. A sceptical third view would suggest that increasingly physiological ventricular activation does not have clinically relevant benefits.

We think that there is insufficient data in current literature to provide a definitive answer to this question due to the lack of randomised controlled trials for His bundle pacing. However, we believe his second explanation, that septal pacing and His bundle pacing are not equivalent, is the most plausible one. Regardless of whether pacing is performed from the right ventricular outflow tract, septum or apex, the activation of the left ventricle (LV) occurs via slow cell-to-cell myocardial activation. Therefore, although the severity may vary, any lead position that captures RV myocardium rather than conduction system tissue will result in deleterious intra-ventricular LV dyssynchrony. His bundle pacing, however, is thought to obviate pacing-induced intra-LV dyssynchrony, by its very nature, as activation occurs rapidly through the His–Purkinje network. An important caveat to this is non-selective His bundle capture, which is likely to induce intra-RV dyssynchrony and therefore a degree of inter-ventricular dyssynchrony. The clinical significance of this is not yet known.

It is possible that study design has impacted the ability of randomised trials to detect a difference between septal and apical pacing, but this is not necessarily limited to follow-up duration (although this appears to be a factor). Recruiting patients with preserved LV systolic function means that the trial is designed to prevent, rather than treat, pacing-induced cardiomyopathy. Although this might be a better clinical strategy for patients, it may underpower trials as some patients experience lifelong RV apical pacing without developing heart failure. Furthermore establishing a definition of high or mid septal pacing that differs from apical pacing, and is achievable in the vast majority of patients randomised to septal pacing, can be difficult.

Irrespective of trial design, His bundle pacing differs from septal pacing in terms of implant technique. Septal pacing is based on a fluoroscopic, anatomical assessment of the position of the septum. Varying rotation of the heart can result in an apparently high septal lead position being, in actuality, relatively posterior/anterior, or even lateral. This is difficult to detect using fluoroscopy alone but is important because these alternative positions might be expected to have worse characteristics of ventricular activation than apical pacing. His pacing, however, is a combined electrophysiological and anatomical technique. The presence of a His signal, His injury current and formal ECG and electrogram criteria mean that His bundle pacing can be verified more robustly than septal pacing.

Randomised evidence for His bundle pacing

Dr Zografos highlights the need for randomised trials to support routine use of His bundle pacing in clinical practice. He points out that while the acute benefits may be similar to cardiac resynchronisation therapy (CRT), this does not necessarily mean this will be the same for clinical outcomes.

Randomised controlled trials (RCTs) remain the gold standard for evidence based medical interventions. For His bundle pacing in heart failure to be recommended for routine clinical practise, existing observational data are insufficient. Important confounders and biases that limit observational data may be responsible for the positive findings that existing studies report. There are potential pitfalls of His bundle pacing that have not been fully addressed by current technology, some of which may mitigate its efficacy, such as programming and long-term threshold issues.

The absence of recommendation for routine His pacing limits the ability for operators to gain implant experience. This, combined with the encouraging acute and observational findings, mean that RCTs are now urgently required. We are currently addressing this in the HOPE-HF trial where we are objectively measuring differences in exercise capacity in individuals with PR prolongation and LV impairment where individuals are randomised to having AV optimised His bundle pacing and conventional back-up pacing in a crossover design. The results of the His-SYNC study should provide further information about the use of His pacing to reverse left bundle branch block (LBBB) (NCT 02700425). A trial for His bundle pacing for bradycardia indications is awaited.

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2. Victor F, Jackson G, Maio P, et al. Optimal right ventricular pacing site in chronically implanted patients: a prospective randomised crossover comparison of apical and outflow tract pacing. JACC 1999;33:311–16. https://doi.org/10.1016/S0735-1097(98)00589-0; PMID: 9973008.
3. Shemyan G, Eilander MB, Fiksen KI, Ampt O. Beneficial effects of right ventricular non-apical vs. apical pacing: a systematic review and meta-analysis of randomised-controlled trials. Europace 2011;14:91–9. https://doi.org/10.1093/europace/euq246; PMID: 21798881.
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5. Keene D, Arnold A, Shun-Shin Mi et al. Rationale and design of the randomized multicentre His Optimized Pacing Evaluated for Heart Failure (HOPE-HF) trial. ESC heart failure 2018.