Focused Perspective

Single Site Left Ventricular Pacing for Cardiac Resynchronization

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Chronic, dilated heart failure is often accompanied by delayed ventricular electrical activation manifested as prolonged QRS duration, most commonly in the form of left bundle branch block (LBBB). Exploration of the link between the sequence of cardiac electrical activation and mechanical function is one of the most exciting contemporary areas of research in heart failure, but recognition of the importance of normal ventricular activation patterns for optimal myocardial mechanical performance dates back 75 years. Wiggers observed that asynchronous delayed activation of the ventricular musculature induced by electrical stimulation had adverse hemodynamic consequences in mammals, and he proposed that the more muscle activated before excitation of the Purkinje system, the greater the asynchrony and the weaker the resulting contraction. Forty years later, Schlant concluded that asynchronous ventricular activation and the weaker the resulting contraction. In 1984, de Teresa et al. demonstrated that changing the sequence of ventricular activation by pacing could improve cardiac function. Pacing from epicardial leads placed on the right atrium and lateral left ventricular (LV) free wall in patients with LBBB after aortic valve replacement, they noted that left ventricular ejection fraction was maximal when septal and free wall contraction were simultaneous and diminished when septal and free wall motion were dysynchronous. Ten years later, Cazeau and colleagues applied the term “cardiac resynchronization” to the favorable modification of cardiac activation sequence by pacing in patients with cardiomyopathy and LBBB.

Early attempts at epicardial LV pacing via the coronary veins using pacing leads designed for the right ventricular (RV) apex or left atrium via the coronary sinus met with difficulty lead placement and instability and high pacing thresholds. With the development of pacing systems designed for the task, progress has been swift. A meta-analysis of randomized trials of cardiac resynchronization therapy (CRT) using these first generation pacing systems in 1634 patients found that heart failure deaths were reduced by 51% (from 3.5% to 1.7%) and heart failure hospitalizations were reduced by 29%. The demonstrated benefit is remarkable in view of the failure of approximately 20% to 30% of patients to respond with symptomatic improvement to CRT and that methods to optimize lead placement and patient selection are still unresolved.

Failure to respond favorably to CRT may simply indicate that mechanical activation is not dysynchronous despite delayed ventricular activation. It is likely, however, that inability to select or achieve adequate pacing sites is an important factor. Success of resynchronization is dependent on pacing from a site that changes the sequence of ventricular activation in a manner that translates to an improvement in cardiac function. Ideally, pacing sites that produce the best hemodynamic effect would be selected. Methods for identifying the best site during implantation are not yet of proven clinical benefit. Pacing from the site that produces the greatest decrease in QRS duration makes intuitive sense, but the correlation between decrease in QRS duration and hemodynamic effect has been poor; hemodynamic improvement can occur without shortening of the QRS duration. Acute hemodynamic studies have shown that pacing from the LV free wall is generally superior to pacing from the anterior interventricular vein, near the septum. Furthermore, pacing from anterior LV sites can exacerbate asynchrony and be disadvantageous in some patients. Individual responses, however, reveal important exceptions. A few patients have a better acute hemodynamic response to RV rather than LV or biventricular pacing, possibly related to the ability to rapidly activate a portion of the LV during RV apical pacing in these individuals (Angelo Auricchio, MD, Otto-von-Guericke University, University Hospital, Magdeburg, Germany, unpublished data, 2003).

Even if optimal LV pacing sites could be identified a priori, access to such sites is potentially constrained by variations in coronary venous anatomy, high pacing thresholds related to epicardial scar, or unacceptable phrenic nerve stimulation.
With present systems a suitable pacing site on the LV free wall cannot be achieved in 5% to 10% of patients. Surgical placement of epicardial LV pacing leads or endocardial LV stimulation may be options when the coronary venous approach fails.18

The initial randomized trials of CRT have utilized devices incorporating RV and LV pacing sites, largely because of familiarity with, acceptance of, and demonstrated safety of the RV pacing lead, rather than evidence that RV pacing was required for hemodynamic benefit. An RV pacing site is not required, however, for hemodynamic benefit in many patients. Left ventricular pacing alone has short-term hemodynamic benefits similar or superior to those achieved with biventricular pacing in many patients.3,19–21 Two small studies suggested that benefit of single site LV pacing is persistent at 4 weeks and 6 months.17,22

In this issue of Circulation, Blanc and coworkers extend the follow-up observations of single site LV pacing. Functional capacity (6-minute walk and maximal O2 uptake), ventricular size and function, and blood norepinephrine levels before and after 12 months of left univentricular pacing were evaluated in 22 patients with dilated cardiomyopathy, LBBB, and New York Heart Association class III or IV heart failure. The LV lead was placed in a lateral coronary vein when possible and all patients had sinus rhythm to allow atrial synchronous left univentricular pacing with an AV delay initially programmed to 100 ms. Significant improvements in functional capacity, echocardiographic mitral regurgitation, and LV end diastolic diameter were observed with favorable trend toward improvement in LV ejection fraction.

It should be recognized that the design of the study likely selected CRT “responders.” Of the initial 43 patients who underwent implantation, 7 died before 1 year and thus could not be evaluated. An additional 13 patients had not yet reached 1 year of follow-up and their data were not reported. There was no control group. These results in the remaining 23 patients are encouraging, however, supporting persistent benefit (at least to 1 year) of left univentricular pacing in some patients who respond to CRT.

How should this information be used? Given individual variations in heart failure etiologies, severity, patterns of delayed ventricular activation, location of regions of scar, and extent of mitral regurgitation, it seems unlikely that one pacing site will “fit all.” At present, it is not possible to identify patients who will respond better to LV pacing alone compared with biventricular pacing or neither, and it is not clear how to identify the optimal pacing site. Biventricular pacing systems with separately programmable LV and RV stimulation outputs and timing delay will allow adjustments to be made during follow-up that will facilitate further studies and hopefully clarify some of these issues.24 Other factors will continue to warrant RV lead placement in many patients. Although no LV lead dislodgements were observed in the study by Blanc et al,23 the incidence has been reported at 5% to 10% in larger studies.11,25 Patients with poor LV function are at risk for sudden cardiac death from ventricular arrhythmias. Present implantable defibrillator systems require a RV lead for tachyarrhythmia sensing and high voltage therapies and have a long record of safety and reliability in this regard.

Further data defining the safety and reliability of LV leads for tachyarrhythmia sensing and possibly defibrillation are essential before RV leads are abandoned in CRT pacing and CRT defibrillation systems.

Better understanding of the link between activation sequence and mechanical function may also have important implications for the large number of patients who receive pacemakers for bradycardias. QRS duration is prolonged during RV apical pacing. Ventricular desynchronization imposed by RV pacing even when AV synchrony is preserved causes increased left atrial diameters and reduced LV fractional shortening and is associated with increased atrial fibrillation, heart failure, and death among patients with normal baseline QRSd.28,29 In a canine model, pacing at the LV septum or apex maintains ventricular pumping function at normal levels despite pacing-induced QRSd prolongation.30 It is likely that systems incorporating an RV lead will continue to predominate. If LV pacing systems can become as reliable as RV pacing systems, the paradigm could shift.

References


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