

# ArrhythmiaNEWS

From the Al-Sabah Arrhythmia Institute at St. Luke's-Roosevelt Hospital Center

*Arrhythmia News* is a physician bulletin providing arrhythmia updates and information on services at **St. Luke's-Roosevelt Hospital Center** which may benefit your practice and your patients.

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## Cardiac Resynchronization Therapy: An Update

Current practice guidelines support cardiac resynchronization therapy (CRT) in patients **in sinus rhythm, left ventricular ejection fraction (LVEF) ≤ 35% (irrespective of etiology), a QRS duration ≥ 0.12 seconds,** and New York Heart Association (NYHA) functional **class III or ambulatory class IV heart failure symptoms** on optimal recommended medical therapy.<sup>1</sup> In these patients, CRT improves quality of life, exercise capacity, functional status, and overall survival. CRT mitigates the adverse hemodynamic impact of prolonged ventricular conduction; specifically, there is reduction in mitral regurgitation and left ventricular reverse remodeling.<sup>2</sup> The latter is characterized by reductions in LV end-systolic volume and improvements in LVEF.

Despite the impressive clinical data favoring CRT, there have been two important unanswered questions. **The first question** is how to identify patients in advance who meet clinical criteria for CRT yet fail to demonstrate either subjective and/or objective long-term improvement. For example, in the Multicenter InSync Random-

ized Clinical Evaluation (**MIRACLE**), **34% of patients** did not demonstrate an improvement in a heart failure clinical composite score that combined all-cause mortality, heart failure hospitalization, NYHA class, and patient global assessment into an outcome measure.<sup>3</sup> **The second question** is whether patients with a narrow QRS (QRS duration < 120 msec) and advanced congestive heart failure can also benefit from CRT. Two recent studies have shed light on both issues.

It has been suggested that QRS duration is an inadequate marker of ventricular dyssynchrony. For example, some patients with ventricular dysfunction and a prolonged QRS duration do not have echocardiographic evidence of intraventricular dyssynchrony, which may explain why some patients fail to respond to CRT. To date, multiple single center studies have proposed the utility of various echocardiographic parameters to identify patients most likely to respond to CRT. These parameters have most commonly incorporated traditional techniques (e.g. M-mode defined septal to posterior wall motion delay) and tissue Doppler imaging. However, the optimal echocardiographic parameter remains undefined.

### Is Echo the Best Predictor?

The Predictors of Response to CRT (**PROSPECT**) was a prospective, multi-center, non-randomized study designed to evaluate selected, predefined baseline echocardiographic parameters for their ability to predict

clinical and echocardiographic response to CRT.<sup>3</sup> This study evaluated 12 separate echocardiographic parameters thought to differentiate responders from non-responders. Responders were defined by improvement in a heart failure clinical composite score and a 15% reduction in end-systolic left ventricular volume assessed 6-months post-CRT. In this study, echocardiographic parameters were associated with only modest inter- and intra-observer variability. Furthermore, not a single echocardiographic variable could reliably differentiate responders from non-responders. **The authors conclude that current technology, degree of training standards, and analytic methods do not allow tissue Doppler imaging to be incorporated into a generalized setting for predicting outcomes to CRT.**

### Additional Studies Conducted

Given the favorable response to CRT in most patients with advanced heart failure and the suggestion that some patients with a narrow QRS also have echocardiographic evidence of intraventricular dyssynchrony, it was natural to wonder whether some patients with a narrow QRS and advanced heart failure in the setting of LV dysfunction could also benefit from CRT. The **Cardiac Resynchronization Therapy in Patients with Heart Failure and Narrow QRS (RethinQ)** study enrolled patients with LV dysfunction (EF ≤ 35%, irrespective of etiology), class III heart failure, and a QRS duration < 130 msec.<sup>2</sup>

All patients underwent implantation of a CRT device. However, prior to device implantation, all patients underwent a 6-minute hall walk test and an echocardiographic examination to assess intraventricular dyssynchrony and LVEF. Intraventricular dyssynchrony was defined by M-mode criteria (**septal to posterior wall motion delay  $\geq 130$  msec**) as well as tissue Doppler criteria (opposing wall mechanical delay [**antero-septal-to-posterior or septal-to-lateral**] of  $\geq 65$  msec). Although all patients received a CRT device, patients were randomized to have the LV lead either turned on or off.

The primary endpoint of the study was the proportion of patients who had an exercise of at least 1.0 ml per kilogram of body weight per minute in peak oxygen consumption during cardiopulmonary exercise testing at 6-months after baseline. Although the patients undergoing CRT had a significant (subjective) improvement in NYHA as compared to patients in whom the LV lead was turned off (54% vs 29%,  $p=0.006$ ), **no difference was observed in the primary endpoint or in quality of life scores, 6-minute hall walk distance, echocardiographic indices of LV reverse remodeling, and survival. These two recent studies provide**

**important data regarding the selection of patients for CRT.** First, in the setting of LV dysfunction and advanced heart failure, QRS duration remains the only viable variable for selection of patients who are candidates for CRT. **Current data do not support using echocardiography for patient selection.** Importantly, there are insufficient data to suggest withholding CRT in patients with a prolonged QRS duration who do not have echocardiographic evidence of intraventricular dyssynchrony. Second, the data not support CRT in patients with advanced heart failure and a narrow QRS duration.

## References

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