EDITORIAL COMMENT

Selection of Permanent Ventricular Pacing Site

How Far Should We Go?*

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Almost a half-century after the initial description of the use of a transvenous endocardial lead for pacing in humans (1), the right ventricular (RV) apex has been selected as the traditional site for lead positioning. This is because of the easy accessibility of the RV apical site and because it allows safe and stable long-term pacing using a passive endocardial pacing lead. However, the acute adverse hemodynamic effects of nonphysiological left ventricular (LV) activation because of RV apical pacing had been recognized by Wiggers (2) as early as 1925. Indeed, emerging clinical data have shown that chronic RV apical pacing can lead to adverse clinical outcomes (3,4). In patients with congenital (5) or acquired (6) atrioventricular (AV) block, chronic RV apical pacing is associated with LV dyssynchrony and deterioration of LV diastolic and systolic function. Recent studies have shown that up to 31% to 50% of pacemaker patients have asymptomatic LV dysfunction (7–9).

In this issue of the Journal, Tops et al. (10) provide further evidence showing that RV pacing induces LV dyssynchrony in a substantial proportion of patients who received permanent ventricular pacing after AV junction ablation for permanent atrial fibrillation. In this study, all patients had normal QRS duration and no evidence of intraventricular or interventricular dyssynchrony on baseline echocardiogram. After a mean of 3.8 years of follow-up, in up to half of these patients, new-onset echocardiographic evidence of intraventricular and/or interventricular dyssynchrony had developed. Furthermore, worsening of LV function and clinical status were observed in those patients with ventricular dyssynchrony after RV pacing. Similar to the findings from previous studies (6,11), long-term RV pacing induced ∼5% to 10% absolute reduction in LV ejection fraction in patients with baseline preserved LV function. This study extends the findings from previous studies (3–6) and shows that ventricular dyssynchrony induced by RV pacing resulted in progressive ventricular remodeling and deterioration of LV function. The use echocardiographic techniques, such as M-mode and tissue Doppler imaging to detect LV dyssynchrony after RV pacing, could also identify those patients who are at risk of developing long-term LV dysfunction. Because this study was performed in patients with permanent atrial fibrillation, the impact of AV synchrony on the development of intraventricular and interventricular dyssynchrony was eliminated. Unfortunately, the patient’s baseline clinical characteristics in this study did not predict the development of ventricular dyssynchrony after RV pacing. Furthermore, no detailed analysis on the relationships between the occurrence of ventricular dyssynchrony and the RV pacing site or other pacing parameters, such as duration of pacing, average pacing rate, and pacing QRS duration and morphology, were performed in this study. This information may provide further insights on the optimal selection of ventricular pacing site or parameters to avoid ventricular dyssynchrony induced by RV pacing. In addition, the data were derived from iatrogenic AV nodal block from ablation, and the application of those findings to degenerative AV block is uncertain.

Another article in this issue of the Journal attempts to identify the optimal ventricular pacing site in patients with or without LV dysfunction. Lieberman et al. (11) studied the acute hemodynamic effects of AV synchronous pacing at 3 different RV sites (apex, free wall, and septum), at the LV free wall, and at both the RV septum and the LV free wall (biventricular [BV]) during electrophysiological studies in patients with or without preexisting LV dysfunction. In this study, all patients had normal QRS duration and no conventional indication for cardiac pacing. During the acute pacing protocol, comprehensive invasive hemodynamic assessment of the LV pressure-volume loop was obtained. The results of this study show that ventricular pacing sites have a significant impact on LV function. In this study, the acute cardiac hemodynamics and functions were better during LV and BV pacing than during RV pacing at 3 different sites, especially in patients with preexisting LV dysfunction. In patients with LV dysfunction, acute RV pacing at any site resulted in worsening of cardiac performance. However, in patients without LV dysfunction, individual optimization of RV pacing sites could preserve cardiac performance. Furthermore, there were substantial individual variations in the optimal RV pacing sites, and no consistent RV pacing site was superior to others. This study suggests that ventricular pacing sites need to be individually optimized. In patients with preexisting LV dysfunction, an LV-based pacing approach can avoid RV pacing–induced LV dyssynchrony and may further improve LV performance. However, the clinical implication of this finding remains unclear. First, whether the acute hemodynamic effects of pacing predict a chronic functional benefit is unknown. In patients with heart failure and prolonged QRS duration, an acute hemodynamic benefit did not predict the
response to cardiac resynchronization therapy (12). Second, the invasiveness of this method will significantly limit its applications. On the other hand, other less invasive methods, such as arterial pulse pressure or pulse oximetry, are unlikely to be sensitive enough to detect the differences in cardiac performance during pacing at different sites, especially in patients with normal LV function. Third, the pacing sites tested in this study were poorly defined. There was no detailed description on whether the LV pacing was performed inside the coronary venous sites or within the LV, and which part of the LV free wall was selected for pacing. Furthermore, RV septum pacing was performed with an electrophysiological catheter lying along the endocardium, whereas an active fixation electrode is used in permanent pacing during RV septal pacing. A recent experimental study (13) has shown that pacing at the RV septum with a screw-in electrode can potentially lead to stimulation of the native conduction system deep into the septum and can result in normal LV activation sequence. Finally, the study was performed in patients with preserved AV conduction who did not require ventricular pacing, and a variable degree of fusion during pacing will make data interpretation difficult.

The findings from these 2 studies (10,11) provide important mechanistic insight into the adverse hemodynamic effects of nonphysiological LV activation induced by pacing. Obviously, in view of the potential harmful effect of ventricular pacing, every effort should be made to minimize ventricular pacing if possible. However, in patients who require ventricular pacing, there are still very limited data to guide the selection of the optimal permanent ventricular pacing site (14). Therefore, several important issues still need to be addressed in future studies.

First, it would be useful to identify a subset of patients who are susceptible to the adverse effects of RV apex pacing before a pacemaker implantation. Currently, only patients with preexisting LV dysfunction seem more likely to develop LV dyssynchrony after RV pacing. In those patients, alternative site pacing should be considered to prevent LV dyssynchrony and deterioration of LV function. However, in addition to LV dyssynchrony, there are several other potential mechanisms, such as change in myocardial perfusion and histology (6,7,14), that can contribute to progressive LV dysfunction after RV pacing. Therefore, it remains unclear whether improvement of LV synchrony with alternative-site pacing can prevent LV dysfunction. Indeed, several ongoing trials are underway to determine whether biventricular pacing is superior to RV apical pacing in patients with a conventional pacing indication and impaired LV function (15).

Second, in view of the high prevalence of asymptomatic LV dysfunction in pacemaker patients (5–9), these patients should be closely monitored for progressive worsening of LV function. Recent studies have shown that upgrading to biventricular pacing can improve functional status and cardiac function in those patients in whom heart failure developed after RV apical pacing (16). Therefore, there is a need to identify those patients with RV pacing who may benefit from prophylactic or therapeutic upgrading to biventricular pacing. Previous studies (17,18) have shown that paced QRS was a major independent predictor for long-term deterioration of LV function and development of heart failure. However, recent studies (19) have failed to show a correlation between paced QRS duration and the degree of LV dyssynchrony. Although Tops et al. (10) have shown a similar pattern of LV dyssynchrony in RV-paced patients as in patients with heart failure and prolonged QRS duration, the optimal LV lead location for biventricular pacing in patients with heart failure induced by RV pacing remains unclear. Therefore, future studies should investigate the potential roles of different echocardiographic techniques, such as tissue Doppler imaging and strain rate, to select candidates for biventricular pacing upgrade and to guide the optimal location for LV lead placement. Furthermore, the risk and benefit of a prophylactic approach to upgrading the device to biventricular pacing in patients with asymptomatic LV dyssynchrony and dysfunction should be considered because the complication rates for device upgrades are much higher than for the initial implant.

Finally, a future strategy to individualize the optimal pacing site should be developed. Recent studies (20) have shown that prophylactic biventricular pacing in patients with bradycardia resulted in better LV function, quality of life, and exercise capacity as compared with RV apical pacing. However, except in a subset of pacemaker patients as previously discussed, the routine use of LV-based pacing for bradycardia in the majority of patients is impractical compared with the longer procedure time, shorter battery life, and higher cost and complications rates, such as lead dislodgement and less reliable long-term pacing. With the recent advances in the active-fixation endocardial lead systems (21), different alternative RV pacing sites, such as RV outflow tract, RV septum, and His and para-His bundle have been explored to replace the RV apex. In patients without significant distal conduction abnormalities, such as those patients who underwent AV node ablation for atrial fibrillation, His or para-His bundle pacing have been shown to preserve the LV activation sequence and LV function (22,23). However, the technique for achieving successful His or para-His bundle pacing remains challenging. Interestingly, the RV septum site has been used in the first human implantation of the endocardial pacing lead (1). Indeed, RV septum pacing is not inferior to RV apical pacing in terms of long-term stability and efficacy, and seems to be practical because it is associated with a low risk of RV perforation and diaphragmatic stimulation, and is easy to extract. Furthermore, recent studies (6,24) have shown that the use of RV septum pacing to achieve a narrow QRS duration could avoid the deleterious effects of RV pacing and preserve LV function. It is likely that pacing at the RV septum results in stimulation of the interventricular conduction system to cause a more synchronous ventricular
activation pattern with a narrow QRS duration (13). One of the major issues related to RV septal pacing is that it is difficult to define the optimal site for lead placement in the septum, but QRS width seems to be a practical method that has been used in at least these 2 clinical studies (6,24). Therefore, future studies are needed to define the potential role of alternative RV pacing sites, in particular the RV septum location for long-term pacing in patients with bradycardia. In addition, the use of different parameters such as fluoroscopic landmarks, paced QRS width, or morphology or echocardiographic indexes alone or in combination to select optimal RV pacing sites merit further studies.

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