Role of dyssynchrony in optimization of CRT implantation: a time to re-think?

Cheuk-Man Yu* and Fang Fang

Optimizing the treatment strategy and patient selection have been the challenging areas for cardiac resynchronization therapy (CRT) since the introduction of the therapy in the beginning of the Millennium. To optimize the treatment strategy, it is commonly related to the implantation of the left ventricular (LV) lead—its location with respect to the anatomical location of the LV, the presence of transmural scar tissue in the pacing site, its relationship with respect to the mechanical delay, and also the number of LV pacing sites. To achieve this task, there are two prerequisites that need to be fulfilled—the use of an appropriate imaging technology that allows the identification of the potentially optimal LV lead location and the use of a right implantation strategy that permits the secure placement of the LV lead in the target location.

Factors that may affect the efficacy of LV pacing may include the presence of transmural scar tissue and the degree of the mechanical contractile delay at the location where the LV lead is placed. To assess the transmurality of LV scar tissue, cardiac MRI with delay enhancement is currently the preferred imaging choice. It has been observed that patients who had a transmural scar at the posterolateral wall in which the LV lead was placed would have a significantly lower response rate than those with a non-transmural or without scar tissue in such location.1 However, cardiac MRI is limited by its availability and the high cost. On the other hand, echocardiography has the advantages of being versatile, cheaper, and quantitative in nature. The study in the current issue of the Journal by Kristiansen et al.2 described the role of employing 2D speckle tracking technology in the assessment of LV segmental function and regional dyssynchrony in heart failure patients before receiving CRT. Although speckle tracking is unable to measure directly the amount of scar tissue in a LV segment, a low value of regional strain is a surrogate measure of a high scar burden and a lack of contractile reserve.3,4 Nonetheless, it remains unclear whether the total scar burden or the distribution of scar is a more important determinant of the lack of response to CRT.

The concept of a comprehensive implantation strategy is to place the LV lead at a site not only with viable myocardium, but also has the greatest amount of systolic dyssynchrony. In this regard, the speckle tracking measurement of the delay in strain is increasingly recognized as a useful tool to guide the optimal placement of LV lead. One of the commonest methods is to measure the amount of the antero-posterior wall delay in radial strain in the LV mid-cavity level (cutoff > 130 ms).5 This parameter predicts a favourable long-term clinical outcome after CRT, as similar to tissue Doppler imaging that measured Ts-SD > 33 ms in a six-basal, six-middle segmental model.6 Previous single-centre studies supported the placement of the LV lead in a free wall segment concordant with the greatest systolic delay on echocardiography would result in a greatest extent of LV reverse remodelling and lower mortality and/or heart failure hospitalization than those with a discordant relationship.7–9 Recently, a single-centre randomized trial (TARGET) that compared speckle tracking-guided vs. the conventional approach of LV lead placement has shown the superiority of the former strategy in achieving better LV reverse remodelling (the primary end-point), a lower heart failure hospitalization, and a higher volumetric responder rate (83% vs 65%), although there was no difference in all-cause mortality.10 Furthermore, a concordant relationship was associated with the best clinical outcome, with the intermediate outcome for patients with the adjacent relationship, and was the worst in those with the discordant relationship.10 Interestingly, LV pacing at a low strain region (defined as < 10% of radial strain) reflecting the presence of significant scar tissue was also associated with a worse clinical outcome. The study by Kristiansen et al.2 corroborates with the TARGET trial, which affirmed the usefulness of radial strain-measured dyssynchrony parameter to enhance the volumetric response. Perhaps, the new finding of the study provides, for the first time, a direct relationship between dyssynchrony-targeted LV lead placement and the beneficial result of mechanical resynchronization. The study group defined responders of mechanical resynchronization as those having ≥ 50% reduction in the anteroposterior wall strain delay. This was observed in 66% of patients with concordance between LV lead location and dyssynchrony, 48% with the adjacent (one segment) relationship, and 0% with the discordant relationship. Therefore the message is that if one can place the LV lead in the free wall region that has the most
severe contractile delay, a maximal reduction in dyssynchrony could be achieved that will be translated to the greatest amount of LV reverse remodelling and best long-term clinical outcome. Furthermore, it is imperative to avoid the location with significant scar tissue as reflected by a low regional strain value.

There remain unanswered issues related to the dyssynchrony-guided strategy of LV lead placement. The LV lead dislodgement rate is relatively high of 7% as reported by Kristiansen et al. It is unclear how to tackle the situation when the latest contraction occurs at the site of low strain. Since these patients will likely be falling into the group of discordant lead location according to the above strategy, a low response rate is anticipated. Knowing the currently high CRT non-responder rate of at least 30%, whether these patients shall be excluded from CRT needs to be addressed by further prospective studies. The unavailability of a sizable coronary vein in the tentative segment for LV lead placement is another challenge of such approach, in which endocardial lead implantation could be a potential solution. Of note, the study by Kristiansen et al. and the TARGET trial, as similar to earlier reports, are single-centre design. In real-life experience, the measurement of speckle tracking strain parameters is subjected to significant inter- and intra-observer variability, which is particularly problematic when measured the absolute strain value than its time domain. Therefore, whether the use of speckle tracking strain can be generalized to average echocardiographic laboratories need to be validated by the future multicentre trial. It has been shown that a dedicated training programme plays a crucial role to maintain the high reproducibility of new echocardiography technologies. Lastly, the measured strain parameters may vary among vendors due to the use of non-unified algorithms, which need further validation and unification.

References