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Editorial

Speckle Tracking for Cardiac Resynchronization Therapy Implantation: Have We Found the Perfect Match?

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See article by Appert et al., pages 27–34 of this issue.

Cardiac resynchronization therapy (CRT) in patients with advanced heart failure improves left ventricular (LV) function, exercise capacity,[1] and reduces morbidity and mortality compared with medical treatment.[2,3] As with any intervention, when considering individual patient's risks and benefits of the procedure, we would like to be able to select those likely to derive the greatest benefit, identify those at the greatest risk after the procedure, and seek ways to optimize response to therapy in patients selected to receive it.

Unfortunately, despite meeting the guideline criteria for CRT implantation, the rate of CRT nonresponders remains high at 30% to 40%.[4-6] Teasing out the reasons for lack of response to CRT and fine-tuning CRT selection criteria remain the cornerstone for research in this field. The type of substrate, scar burden and location, LV lead location, and the pattern of dyssynchrony seem to be the main determinants of outcomes. In a recent meta-analysis, classic features such as the presence of left bundle branch block at baseline, nonischemic cardiomyopathy, female sex, sinus rhythm, and a wider QRS duration were also associated with better CRT response and long-term outcomes.[7]

The use of echocardiography to optimize CRT response is still controversial.[8] In fact, the 2016 European Society of Cardiology guidelines for the diagnosis and treatment of heart failure only suggest the use of echocardiography in patients with poor response to CRT.[5] In the Results of the **Pr**edict**or**s of Res**p**ons**e** to **C**R**T** (PROSPECT) trial, 426 patients eligible for CRT were evaluated using 12 echocardiographic parameters to predict CRT response. Although intellectually promising, these parameters showed low sensitivity and specificity for CRT response, leading the authors to recommend clinical criteria rather than echocardiography as the standard for patient selection.[9]

Over the last few years, speckle tracking has emerged as a promising echocardiographic technique to assess cardiac resynchronization and optimize lead positioning.[10,11] Strain rate has been described as a useful parameter to define septal dyssynchrony patterns that can predict response to cardiac resyncronization.[12]

Echocardiography has also been used to optimize lead placement during CRT. In the **Tar**geted Left Ventricular Lead Placement to **G**uide Cardiac R**e**synchronisation **T**herapy (TARGET) study, the authors' randomized 220 patients eligible for CRT to have a standard or a speckle tracking guided procedure. Patients in the first group, where strain rate was used to identify scar and position the LV lead in a healthy location, had better clinical response and a lower rate of combined endpoint (all-cause mortality and heart failure–related hospitalization). This approach was further supported by other studies.[13]

Electrocardiographic QRS narrowing is another known predictor of CRT response with lack of improvement of the functional status or LV reverse remodeling in patients without QRS narrowing after CRT implantation and increased mortality and hospitalization in patients with QRS widening after the procedure.[14,15]

In the prospective cohort study published in this issue of the *Canadian Journal of Cardiology*, Appert et al.[16] sought to determine the correlation between preoperative dyssynchrony as qualified using various echocardiography strain patterns and QRS narrowing with clinical CRT response and outcomes.

The authors enrolled 233 ambulatory patients eligible to receive CRT according to the current guidelines (New York Heart Association [NYHA] class II-IV despite optimal medical therapy, LV ejection fraction $< 35\%$, and QRS duration > 120 ms with left bundle branch block or >150 ms with right bundle branch block). Patients underwent an echocardiogram before the procedure, where in addition to standard echocardiographic measurements, longitudinal strain and strain rate values were collected. Patients were classified into 3

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septal deformation patterns. These patterns have been previously described as associated with diverse CRT response;[17] patterns 1 and 2 were previously shown to correlate with greater CRT response compared with pattern 3, which was not. Maximum QRS duration from earliest onset in any lead to latest offset in any lead was also measured a day before and a day after device implantation. Instead of using quantitative data, patients were classified into 2 groups: those with or without any QRS narrowing after CRT. The primary endpoint of the study was overall mortality with a mean follow-up of 48 months. Clinical and echocardiographic response were also measured and defined as an improvement of at least 1 NYHA functional class and ΔLV end-systolic volume $\geq$ 15% nine months after initiation of CRT.

Consistent with the results of previous studies, QRS narrowing was seen after CRT implantation in 79% of the patients, and as expected, more patients with patterns 1 and 2 experienced QRS narrowing compared with those with pattern 3 (88%, 86%, and 69%, respectively). Both absence of postoperative QRS narrowing and echocardiographic pattern 3 were found to be independently associated with increased mortality. When comparing all groups, patients with pattern 3 had greater cardiovascular mortality during follow-up compared with patients exhibiting patterns 1 and 2, among both patients who experienced QRS narrowing as well as those patients who did not (odds ratios 2.81 and 6.27, respectively). Clinical response was not significantly different between the 3 groups. Only 63% of patients with pattern 3 and QRS narrowing and 23% of those with pattern 3 without QRS narrowing responded to CRT. This compares poorly with patients with patterns 1 and 2 with or without QRS narrowing who exhibited much higher rates of response to CRT (88% and 70%, respectively).

None of the patients in this study had a cardiac magnetic resonance imaging preprocedure to assess scar burden and distribution previously described to predict CRT response.[18]

These results are consistent and validate previous studies supporting the limited role of echocardiography to prognosticate response to CRT. The novel contribution of this study is the interaction between QRS narrowing and echocardiographic patterns. The authors demonstrate that:

1. Patients with echocardiographic pattern 3 are less likely to exhibit QRS narrowing with CRT and those with pattern 3 and lack of QRS narrowing with CRT have the worst survival.
2. Patients with patterns 1 and 2 respond to CRT regardless of whether or not they demonstrate QRS narrowing with CRT.
3. Clinical response to CRT as measured by improvement in NYHA functional class rather than some of the more sophisticated functional assessment tools remains constant irrespective of underlying dyssynchrony as evidenced by echocardiography or electrical resynchronization as demonstrated by QRS narrowing.

When we take a closer look at the baseline demographic and echocardiographic characteristics among the patients in the study, it becomes apparent that there is an association between lack of QRS narrowing and the presence of the classical clinical features associated with poor outcomes: sex ($P = 0.01$), baseline QRS width ($P \leq 0.001$), LV end-diastolic volume ($P = 0.03$), and scarred segments ($P = 0.003$). Without further modeling including clinical and magnetic resonance imaging predictors of CRT response, the incremental unique predictive value of the echocardiographic patterns described by the authors for patients considered for CRT remains unclear. As echocardiography is ubiquitously available, it is enticing to continue to search for echocardiographic signs that could help us select patients for CRT and optimize their clinical response and ultimate survival; for the time being this goal remains elusive.

Disclosures

The authors have no conflicts of interest to disclose.

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