Cardiac resynchronization therapy (CRT) has emerged as a highly effective treatment for selected patients with heart failure. It has been shown to improve symptoms, reduce hospitalizations and improve survival. It is well recognized, however, that the response to CRT is variable, even when CRT is delivered according to current guidelines.

According to the accepted paradigm of CRT, cardiac dyssynchrony contributes to the syndrome of heart failure and its correction leads to a clinical benefit. Intuitively, therefore, the degree of dyssynchrony present prior to CRT device implantation should relate to treatment response. Based on this premise, a panoply of echocardiographic studies have explored pre-implant dyssynchrony in relation to clinical response after CRT. In the PROSPECT study,1 the only randomized controlled study of dyssynchrony variables in relation to response after CRT, no single echocardiographic measure was found to predict CRT response, defined in terms of a composite clinical endpoint. This included the standard deviation (SD) of the time to peak systolic motion in 12 myocardial segments (Ts-SD), developed and validated by Yu et al.2

An important aspect of the conventional Ts-SD index is that it uses TDI-derived velocities in the ejection period, which comprises both active and passive motion. It is well recognized, however, that velocity peaks are also present in the pre-ejection period, where active contraction is most likely to occur. Temporal dispersion of the times to peak velocity within the pre-ejection period, therefore, is most likely to reflect temporal dispersion of contraction, rather than passive wall motion.

In this issue of the Journal, Sakamaki et al3 explore whether a modified TDI index using peak velocities during the pre-ejection period, is a better predictor of response to CRT than the conventional Ts-SD index. In their study of 61 patients, 57% were classified as responders (≥15% reduction in LV end-systolic volume). In receiver-operator characteristic (ROC) analysis, the modified Ts-SD was superior to the conventional Ts-SD in predicting the response to CRT.

Systolic function is reflected in the velocity of pressure rise (dP/dtmax), the velocity of ejection, and the magnitude of ejection. The pre-ejection period includes excitation-contraction coupling and isovolumic contraction. Accordingly, a normal ventricle has a short pre-ejection period whereas an abnormal ventricle has a long pre-ejection period and a short ejection time. Dyssynchrony within the pre-ejection period, therefore, may therefore lead to a shortened ejection time. Mechanistically, inclusion of a dyssynchrony measure from the pre-ejection period makes sense. For example, the so-called septal flash, which occurs during this period, has been linked to a favorable outcome. A peak in velocity in the pre-ejection period may well be a marker for this phenomenon.

From the clinical standpoint, the modified Ts-SD index, although better than the conventional Ts-SD, has an accuracy of approximately 80% at predicting LV remodeling after CRT. It is, therefore, not a perfect biomarker. As the authors point out, although the LV reverse remodeling response predicts survival after CRT, it does not predict a symptomatic response. The authors have included intra- and interobserver variabilities, but the true test of a new biomarker, such as the modified Ts-SD index, is in large, multicenter, randomized, controlled studies. Had we invested more in such studies over the past 10 years, we would not be revisiting so many debates in relation to echocardiography and CRT.

Disclosures
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References