Large response to cardiac resynchronization therapy in a patient with segmental paradoxical systolic expansion identified by strain imaging

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An 84-year-old man with non-ischaemic cardiomyopathy underwent cardiac resynchronization therapy (CRT) based on the presence of drug-refractory heart failure, depressed left ventricular ejection fraction (25%), and wide QRS complex (160 ms). Longitudinal tissue velocity revealed no significant dyssynchrony (23 ms in Yu index and 35 ms in opposing wall delay). However, longitudinal tissue Doppler strain revealed unique appearances in apical four-chamber and long-axis views. The anterior and inferior septum at basal and mid-levels had reversed strain (becoming positive), indicating paradoxical systolic expansion. Ejection fraction dramatically improved from 26 to 50% the day following CRT, and this beneficial effect of CRT was sustained 12 months following CRT. The presence of the segmental reversed strain might have a potential to predict a large response to CRT in the assessment of longitudinal dyssynchrony.

KEYWORDS
Echocardiography; Tissue Doppler imaging; Pacing therapy

Case report
An 84-year-old man with non-ischaemic cardiomyopathy was admitted to the hospital to refer for cardiac resynchronization therapy (CRT). Despite optimized medical therapy including maximum tolerated dosages of furosemide, enalapril, and carvedilol, he experienced continued heart failure (HF) with New York Heart Association functional class III. His electrocardiogram demonstrated a sinus rhythm with a wide QRS complex of 160 ms with a left bundle-branch block (Figure 1A). Echocardiographic examination was performed to assess left ventricular (LV) function and mechanical dyssynchrony (Vivid 7 GE-Vingmed, Horten, Norway). The ejection fraction (EF) was 25% by biplane Simpson’s rule (Supplementary data online, Video 1). Colour-coded longitudinal tissue Doppler imaging was recorded in apical four-chamber, two-chamber, and long-axis views and a sample volume was positioned at basal and mid-levels from each view (12 sites). Longitudinal dyssynchrony by myocardial velocity was as follows: 23 ms in Yu index and 35 ms in opposing wall delay, indicating no significant longitudinal dyssynchrony1,2 (Figure 1B). However, longitudinal tissue Doppler strain revealed unique appearances in apical four-chamber and long-axis views. The anterior and inferior septum at the basal and mid-levels had reversed strain (becoming positive), indicating paradoxical systolic expansion (Figure 2A).

On the basis of the presence of drug-refractory HF, depressed LV function (≤35%) and wide QRS complex (≥120 ms), a biventricular pacemaker was implanted. The implantation of the device was uneventful with the right ventricular pacing lead positioned in the RV apex and the LV lead positioned in a lateral branch of epicardial vein via the coronary sinus. The patient subsequently had a repeat two-dimensional echocardiographic and tissue Doppler study the day following CRT. EF dramatically improved from 25 to 50% (Supplementary data online, Video 2), and reversed strain by longitudinal tissue Doppler imaging was disappeared in apical four-chamber and long-axis views (Figure 2B). This beneficial effect of CRT was sustained 16 months following CRT (Supplementary data online, Video 3).

Discussion
CRT has made a large impact on improving symptoms and survival in patients with drug-refractory HF and wide QRS
complex, but a subset of patients does not favourably respond to CRT with standard clinical selection criteria. Accordingly, quantification of LV dyssynchrony by echocardiography has emerged as an important potential means to predict response to CRT. Several echocardiographic studies have demonstrated that the presence of mechanical dyssynchrony is an important factor determining response to CRT. The largest body of studies to quantify LV dyssynchrony and predict response to CRT has focused on longitudinal dyssynchrony by tissue Doppler imaging from the apical views or radial dyssynchrony by speckle tracking strain from the LV mid-short-axis view. Longitudinal myocardial velocity assessed by tissue Doppler imaging is the most commonly used technique for quantifying LV dyssynchrony. The greatest sensitivity and specificity for predicting response to CRT appears to be attained when limiting peak longitudinal velocities for dyssynchrony analysis to the interval from aortic valve opening to aortic valve closure. Therefore, longitudinal dyssynchrony by tissue velocity generally limits analysis to LV ejection interval. However, patients with conduction delay and impaired systolic function often show more prominent positive velocities during isovolumic contraction or in the post-systolic period than in the ejection interval and sometimes do not show a distinct peak during the ejection interval. In this case, the patient with segmental paradoxical systolic expansion identified by strain imaging had a large response to CRT in spite of no longitudinal dyssynchrony by current criteria. The precise reason why this patient had significant dysynchronous wall motion abnormalities, but no longitudinal dysynchrony by myocardial velocity is unknown. However, the presence of patients with a heterogeneous pattern of either longitudinal dyssynchrony by myocardial velocity or radial dyssynchrony by speckle-tracking strain in HF patients with left bundle-branch block was reported. In fact, this patient had a significant radial dyssynchrony by speckle-tracking strain of 380 ms \( \pm 130 \) ms, defined as a time difference between anterior-septum and posterior wall (Figure 3).

An important limitation of this present study is that this was an isolated case report, and further clinical studies are required to confirm this result. However, we previously investigated the acute response to CRT in patients with segmental reversed strain assessed by tissue Doppler strain imaging in 27 HF patients. We showed that EF response to CRT was significantly higher in HF patients with segmental reversed strain than those without segmental reversed strain. Another limitation is the variation of longitudinal tissue Doppler strain. This might have affected the objectiveness of segmental reversed strain.

**Figure 1** (A) The 12-lead electrocardiogram before cardiac resynchronization therapy (CRT), demonstrating a QRS width of 160 ms with a left bundle branch block. (B) Longitudinal dyssynchrony by myocardial velocity before cardiac resynchronization therapy was as follows: 23 ms in Yu index and 35 ms in opposing wall delay, indicating no longitudinal dyssynchrony. AVO, aortic valve opening; AVC, aortic valve closure. Apical four-chamber view: yellow, basal-interior septum; blue, mid-inferior septum; red, basal-lateral; green, mid-lateral. Apical two-chamber view: yellow, basal-anterior; blue, mid-anterior; red, basal-inferior; green, mid-inferior. Apical long-axis view: yellow, basal-anterior septum; blue, mid-anterior septum; red, basal-posterior; green, mid-posterior.
Figure 2  (A) Longitudinal tissue Doppler strain before cardiac resynchronization therapy (CRT). The anterior and inferior septum at basal and mid-levels had reversed strain (becoming positive), indicating paradoxical systolic expansion (white arrow).  (B) Longitudinal tissue Doppler strain the day following cardiac resynchronization therapy. The reversed strain was disappeared. Apical four-chamber view: yellow, basal-interior septum; blue, mid-inferior septum; red, basal-lateral; green, mid-lateral. Apical long-axis view: yellow, basal-anterior septum; blue, mid-anterior septum; red, basal-posterior; green = mid-posterior.

Figure 3  Speckle-tracking radial time strain curves from a mid-left ventricular short-axis image before cardiac resynchronization therapy. Significant dyssynchrony is shown as a time difference (white arrow) between time-to-peak strain in the anterior septum (yellow line) and posterior wall peak strain (purple line) of 380 ms.
In conclusion, the presence of the segmental reversed strain might overcome the limitation of tissue velocity dysynchrony analysis and have a potential to predict a large response to CRT in the assessment of longitudinal dyssynchrony.

Supplementary data
Supplementary data are available at European Journal of Echocardiography online.

References