Gated SPECT MPI and CT venography fusion: A new approach for appropriate CRT-pacemaker lead placement?

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Cardiac resynchronization therapy (CRT) is a disease-modifying therapy and has been shown to improve left ventricular ejection fraction (LVEF), reduce heart failure (HF) related hospitalization and decrease all-cause mortality in selected HF patients.^{1,2} CRT is currently recommended as a class IA indication in symptomatic HF patients with LVEF is $\leq 35\%$, sinus rhythm and a QRS duration ≥ 150 ms.³ However, one-quarter to one-half of the subjects who receive a CRT are “non-responders” and do not benefit from CRT device implantation.^{4,5} Suboptimal pacemaker lead positioning is one of the multifactorial factors associated with non-response to CRT.⁶ In general, pacing the posterolateral LV results in the best haemodynamic response.⁷ However, scar in the paced region seems to be associated with poor response to CRT.⁸ Speckle-tracking echocardiography and late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) have shown that LV CRT-pacemaker lead placement in viable segments with the latest mechanical activation is associated with acute haemodynamic response and better outcome.⁹⁻¹² Shetty et al. showed that it is feasible to acquire, overlay, and accurately register CMR-derived anatomical, scar, and dyssynchrony data to guide CRT device implantation.¹¹ Unlike CMR, gated SPECT

myocardial perfusing imaging (MPI) is widely available at relatively low costs. Therefore, gated SPECT MPI has been evaluated for optimal LV CRT-pacemaker lead positioning.^{13,14} Recently, Zhang et al. demonstrated in 79 patients that CRT response improved when LV CRT-pacemaker lead position was based on gated SPECT MPI [response was defined as a reduction of $\geq 15\%$ in LV end-systolic volume (LVESV)].¹⁵ After excluding 11 patients with LV CRT-pacemaker pacemaker lead placement in apical of scarred segments, 75.6% of the patients with LV CRT-pacemaker lead position based on gated SPECT MPI ($n = 41$) responded to CRT while only 51.9% of patients where LV CRT-pacemaker lead position was not based on gated SPECT MPI ($n = 27$) showed CRT response ($P = 0.043$). Furthermore pacing in the recommended LV segments, identified using gated SPECT MPI, was associated with long-term prognosis. Over a median follow-up of 49 months, 4 patients died (9.8%) in the recommended group, 7 (25.9%) in the non-recommended group, and 5 (45.5%) in patients where the LV CRT-pacemaker lead was positioned in the apex or scar. There were 9 (22.0%) composite events (all-cause mortality or HF hospitalization) in the recommended group, 14 (51.9%) in the non-recommended group, and 7 (63.6%) in the apex or scar group.

Although identifying the optimal LV CRT-pacemaker lead position by excluding scar tissue is key, the optimal LV CRT-pacemaker lead position is not always feasible due to variations in coronary sinus (CS) anatomy. Cardiac CT has been shown to have additional value for non-invasive visualizing myocardial anatomy, including the CS anatomy. Combining viability and known CS anatomy can result in optimal LV CRT-pacemaker lead placement, reducing fluoroscopy time, reducing procedure time, and last but not least reducing peri-procedural complications. In this issue of the

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Journal of Nuclear Cardiology Tada et al. evaluated in a proof-of-principle study the feasibility of a novel approach, named the FIVE STaR method (Fusion Image using CT Venography and perfusion SPECT applied for cardiac Resynchronization therapy), to optimize the efficacy of CRT device implantation.¹⁶ Four patients referred for CRT device implantation underwent rest SPECT MPI and CT venography prior to CRT implantation. The authors chose as definition of CRT response $\geq 15\%$ decrease of LVESV, $\geq 5\%$ increase of LVEF and decrease of at least one NYHA class at follow-up (3 months or later after CRT implantation). All patients ($n = 4$) that were evaluated using the FIVE STaR method showed CRT response according to all the different criteria used by the authors. In addition, there were no peri-procedural complications. Although a comparison with standard procedures is missing, not allowing for comparison in overall procedure time, fluoroscopy time and complications, this new method seems feasible.

Despite it has been 2 decades after the introduction of CRT into the clinical arena a consensus on how to define CRT response is still lacking. Clinical trials and registries used a variety of different outcome measures without a unified composite endpoint.¹⁷ Early studies used parameters reflecting functional improvement (6-minutes walk test and NYHA functional class).^{18,19} More recent CRT trials used HF hospitalization and death as a more objective, hard clinical endpoints.^{1,2} Besides clinical events and mortality, surrogate outcomes such as LV remodeling measures (i.e. improvement of LVEF, LVESV, and end-diastolic volume (LVEDV)) were also used in clinical trials. Consequently, different means of measuring response to CRT yield dissimilar response rates as they examine different aspects and severity of HF, in different populations, over different periods of time. This hampers comparison between different studies and will limit in obtaining the real clinical value of CRT.

Tada et al. chose a $\geq 5\%$ increase of LVEF measured by echocardiography. However, this cut-off value lies within the inter- and intra-operator variability of LVEF measurement by echocardiography.²⁰ Therefore, it is advisable to choose another cut-off value of LVEF. Furthermore, using a decrease in NYHA class as an endpoint is limited by subjectivity in assessing NYHA classification. As the FIVE STaR method by Tada et al. seem to be promising, it should be evaluated in larger cohorts of patients referred for CRT. However, as long as there is no consensus on how to best define CRT response, it is advisable to limit to hard clinical endpoints and more objective endpoints with limited inter- and intra-operator variability and excellent reproducibility such as LV remodeling measures as assessed with gated SPECT MPI.

Disclosure

Derk O. Verschure and Hein J. Verberne have no conflict of interest to declare.

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