JACC: CLINICAL ELECTROPHYSIOLOGY
VOL. 2, NO. 7, 2016

ISSN 2405-500X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jacep.2016.06.003

EDITORIAL COMMENT

Left Ventricular Endocardial Stimulation in Patients With a Poor Response to Cardiac Resynchronization Therapy

What Is Next?*

Nathaniel Thompson, MD, Nicolas Derval, MD

Cardiac resynchronization therapy (CRT) significantly improves the cardiac function, clinical outcomes, and survival of patients who present with advanced drug-refractory congestive heart failure (HF). This was clearly demonstrated in patients with an ejection fraction of <35% and QRS duration of >120 ms, and is now considered standard of care. However, the magnitude of response to CRT may vary among patients, with the greatest responders being female patients with idiopathic dilated cardiomyopathy, typical left bundle branch block, and a wide QRS (≥150 ms) (1). Initial work on the relationship between the pacing site and the hemodynamic response has suggested that the lateral left ventricular (LV) wall was the optimal position for LV lead placement in CRT. However, due to the varied individual response to CRT (including nonresponders), there has been growing interest in creating a tailored approach to LV lead placement. There has also been interest in pacing the LV from the endocardium, particularly with the development of wireless pacing devices.

SEE PAGE 799

In this issue of the *JACC: Clinical Electrophysiology*, Behar et al. (2) present investigations of an individualized approach to both epicardial and endocardial lead placement in patients with severe ischemic cardiomyopathy who demonstrated poor response to CRT. The investigators created a 2-step protocol. First, regions of scar in the LV were delineated with an endocardial voltage map (voltage <0.5 mV), and the LV cavity was divided into 12 segments. In the second step, each of the 12 segments was targeted for pacing. A mean of 10.4 ± 4.8 endocardial positions and a mean of 5.8 ± 0.5 epicardial positions were targeted. The epicardial sites were targeted with a temporary pacemaker lead. Acute hemodynamic response (AHR) was measured to assess efficacy. The investigators demonstrated that endocardial pacing was superior to epicardial stimulation, regardless of the endocardial pacing position (+11.8% vs. +6.5% increase of AHR from baseline; $p = 0.025$). After individual optimization of the pacing site, endocardial pacing remained superior to epicardial pacing, and endocardial stimulation was also superior to epicardial pacing at approximately the same position. The optimal LV site was highly variable between individuals and was not associated with the area of the latest electrical activation.

These results are consistent with previous work that demonstrated the superiority of pacing at optimized endocardial positions versus conventional LV pacing positions (3,4). Taken together with the work provided here by Behar et al. (2), this provides strong evidence that patients who improve by conventional CRT use may not be optimally improved. On average, optimal biventricular pacing doubles the AHR compared with conventional strategy. Moreover, the wide intraindividual AHR of the work discussed currently highlights the critical need for dedicated tools to improve pacing site selection.

There is some debate over the physiological differences between endocardial and epicardial pacing. In animal studies, endocardial pacing resulted in

*Editorials published in *JACC: Clinical Electrophysiology* reflect the views of the authors and do not necessarily represent the views of *JACC: Clinical Electrophysiology* or the American College of Cardiology.

From the Hopital Cardiologique du Haut Lévêque, CHU Bordeaux, Pessac, France. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

better resynchronization of ventricular activation and larger acute hemodynamic effects than with epicardial pacing. However, direct comparison of opposing endocardial and epicardial pacing sites in patients with heart failure was more equivocal, with no significant superiority of endocardial pacing. In addition, epicardial pacing was not optimized, and therefore, the intrinsic superiority of endocardial pacing could not be demonstrated (5,6). In the current study, endocardial pacing was found to be superior in all of the different tested comparisons (direct comparison, optimized pacing site, or mean response). As the investigators pointed out, a recent animal study demonstrated that there was increased electrical resynchronization with endocardial pacing caused by a shorter activation path length and faster impulse conduction in these layers (7). The investigators' hypothesized that the His-Purkinje network might make a contribution to conduction. However, further studies are needed to confirm this hypothesis.

An advantage of the endocardial approach, and a limitation of the study, is that the epicardial approach is limited by the coronary venous anatomy. Therefore, not all 12 of the LV segments could be compared or assessed for optimization. Without a true epicardial optimization, the comparison appears to be always biased. The population of the study is small and limited to patients with ischemic cardiomyopathy. Three patients had a typical left bundle branch block, and nearly 40% of the small population had a baseline electrical condition that is strongly associated with a good response to CRT. Furthermore, although there was immediate evidence of improvement of cardiac output with endocardial LV pacing, there currently are no practical means to assess longer term clinical efficacy.

In summary, endocardial LV pacing remains an enticing potential option for those patients with little to no demonstrable improvement with conventional CRT. What remains before being accepted into daily practice is a safe and easy way to deliver endocardial devices. The current methods by the transseptal or transapical route are technically challenging and associated with significant risk, including endocarditis, mitral insufficiency, and systemic thromboembolism. New technology such as leadless pacemakers might represent a promising future for CRT. Noninvasive technology including imaging and magnetic resonance imaging will be useful to anticipate and evaluate the optimal pacing site locations. Noninvasive body surface mapping technology has already demonstrated its usefulness in better selecting CRT candidates, and ongoing studies are evaluating its usefulness in the identification of the optimal pacing site (8). We must thank the investigators for reporting on a potential therapy for patients that may be of great benefit, and we look forward to further work to come.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Nicolas Derval, Hopital Cardiologique du Haut-Lévêque, CHU Bordeaux, 1, Avenue Magellan, 33600 Pessac, France. E-mail: dervalnicolas@gmail.com.

REFERENCES

1. Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: The Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association. Eur Heart J 2013;34:2281–329.

2. Behar JM, Jackson T, Hyde E, et al. Optimized left ventricular endocardial stimulation is superior to optimized epicardial stimulation in ischemic patients with poor response to cardiac resynchronization therapy: a combined magnetic resonance imaging, electroanatomic contact mapping, and hemodynamic study to target endocardial lead placement. J Am Coll Cardiol EP 2016;2:799–809.

3. Spragg DD, Dong J, Fetics BJ, et al. Optimal left ventricular endocardial pacing sites for cardiac resynchronization therapy in patients with ischemic cardiomyopathy. J Am Coll Cardiol 2010;56:774–81.

4. Derval N, Steendijk P, Gula LJ, et al. Optimizing hemodynamics in heart failure patients by systematic screening of left ventricular pacing sites: the lateral left ventricular wall and the coronary sinus are rarely the best sites. J Am Coll Cardiol 2010;55:566–75.

5. van Deursen C, van Geldorp IE, Rademakers LM, et al. Left ventricular endocardial pacing improves resynchronization therapy in canine left bundle-branch hearts. Circ Arrhythm Electrophysiol 2009;2:580–7.

6. Bordachar P, Grenz N, Jais P, et al. Left ventricular endocardial or triventricular pacing to optimize cardiac resynchronization therapy in a chronic canine model of ischemic heart. Am J Physiol Heart Circ Physiol 2012;303:207–15.

7. Strik M, Rademakers LM, van Deursen CJM, et al. Endocardial left ventricular pacing improves cardiac resynchronization therapy in chronic asynchronous infarction and heart failure models. Circ Arrhythm Electrophysiol 2012;5:191–200.

8. Ploux S, Lumens J, Whinnett Z, et al. Noninvasive electrocardiographic mapping to improve patient selection for cardiac resynchronization therapy: beyond QRS duration and left bundle branch block morphology. J Am Coll Cardiol 2013;61:2435–43.

KEY WORDS cardiac resynchronization therapy, endocardial pacing, pacing site