

# Challenges for the Basis of Practice

## Guideline Challenge

### Has CRT Earned a Class I Recommendation?

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The biventricular pacemaker has become a cornerstone in the management of chronic heart failure, despite the fact that at least 30%, and perhaps as many as 50%, of implanted patients do not benefit from such a therapy.<sup>1</sup> The 12-lead ECG was used to select patients in the majority of randomized controlled trials performed to date, and the inaccuracy of QRS complex width in the identification of appropriate candidates for pacing has been viewed as the principal cause underlying nonresponse to cardiac resynchronization therapy (CRT).<sup>1</sup> Indeed, numerous studies subsequently showed that mechanical, more than electric, dyssynchrony identified by echocardiography is a fundamental prerequisite for the success of CRT.<sup>1</sup> However, these studies were primarily single-centered, presented significant methodological differences—definition of “dyssynchrony” and of “responder” for example—and enrolled a limited number of patients. In addition, although promising results have been obtained when dichotomizing echocardiographic parameters, a linear relationship between the degree of resynchronization offered by CRT and improvement at echocardiography after implantation has not been consistently reported.<sup>2</sup> Finally, and most importantly, nonresponders in the aforementioned randomized controlled trials did not undergo in-depth echocardiographic evaluation and, consequently, treatment failure cannot be automatically ascribed to an absence of mechanical dyssynchrony.

The PROSPECT trial<sup>3</sup> was the first, and remains the only, large-scale, prospective study to investigate the role of echocardiography in CRT. Several indices with varying complexity were examined, but all of them had an unacceptably low predictive value in terms of reverse remodeling. Is such a finding unexpected? It should not be. Evaluation of intraventricular dyssynchrony per se does not take into account several key factors that may condition response to CRT, such as pacing site and presence of viable myocardium.<sup>4</sup> One should also keep in mind that heart failure is a complex clinical syndrome that involves not only the heart but also every other system—vascular, respiratory, renal, muscular, central nervous, peripheral nervous, endocrine, gastrointestinal, reproductive, immune, hematologic—of the human body. Heart failure, therefore, cannot be boiled down to a matter of intraventricular dyssynchrony. As demonstrated by

**Table. Comparison of American and European Guidelines on CRT**

Guideline	Recommendation
AHA/ACC 2008 guidelines for device-based therapy of cardiac rhythm abnormalities <sup>5</sup>	“For patients who have LV ejection fraction $\leq 35\%$ , a QRS duration $\geq 0.12$ s, and sinus rhythm, CRT with or without an ICD is indicated for the treatment of NYHA functional Class III or ambulatory Class IV heart failure symptoms with optimal recommended medical therapy.” Class of recommendation I, level of evidence A
ESC 2008 guidelines for the diagnosis and treatment of acute and chronic heart failure <sup>6</sup>	“CRT-P is recommended to reduce morbidity and mortality in patients with NYHA III to IV class who are symptomatic despite optimal medical therapy and who have reduced EF (LVEF $\leq 35\%$ ) and QRS prolongation (QRS width $\geq 120$ ms).” Class of recommendation I, level of evidence A
ESC 2007 guidelines for cardiac pacing and cardiac resynchronization therapy <sup>7</sup>	CRT is indicated for “patients with heart failure who remain symptomatic in NYHA classes III to IV despite OPT, with LVEF $\leq 35\%$ , LV dilatation, normal sinus rhythm, and wide QRS complex ( $\geq 120$ ms).” Class of recommendation I, level of evidence A
AHA/ACC 2005 guidelines for the diagnosis and management of chronic heart failure in the adult <sup>8</sup>	“Patients with LVEF $\leq 35\%$ , sinus rhythm and NYHA functional class III or ambulatory class IV symptoms despite recommended, optimal medical therapy and who have cardiac dyssynchrony, which is currently defined as a QRS duration $>0.12$ ms, should receive cardiac resynchronization therapy unless contraindicated.” Class of recommendation I, level of evidence A

ACC indicates American College of Cardiology; AHA, American Heart Association; CRT-P, CRT without an implantable cardioverter-defibrillator; EF, ejection fraction; ESC, European Society of Cardiology; ICD, implantable cardioverter-defibrillator; LV, left ventricular; NYHA, New York Heart Association; OPT, optimal medical therapy.

the PROSPECT trial, the existence of dyssynchrony is not closely correlated to clinical response after CRT.

Although the methodology currently used to select candidates for CRT is far from perfect, both American and European cardiological societies have nevertheless recently assigned a class I, with level of evidence A, recommendation to CRT in chronic heart failure.<sup>5,6</sup> According to these new guidelines and similar documents published in the past<sup>7,8</sup> (Table)—in addition to NYHA class, ejection fraction, and concomitant medical therapy—clinicians should assess QRS

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complex width despite the uncertainties surrounding the predictive value of intraventricular dyssynchrony. Would not it be wise then, also in light of the potential long-term complications and costs associated with device implantation, to downgrade the recommendation to IIa until we truly understand how to identify responders? Or alternatively, if the authors of the guidelines consider a class I recommendation to be of vital importance, should not they also highlight the importance of searching for potential predictors of non-response, such as extreme left ventricular dilatation, unfavorable venous anatomy, and extensive myocardial scar?<sup>4</sup>

## Disclosures

None.

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