Identification of Wasted Energy Is a Key to Predict Positive Response to Cardiac Resynchronization Therapy

Is Strain Imaging the Answer?

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The introduction of cardiac resynchronization therapy (CRT) more than 10 years ago has been a major progress in heart failure therapy, and it has been shown clearly that CRT is beneficial to patients with intraventricular conduction delay in terms of reduced hospitalization and mortality. On the basis of clinical and ECG criteria alone, up to 70% of the patients with nonischemic cardiomyopathy respond positively to CRT, but only about 50% of the patients with ischemic cardiomyopathy respond. Recently, clinical and ECG criteria have been revised to limit the class I indication to QRS ≥150 ms and left bundle branch block (LBBB), but to include those with NYHA class II. Although echocardiography seemed to be an ideal tool to identify patients who would benefit positively from CRT, the 2012 device-based therapy guideline does not include echocardiography as one of selection criteria.

Initial results using different tissue Doppler imaging velocity-derived dyssynchrony indices from single-center studies were encouraging. However, the results of the multicenter study, PROSPECT, were disappointing as they demonstrated that all previously promising dyssynchrony indices had at best moderate predictive value for CRT response, if any. Although a substantial interobserver variability in PROSPECT was blamed for its poor result, our CRT working group confirmed that none of temporal dyssynchrony measures determined by M-mode, 3-dimensional volumetric, tissue Doppler, or strain echocardiography imaging was able to predict CRT response satisfactorily. A major reason for the failure of temporal dyssynchrony by echocardiography is that even if dyssynchronous activation can be corrected by CRT, mechanical dyssynchrony or discoordination may not be satisfactorily improved or corrected, especially when there are few viable myocardium or none. Therefore, an ideal parameter that predicts CRT response should be able to identify the sufficient amount of viable myocardium with dyssynchronous contraction, which can be corrected by CRT.

To achieve this, we need to identify not only differences in the timings of the peak contractions of various left ventricular (LV) segments, but also the viability or contractibility of the dyssynchronous segments.

In this issue of Circulation: Cardiovascular Imaging, Kydd et al report a parameter incorporating the regional timing (electrical dyssynchrony) and peak amplitude of myocardial deformation (indirectly reflecting viability) for predicting response to CRT. This proposed parameter, the radial strain delay (RSDc), adapted from the work by Lim et al, is derived from speckle-tracking radial strain and calculated as a segment’s peak amplitude minus the amplitude at aortic valve closure averaged for the 12 nonapical segments. The authors also calculated RSD from 6 midlevel LV segments. The higher the RSD value, the more potentially contractile energy is wasted. Kydd et al showed that RSD has a good correlation with reduction in LV end-systolic volume and a cutoff value of 40% for RSDc predicted response to CRT (defined as >15% reduction in LV end-systolic volume) with a sensitivity of 87% and specificity of 88%. The use of RSDc also displayed a better sensitivity and specificity than other temporal dyssynchrony parameters previously reported by other studies. RSDc value of more than 40% was related to improved survival, which could be explained not only by better response to CRT, but also by the fact that lower RSDc reflects less temporal delay or more scar tissue. Interestingly, ischemic and nonischemic patients did not differ significantly in their baseline RSDcs (52% versus 60%), which were somewhat different than what one would expect, given that more scar tissue should result in lower RSDc. This may be explained by the relatively small cohort size or the fact that the use of averaging in this parameter decreases the relative effect of scar tissue on total RSDc. The contribution of this study is to point out the importance of incorporating the concept of wasted energy, which takes into account temporal delay and myocardial viability in predicting CRT response. Because scarred tissue does not contribute too much to myocardial contraction even in the perfect synchronous setting, its dyssynchronous motion is not a wasted energy although it is dyssynchronous in timing.

**Mechanical Discoordination and Wasted Energy From LBBB**

It is an agreed fact that CRT works best for the patients with classical mechanical discoordination or contraction abnormality associated with LBBB. It has been well characterized that LBBB results in 2 phases of myocardial shortening followed by myocardial stretching or thinning. An early septal...
contraction begins even before the opening of the aortic valve (described as pre-ejection septal flash), which is followed by stretching during an early part of systole before contracting again with reduced force at late systole and even into postsystolic period. Opposing (lateral and posterior) walls are stretched at the time of septal contraction during the isovolumic contraction period followed by late systolic contraction with elevated cavity pressure caused by septal stretching.

How Strain Helps to Evaluate Wasted Energy

Strain imaging displays the timing and extent of myocardial thickening and stretching and hence is well suited to estimate the amount of mechanical wasted energy attributable to electrical dyssynchrony. Strain imaging also demonstrates classical mechanical dyssynchrony or discoordination pattern, which was associated with an excellent response rate to CRT, much superior to time-to-peak dyssynchrony parameters. The extent of stretch of LV segments depends on their viability because scarred myocardium cannot stretch as much as normal myocardium. The more the LV segments can stretch, the more is the wasted energy of the myocardium, which can be corrected by CRT. Because scarred myocardium has a similar timing of systolic movement or contraction as viable myocardium within a given electrical dyssynchrony setting, any measurement that just measures the timing difference in contraction of various myocardial segments, as done in initial attempts to identify an echocardiographic dyssynchrony parameter, does not accurately predict CRT response satisfactorily because it does not take viability of the myocardium into account. Most recently, Lumens et al elegantly used multiscale computer simulations of cardiac mechanics and hemodynamics to show that temporal dyssynchrony measures have a discontinuous relationship with LV volume response to CRT because of data clusters. Russell et al used LV pressure-strain loops to demonstrate beautifully marked intersegment differences in myocardial work in LBBB and other conditions producing dyssynchrony such as myocardial ischemia or infarction. As the authors suggested, RSDc is one of many means to estimate the extent of wasted energy caused by conduction delay. While Rism et al and Lim et al used longitudinal strain, the investigators of the current article used radial strain imaging. Our group reported a different approach to quantify the extent of wasted energy using speckle-tracking radial strain and strain rate from the short axis view of the LV. Radial strain rate displays thickening and stretching above and below the baseline, respectively (Figure 1). The area drawn by the averaged strain rate curve above and below the zero baseline provides the extent of thickening and stretching (Figure 2). Radial discoordination index was calculated by dividing the summed strain rate (hence, strain) of the summed myocardium by the summed strain rate of thickened myocardium during the ejection period. We were able to show that positive and negative CRT responses to CRT could be predicted best by radial discoordination index obtained from midventricular 6 segments with 38% as a cutoff value. Kydd et al also showed that RSD from 6 segments had a similar, although slight less, predictability as RSDc from 12 segments. One of the most attractive aspects of RSDc or radial discoordination index is that these measures are simple and use 1 to 3 standard echocardiography views from the parasternal short axis. Radial strain rate can also be displayed as a curved color M-mode, which instantaneously provides the extent of stretch or wasted energy (Figures 1 and 2).

Radial strain imaging has been also used to identify the optimal location for coronary sinus lead placement. Target trial demonstrated that response rate was much higher when the lead placement was guided by radial strain imaging. Can the radial strain imaging be the preferred way to identify patients who do or do not respond well to CRT? Although RSDc or radial discoordination index method seems more logical and more practical than time-based dyssynchrony, they need to be validated by multicenter trials and compared with other possible parameters such as apical rocking motion, which can be quickly assessed visually. It will take some time for the CRT community to have confidence in an echocardiographic parameter to be used for the selection of patients for CRT. We now have learned that any future echocardiography parameter for prediction of CRT response should use the concept of wasted energy and not rely on temporal dyssynchrony alone, as Kydd et al demonstrated. It is also becoming apparent that speckle-tracking strain and strain rate imaging is the modality echocardiography can rely on to demonstrate the extent of wasted energy. Therefore, we believe that we are ready to validate the finding that the wasted energy is a key to echocardiography evaluation of CRT patients in multicenter clinical trials.

Figure 1. Normal radial strain rate of 6 mid left ventricular wall segments. On the left is the strain rate of 6 segments depicted as a graph. Different colors represent different segments, with black showing an average value. Lines above the baseline indicates thickening and lines below the zero baseline indicates thinning or stretching. On the right is the color M-mode of normal radial strain rate of 6 segments. From top to bottom, color M-mode shows thickening (orange) and thinning (blue) of inferior (top), inferoseptal, anteroseptal, anterior, lateral, and posterior walls. During the ejection period, color is all orange, indicating that all segments are contracting (thickening) radially, and is mostly blue indicating stretching with diastolic filling. AVC indicates aortic valve closing; and AVO, aortic valve opening.
Disclosures

Drs Oh and Vatury are involved in RAISE-CRT multi-center trial as Echocardiography Core Lab.

References


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