# Parameters of left ventricular systolic and diastolic dyssynchrony on radionuclide imaging to improve cardiac resynchronization therapy in heart failure patients with dilated cardiomyopathy

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Cardiac resynchronization therapy (CRT) is a proven therapeutic intervention for selected patients with heart failure with reduced ejection fraction and electrical conduction delay.[1] However, studies have shown that at least one-third of patients who undergo CRT based on currently recommended indications experience no significant improvement.[2] Patient selection still remains a challenge despite multiple studies that have investigated predictors of favorable outcomes following CRT.[3,4] Narrower baseline QRS duration, suboptimal left ventricular (LV) lead placement, larger myocardial scar burden, and ischemic cardiomyopathy are a few factors associated with poor response to CRT.[3–5] Multiple different parameters of LV mechanical dyssynchrony have been of recent interest to predict outcomes following CRT.[6,7]

Myocardial scar and non-viable myocardial segments can cause dyssynchronous LV contractility that does not adequately respond to CRT.[6] Initial studies assessing LV dyssynchrony were mainly based on conventional and tissue doppler echocardiography-based parameters like the timing of longitudinal myocardial velocity peaks.[8] Several other echocardiographic parameters were found to be of interest in assessing the CRT response, however, those parameters had significant variability and had demonstrated only modest predictive power.[8] A large study assessing novel echocardiographic findings like visually assessed apical rocking and septal flash as surrogates for myocardial dyssynchrony found that these parameters were associated with better survival following CRT.[7] But a visual assessment by echocardiographic techniques is prone to intra- and interobserver variability, especially in patients with subtle patterns of dyssynchrony.[7,9] In order to mitigate the limitations of echocardiography in dyssynchrony evaluation, phase analysis on gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has been studied as an alternative to echocardiographic assessment of LV systolic and diastolic dyssynchrony.[10,11] Several studies have shown excellent correlation between the SPECT-MPI and echocardiographic assessment of dyssynchrony.[10,11] SPECT-MPI-based assessment of LV dyssynchrony relies on a demonstration of a wider spread in the timing of contraction and relaxation of various LV segments as compared to a narrower peak in normal hearts. The algorithms used for this assessment are highly automated with high reproducibility in contrast to echocardiography.[12]

It is intriguing that, it is not merely the systolic dyssynchrony, the diastolic dyssynchrony is also being increasingly suggested to be a contributor to poor

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response following CRT.[13] A significant proportion of patients with systolic heart failure have been shown to have diastolic dyssynchrony in addition to the often sought out systolic LV dyssynchrony.[13] Studies have shown varied findings in terms of changes in diastolic dyssynchrony pre and post CRT.[13,14] However, the role of LV diastolic dyssynchrony in device responsiveness and functional outcomes is not adequately understood. Whether diastolic dyssynchrony is an independent variable or merely a reflection of systolic dyssynchrony is not entirely clear.

In this issue of the *Journal*, Wang *et al* report their findings on the predictive value of LV systolic and diastolic dyssynchrony in identifying treatment response among patients with dilated cardiomyopathy who underwent CRT.[15] They evaluated 84 consecutive patients who underwent gated SPECT-MPI prior to CRT device implantation. Phase standard deviation and 95% width of phase histogram bandwidth were used to measure the global LV mechanical dyssynchrony. The primary outcome was CRT responsiveness defined as a $\geq$5% improvement in LV ejection fraction at 6-month follow-up. Study participants had a steep positive correlation between systolic and diastolic mechanical dyssynchrony. The study found that both systolic and diastolic mechanical dyssynchrony have incremental predictive value in addition to the conventional clinical predictors of CRT response including QRS duration, non-sustained ventricular tachycardia on telemetry, and optimal LV lead placement.

This study adds to the existing literature that in addition to the established clinical parameters, systolic as well as diastolic mechanical dyssynchrony assessment can help case selection for better prediction of optimal CRT outcomes. The study focused on diastolic dyssynchrony specifically, however, in the serial regression modeling, the diastolic dyssynchrony parameters in addition to systolic dyssynchrony abnormalities did not add significantly to the predictive power to the model in addition to the clinical predictors. The degree of myocardial scar burden which has known impact on CRT response and long-term outcomes was not significantly predictive of CRT responsiveness in this patient population, despite a larger proportion of subjects were reported to have scar burden. The authors have not adequately discussed this issue in their manuscript. Since the study population comprises only non-ischemic cardiomyopathy patients, based on an absence of significant angiographic coronary artery disease, one does not expect a large scar burden in this population. However, various attenuation artifacts and a reduced septal radiotracer uptake in patients with LBBB can contribute to various degrees of apparent perfusion abnormalities. However, caution is required in interpreting these apparent abnormalities as indicative of scar.

Whether diastolic dyssynchrony is just a reflection of the systolic dyssynchrony in patients with severe cardiomyopathy rather than having an independent causal effect by itself on CRT outcomes remains unknown. Besides, it is important for future studies to assess the relationship of diastolic dyssynchrony and functional outcomes in terms of quality of life in patients receiving CRT as the current study did not assess the functional outcomes of patients at follow-up. In addition to dyssynchrony, the investigators showed that pacing at LV segments with both the late contraction and late relaxation as visualized on phase polar mapping was associated with better CRT response. This physiologically instinctive finding suggests the utility of phase analysis on gated SPECT-MPI for assessing optimal lead placement following CRT. Even though the study by Wang *et al* is limited by relatively small sample size, the findings are of important clinical implications in the selection of the most appropriate patients to expect the best outcomes following an invasive and expensive intervention like CRT. Study findings need to be validated over larger prospective cohorts with longer follow-up and clinical endpoints in addition to CRT responsiveness. Overall, this study definitely appeals to our curiosity to further explore currently available imaging techniques for better phenotypical characterization in addition to the clinical selection of patients to streamline the outcomes following CRT.

## Disclosures

*D. Jain is a speaker for Astellas and Pfyzer. Consultant for Astellas and GE. J. Sreenivasan has nothing to disclose.*

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