

Size Might Matter for CRT to Work in Narrow-QRS Heart Failure

Steve Stiles

June 12, 2018

VIENNA — A wide electrocardiographic QRS duration is a key part of the indication for cardiac resynchronization therapy (CRT) in heart failure (HF), but patients with narrow QRS who are of shorter stature and have smaller ventricles might also make good candidates, post hoc analysis of a trial suggests.

The event risk on CRT in patients with HF who have QRS durations less than 130 msec were significantly influenced by left ventricular (LV) size, as gauged by height-indexed end-diastolic volume (LVEDV), in an analysis based on more than 800 patients in the randomized [EchoCRT](#) trial.

Such patients on CRT who had an LV size below the median showed significant survival and HF-hospitalization benefits on CRT compared with those not on CRT. But those with larger ventricles fared significantly worse on than off the pacing therapy, reported Niraj Varma, MD, PhD, Cleveland Clinic, Ohio, here at European Society of Cardiology Heart Failure (ESC-HF) 2018.

LV size was an important modulator of CRT's clinical effects in EchoCRT patients, he said, with implications for potentially using LV size to identify subgroups of patients with narrow QRS in whom CRT might prolong life or prevent hospitalizations.

Importantly, the 115-center trial had entered only patients in NYHA class III to IV HF with an LV ejection fraction of 35% or less, a QRS less than 130 msec, and LV dilatation with signs on echocardiography of ventricular dyssynchrony. It found no clinical advantage and even showed evidence of harm from CRT over a mean of 19 months; the trial had been terminated early for futility.

As previously reported, among the trial's patients randomly assigned to CRT-on compared with CRT-off, there was no significant difference for the primary endpoint of all-cause mortality or HF hospitalization. But CRT was associated with an 80% increase in risk for death from any cause ($P = .02$) and a more than doubled risk for cardiovascular death ($P = .004$), both secondary endpoints.

But patients in the trial varied widely by QRS duration, which is dependent separately on both His-Purkinje conduction velocity and the amount of LV myocardium the pulse wave must traverse; the smaller the ventricle and, therefore, the less the myocardial conduction distance, the shorter the QRS duration.

"I don't want to read too much into this — it was a trend in a prematurely terminated trial, in only a subpopulation — but the primary outcomes seemed to improve with CRT in the shortest patients with the smallest ventricles, whereas everyone else worsened," Varma told *theheart.org* | *Medscape Cardiology*.

Varma and his colleagues, in an accompanying *Journal of the American Heart Association* [report published May 27](#), went beyond his ESC-HF presentation to show that EchoCRT patients who were in the highest quartile for the ratio of QRS duration to LVEDV improved on CRT. But those in quartiles 1 to 3 fared worse on CRT, with a 47% increased adjusted risk for the primary endpoint.

The interaction test for the effect of the QRS duration/LVEDV ratio on outcomes was "marginally significant" at $P = .046$, Varma said.

Men overall have larger ventricles than women, he observed, but sex didn't significantly influence CRT's effect on clinical outcomes, regardless of whether LVEDV was lower or higher than the median.

The findings, Varma said, "raise the provocative notion" that patients with narrow QRS with LV dilatation but with higher ratio of QRS duration to LVEDV would benefit from CRT.

In clinical practice, he said, criteria for selecting patients for the pacing therapy potentially might include LV size and stature, possibly indexed to QRS duration, and perhaps also measures of ventricular thickness.

"All of those things might be in play. None of the studies were designed prospectively to look at that, but I think that is where we are going," Varma said in an interview.

"I think it's pretty bold to do this analysis," said Wilfried Mullens, MD, PhD, Ziekenhuis Oost-Limburg, Genk, Belgium, "and even to suggest to us that we might need to look into the guidelines again."

As invited discussant after Varma's presentation, Mullens reiterated the study's limitations but noted its findings are consistent with a recent [patient-level meta-analysis](#) of five randomized trials that saw better clinical outcomes in shorter patients, independent of QRS duration. Again, sex was not an independent predictor.

That study, Mullens said, combined with the current analysis, suggests that "LV size by itself modulates QRS duration" and that QRS prolongation due to ventricular dilatation is probably not amenable to CRT, but probably will respond to CRT when it is due more to slow His-Purkinje conduction.

"That might explain why bigger ventricles with a similar QRS duration derive less benefit from CRT than smaller ventricles with a similar QRS duration."

In the analysis presented by Varma, the patients with above-median LVEDV worsened significantly for the primary endpoint with CRT switched on vs off, whereas no significant effect was seen in those with below-median LVEDV. The interaction *P* value of .056 indicated only a trend, however.

The analysis was adjusted for country, sex, walking distance, quality-of-life scores, resting diastolic blood pressure, cardiomyopathy etiology, history of myocardial infarction or coronary artery bypass grafting, and diuretic use.

Similar nonsignificant interactions were observed for the primary-endpoint components of all-cause mortality and HF hospitalization individually.

However, patients with above-median LVEDV who had CRT-on vs CRT-off showed a hazard ratio of 5.26 for cardiovascular death (95% CI, 1.93 - 14.30; *P* = .001); no significant increase was seen in the below-median LVEDV group, and the interaction *P* value for the endpoint was significant at .036.

The current study is part of a broad effort to identify further markers that will sharpen the identification of patients' HF and LV dysfunction who are most likely to respond well to CRT, Mullens commented.

But he cautioned not to lose sight of patients who aren't getting CRT despite meeting current indications.

"Every randomized trial with regard to CRT that included patients with a wide QRS was absolutely positive with regard to all-cause mortality, heart failure hospitalizations, and remodeling," he said.

"There is gross underutilization of CRT therapy in Europe and in the States and in Asia," Mullens observed, and the number 1 reason for CRT nonresponse isn't a narrow QRS duration but rather failure to receive a device.

EchoCRT was funded by Biotronik and GE Healthcare. Varma discloses receiving research grants from and consulting, receiving royalties, or being an owner of or stockholder for Biotronik. Mullens has recently disclosed that he has no relevant conflicts.

European Society of Cardiology Heart Failure (ESC-HF) 2018. Late breaking trial III - Innovative and device therapy. Presented May 28, 2018.

J Am Heart Assoc. Published online May 27, 2018. [Full text](#)

Follow Steve Stiles on Twitter: [@SteveStiles2](#). For more from [theheart.org](#) | Medscape Cardiology, follow us on [Twitter](#) and [Facebook](#).

Medscape Medical News © 2018 WebMD, LLC

Send comments and news tips to news@medscape.net.

Cite this article: Steve Stiles. Size Might Matter for CRT to Work in Narrow-QRS Heart Failure - *Medscape* - Jun 12, 2018.