Cardiac Resynchronization Therapy
Location Matters*

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In this issue of the Journal, Giraldi et al. (1) compare transvenous and epicardial lead placement in patients with unfavorable coronary sinus anatomy. Patients who met standard criteria for cardiac resynchronization therapy (CRT) including left ventricular (LV) dysfunction, New York Heart Association class III to IV congestive heart failure, and left bundle branch block, who were on optimal medical therapy underwent pre-operative multislice computed tomography to evaluate coronary sinus (CS) anatomy. Patients with CS veins that were absent, tortuous, angled acutely, or very small were prospectively randomized to LV lead implantation by epicardial minimally invasive thoracotomy versus conventional endocardial lead placement.

Whereas the surgically positioned leads were placed over the mid–basal segments of the posterolateral LV wall, the transvenously positioned leads could not be placed in these segments because of suboptimal CS anatomy. At 1 year, the surgical patients, but not the patients implanted transvenously, had significant improvements in New York Heart Association functional class, LV ejection fraction, LV end-systolic volume, and peak VO$_2$/kg.

In this small but well-designed trial, Giraldi et al. (1) set out to answer an important clinical question: How should an electrophysiologist treat a heart failure patient who needs CRT but has challenging CS anatomy? The answer to this question relies on gaining deeper understanding about electrical and mechanical dyssynchrony. In a landmark article using contact and noncontact mapping to study LV activation, Auricchio et al. (2) demonstrated the complexity and heterogeneity of electrical activation patterns in 24 patients with heart failure and left bundle branch block. Activation of the LV was “U-shaped” in 23 patients because of an anterior, lateral, or inferior line of block, which demonstrated functional behavior. The location of the line of block was unpredictable and independent of QRS duration. Varma et al. (3) used noncontact body surface mapping to examine electrical synchrony in 8 patients undergoing CRT and found that although the location of latest LV activation was in the lateral LV base in 3 patients, it was variable in the remaining patients. The effect of fibrosis on response to LV pacing is also poorly understood, but in 1 study was found to have an important negative effect on response to CRT (4).

Several recent studies have provided insight into CRT and LV lead location that have shattered previous assumptions about this complex matter. Despite impressive benefits from CRT in some patients, 20% to 40% of patients are nonresponders. Many explanations for nonresponders exist, including poor patient selection or suboptimal execution of therapy (5). At Late-Breaking Clinical Trials at Heart Rhythm 2010, Singh et al. (6) presented long-term follow-up from a substudy of MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy) evaluating the impact of LV lead position on clinical outcomes. In 799 patients randomized to CRT-D, LV lead location was classified along the short axis as anterior, lateral, or posterior and along the long axis as basal, mid-ventricular, or apical based on venograms and chest radiographs. Patients whose LV lead was positioned apically had a 22% risk of heart failure and mortality versus 12% risk in patients with a mid-ventricular or basal lead position. Furthermore, there was no difference in clinical benefit or outcome between patients with LV leads positioned on the anterolateral or posterior walls. This finding is important because response to therapy was not measured by acute changes in hemodynamic parameters, but rather by long-term changes in LV volumes. Merchant et al. (7) prospectively evaluated LV lead position along the longitudinal axis in 115 patients at a single center. The primary endpoint was a composite outcome of heart failure hospitalization, cardiac transplantation, or all-cause mortality. During a mean follow-up of 15 months, the primary endpoint of event-free survival was significantly lower (52% vs. 79%) in the patients with apical LV leads. These findings suggest that apical placement of LV leads should be avoided. In the present study (1), 11 of the 20 patients who received a transvenous device had the LV lead placed in an apical posterior vein.

Other recent studies also challenge the assumption that posterolateral lead placement is the only ideal location. Yeim et al. (8) prospectively evaluated 102 patients who received CRT to define demographic, clinical, and electrocardiographic predictors of CRT response. Independent predictors of a clinical response included an idiopathic

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etiology of cardiomyopathy, wider QRS prior to implantation, and narrowing of the QRS after implantation. Interestingly, the anatomic position of the LV lead did not predict clinical benefit from CRT, suggesting that the lateral wall may not be the optimal pacing site in all patients. In a retrospective analysis of 32 super-responders to CRT, defined as patients in whom ejection fraction improved by ≥20%, lead position was not a significant predictor of super-response, but there were trends toward super-responders having more midventricular and fewer laterally placed leads (9). One explanation may be the presence of fibrosis at the pacing site. Lambiase et al. (10) performed noncontact mapping on 10 patients with biventricular pacemakers, all with the LV lead in a posterolateral location.

In 6 patients, 5 with ischemic heart disease, the CS lead was positioned at a site with low amplitude electrograms and slow conduction velocity. Even when the LV lead is positioned in an area of late mechanical or electrical activation, the benefits of biventricular pacing may be limited if the lead is located in an area of myocardial scar or substantial electrical delay.

With regard to LV lead position in biventricular pacing systems, the study from Giraldi et al. (1) suggests that at least in some patients, LV lead location does matter. Although the present paper by Giraldi et al. (1) advances the current state of knowledge on this important topic, there is still a lot we do not know about mechanical and electrical dyssynchrony in heart failure. For example, we do not know whether LV lead position should be dictated by electrical latency or mechanical latency. We have only recently learned in an elegant paper from the Bordeaux group (11) that endocardial pacing is associated with significantly better hemodynamics than epicardial pacing is, and the optimal site of endocardial pacing was not predicted by mechanical latency or typically found to be in the lateral wall. Further research is needed in this critical area. Evolving technologies and implant techniques, such as CS venoplasty, may also improve outcomes by allowing access to more optimal pacing sites. Finally, caution must be taken before recommending routine CT scans to define anatomy in candidates for CRT, as was performed in the present study. Iatrogenic radiation exposure has become an important concern and cardiac patients often have multiple exposures in the cardiac stress, catheterization, and electrophysiology laboratories (12,13). Fluoroscopy times during CRT implants can be prolonged and the long-term risks of performing a CT scan in addition are unknown. We are just beginning to understand the complexity of LV activation in heart failure patients and in patients with biventricular pacing. While we await the results of future trials, we do not feel a change in clinical practice is warranted based on the current state of knowledge, and we do not endorse pre-procedural CT scans because of concern about increased radiation exposure.

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