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Do we need to pace the bundle? Editorial comment on: Nonselective versus selective His bundle pacing: An acute inpatient speckle tracking strain echocardiographic study by Bednarek et al

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Cardiac pacing therapy is the most effective therapy for treating symptomatic bradyarrhythmia. Initially ventricular pacing electrodes were surgically positioned on the left ventricle (LV). When intravenous leads became available in the 1970s, the right ventricle (RV) became the preferred region of implant, largely because of easy accessibility and lead stability. Stimulating the RV, however, results in dyssynchronous electrical activation¹ and uncoordinated ventricular contraction,² with risk of adverse cardiac remodeling, atrial fibrillation, heart failure, and cardiovascular death in the long run.³

His bundle pacing (HBP) reproduces the most physiological sequence of ventricular activation and the clinical evidence for the benefit of HBP is very promising. Compared with RV pacing, studies consistently show that HBP results in better clinical outcome in patients with bradycardia indications and high percentage of ventricular pacing. For example, a nonrandomized trial in patients with a ventricular pacing burden more than 40% showed a lower incidence of heart failure in the HBP group than in the RV pacing group (2% vs. 15%) during a 2-year follow-up period.⁴ After a follow-up of 5-years, permanent HBP was even associated with a significant reduction in the composite endpoint of death or hospitalization for heart failure.⁵

In HBP, selective HBP (s-HBP) and nonselective HBP (ns-HBP) are recognized. In s-HBP, the His bundle is selectively stimulated, and in ns-HBP, there is stimulation of the His bundle as well as some septal myocardium. ns-HBP generates a somewhat wider QRS complexes because of a pseudo-delta wave, suggesting potential electrical ventricular dyssynchrony. However, many implanters accept ns-HBP because s-HBP is not always achievable in a patient, at least not with acceptable pacing threshold

and sensing values. Of note, in a retrospective, multicenter observational study of a large cohort of European patients undergoing HBP at seven centers 55% of all cases were reported to have ns-HBP.⁶ Because it is the pump function rather than the electrocardiogram (ECG) that determines clinical outcome, an important question is whether or not ns-HBP is hemodynamically inferior to s-HBP.

In the current issue of JCE, Bednarek et al.⁷ studied the difference between s-HBP and ns-HBP. The investigators performed a study in 69 patients who underwent pacemaker implantation because of bradycardia and in whom it was possible to obtain both s-HBP and ns-HBP. In each patient, echocardiographic measurements were performed of global function (left ventricular ejection fraction [LVEF], LV global strain for LV function, and TAPSE for RV function) as well as regional function (speckle tracking strains). No significant differences were found between the two pacing modes regarding the global measurements. At the segmental level significant differences were found, as evidenced by larger peak strain dispersion and peak strain delay during ns-HBP. Regional differences were small. Values of the standard deviation of peak strain times in 12 (SD12) and 6 segments (SD6) were on average 50 versus 54 ms, and 56 versus 65 ms, respectively. Time differences between peak septal and lateral wall strain at the basal level in the four-chamber view were on average 30 and 51 ms. The latter numbers indicate that ns-HBP almost doubles mechanical dyssynchrony at the level of the LV base, compared with s-HBP, presumably because the basal septum is near the site of the ns-HBP pacing electrode. However, it should be noted that the ns-HBP values for basal septum-lateral wall delay are still considerably lower than those observed in RV pacing and left bundle branch block (LBBB; and lower than the definition of

significant mechanical dyssynchrony: > 130 ms). The latter value was not reached by any of the patients during ns-HBP. This may be explained by early fusion of activation waves extending from the septal myocardium and His–Purkinje system.

The question is whether these results support the idea that ns-HBP and s-HBP provide similar clinical outcome. An important limitation of this study is that the echocardiographic measurements during the two pacing modes were performed within a short time interval (minutes). In particular the global function measures are highly dependent on the size of the ventricles. Even though a better, more synchronous, way of activation improves coordination of cardiac contraction immediately, this does not translate immediately to changes in global measures. In a cohort of patients with sick sinus syndrome, Nahlawi et al.⁸ found that 2 h after switching from atrial pacing to RV pacing LV ejection fraction (LVEF) had decreased from $66.5 \pm 4.5\%$ to $60.3 \pm 5.2\%$, continuing to decrease to $52.9 \pm 8.3\%$ 1 week later. Similarly, in a study on CRT patients by Yu et al.⁹ LVEF increased 5% within a week after start of CRT and another 7% after 3 months of CRT. Unpublished data from our lab showed no significant increase in LVEF within 1 day of CRT (Verzaal & Van Deursen, unpublished data). Note that the difference in dyssynchrony between atrial and RV pacing and between a LBBB-like conduction pattern and BiV pacing is considerably larger than that between ns-HBP and s-HBP. Therefore, it may not be a surprise that no significant difference in LVEF was found in the Bednarek et al.⁷ study, where LVEF was measured within 5 min after starting a certain pacing mode and the study may therefore not provide the full prove that these two pacing modes are clinically equivalent.

However, the question whether there are functional and clinical differences between s-HBP and ns-HBP should also be regarded in light of the rapidly increasing popularity of left bundle branch pacing (LBBP). After all, this pacing mode also does not achieve the “perfectly narrow” QRS complex and yet seems to provide significant hemodynamic benefit in CRT and preserves function in bradycardia patients.^{10,11} Moreover, also in LBBP selective and nonselective LBBP are recognized. And, as in the field of HBP, also in LBBP it is discussed how important capture of the bundle (in this case left bundle branch) is for ventricular pump function. Even more striking is the observation in our group that pacing at almost any location of the LV septum (LV septum pacing [LVSP]) provides normal function in AV-block dogs¹² and in patients with sick sinus syndrome.¹³ Moreover, in CRT candidates LVSP improves contractility to the same amount as biventricular and HBP.¹⁴ These observations strongly suggest that a perfectly narrow QRS complex is not required for achieving (almost) normal pump function.

Altogether, the moderate effect of ns-HBP on regional mechanics and the abovementioned observations about LBBP and LVSP do support the idea that ns-HBP may provide equivalent hemodynamic effects as s-HBP. The good functional performance during s-HBP, ns-HBP, LBBP, and LVSP indicates not only that

these modes are most likely excellent alternatives to RV and BiV pacing, but also the lack of need to aim at s-HBP. The latter greatly facilitates the implant procedure, reducing procedure time and improving pacing, and sensing properties. Currently, HBP is still performed by only a limited group of pacemaker implanters because of the more complex implantation technique and electrophysiological pacing maneuvers. In contrast, LBBP and LVSP can be performed with only using a 12-lead ECG instead of an electrophysiological system and may therefore become attractive and feasible to a much wider group of pacemaker implanters. In that sense the article by Bednarek et al.⁷ appears to fit in the picture of the novel alternative pacing sites.

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