Incremental value of radial discoordination index for the prediction of response to cardiac resynchronization therapy

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Received 23 March 2012; accepted after revision 6 May 2012; online publish-ahead-of-print 21 June 2012

Aims

Previous studies have identified four baseline characteristics associated with a favourable response to cardiac resynchronization therapy (CRT): female, non-ischaemic aetiology of heart failure, left bundle-branch block (LBBB), and QRS duration ≥ 150 ms. This study evaluated the incremental value of discoordination and dyssynchrony indices over these characteristics for the prediction of the response to CRT.

Methods and results

The speckle-tracking strain analysis was performed in 120 CRT candidates. Patients were divided into subgroups according to the gender (male vs. female), aetiology of heart failure (ischaemic vs. non-ischaemic), QRS morphology (LBBB vs. non-LBBB), and QRS duration (≥ 150 vs. < 150 ms), respectively. Discoordination was measured using the mid-ventricular radial discoordination index (RDI-M), the ratio of the average mid-ventricular thinning to thickening during ejection. Patients with one of the four favourable characteristics were more likely to exhibit other favourable characteristics and had greater amounts of average myocardial thinning during ejection and RDI-M than those without (all P < 0.05). In contrast, dyssynchrony indices failed to demonstrate significant differences between male and female and between ischaemic and non-ischaemic subjects. Of 39 patients who had 6-month follow-up data after CRT, left ventricular reverse remodelling was found in 22 patients (56%). Combining the favourable characteristics and RDI-M provides the best ability to predict reverse remodelling after CRT (area under the curve = 0.85, 95% confidence interval 0.73–0.98, P < 0.001).

Conclusion

Mechanical discoordination rather than mechanical dyssynchrony provides a significant incremental value over the baseline characteristics for the prediction of the response to CRT.

Keywords

Cardiac resynchronization therapy • Discoordination • Dyssynchrony • Echocardiography • Speckle tracking

Introduction

Randomized control trials have demonstrated that cardiac resynchronization therapy (CRT) reduces the morbidity and mortality in patients with advanced heart failure and a wide QRS duration.¹–³ Nevertheless, up to 30% of patients who receive CRT do not benefit from the therapy when selected using current criteria.⁴ ⁵ Previous studies have suggested that, in addition to electrical dyssynchrony, left ventricular (LV) mechanical dyssynchrony (the time delay of a mechanical event) determined by echocardiography can help identify CRT responders.⁵ ⁹ However, the results of the predictors of the response to the CRT trial were disappointing in that no single parameter of mechanical dyssynchrony was able to improve patient selection for CRT beyond the current guidelines.¹⁰

Previous studies have identified four clinical characteristics associated with a favourable response to CRT: female, non-ischaemic aetiology of heart failure, left bundle-branch block (LBBB), and QRS duration ≥ 150 ms⁶–¹⁰. In addition, recent studies have shown that mechanical discoordination (opposite strain within
the left ventricle) may be a better predictor of the response to CRT compared with mechanical dyssynchrony.\textsuperscript{17–20} The aims of this study were to: (i) compare the baseline prevalence of mechanical dyssynchrony and discoordination in CRT candidates with and without favourable characteristics and (ii) evaluate the incremental value of discoordination indices over clinical characteristics for the prediction of the response to CRT compared with dyssynchrony indices.

**Methods**

**Patients**

One-hundred and thirty-six patients with sinus rhythm, LV ejection fraction (EF) ≤ 35%, and QRS duration ≥ 120 ms, who were considered for CRT, were enrolled. Sixteen patients were excluded for technically unsatisfactory images for the speckle-tracking analysis and 120 patients were analysed finally. These patients were divided into subgroups according to their gender (male vs. female), aetiology of heart failure (ischaemic vs. non-ischaemic), QRS morphology (LBBB vs. non-LBBB), and QRS duration (≥ 150 vs. < 150 ms), respectively. Among the 120 patients, the response to CRT was evaluated in 39 patients who had paired echocardiograms at the baseline and 6 months after CRT. The study complies with the Declaration of Helsinki. The study protocol was approved by the local Institutional Review Board. Informed consent was obtained from each participant.

**Echocardiography**

The study protocol included detailed transthoracic echocardiography using a commercially available system (Vivid 7, GE, Horten, Norway). Left ventricular ejection fraction were assessed in the apical two-and-four-chamber views using the biplane Simpson’s rule. Patients with a reduction of ≥15% in the LV end-systolic volume at the 6-month follow-up were defined as CRT responders. Two-dimensional radial strain of the left ventricle was analysed from the parasternal mid-ventricular short-axis view using commercial software (EchoPac version 7.0). The echocardiographic images were recorded with a frame rate of 50–80 Hz. A single beat was analysed for each time and values from three cardiac cycles were averaged to obtain each index. From an end-systolic frame, a region of interest was traced along the endocardial border, and the thickness of the region of interest was adjusted to include the maximal wall thickness.\textsuperscript{21,22} The software automatically tracked the image speckle and produced the radial strain and strain-rate curves in six regional segments. The ejection phase (between aortic valve opening and aortic valve closure) was determined from the Doppler velocity signal at the LV outflow tract. Data of the strain, strain rate, and timing of the ejection phase were exported to a program (MATLAB, MathWorks) to calculate dyssynchrony and discoordination indices.

**CRT procedure**

The pacing leads were positioned at the right ventricular apex or mid-septum, right atrial appendage, and in the posterior or posterolateral branch of the coronary vein. The atrio-ventricular interval was optimized using the established method to ensure adequate LV filling. No adjustments were made to the inter-ventricular interval before the 6-month follow-up.

**Data analysis**

The time to peak radial strain of the mid-LV anteroseptal and posterior walls (AS-P delay) and the standard deviation of the time to peak radial strain over six mid-LV segments (RS-SD) were computed to derive the mechanical dyssynchrony.\textsuperscript{17,21,23} Normal coordinated LV contraction produces myocardial thickening in the radial direction resulting in a positive strain rate signal. During the ejection phase, the disordinated segments become thin in the radial direction resulting in a negative strain rate signal. On the basis, the radial strain rates traces from the six mid-LV segments were divided into positive and negative signals, respectively. The integration of positive and negative strain rate signals over the ejection period resulted in contractile strain ($\varepsilon_c$) and counteracting strain ($\varepsilon_a$), respectively (Figure 1). Contractile strain and counteracting strain represented the amounts of myocardial thickening and thinning during the ejection phase. The mid-ventricular radial discoordination index (RDI-M) was calculated as a ratio of the average myocardial thinning to the average myocardial thickening of six mid-ventricular segments during ejection.\textsuperscript{17,20} Significant discoordination and dyssynchrony were defined using the previously reported cut-off values (the values to predict reverse remodelling are shown in parentheses): RDI-M (38%) and AS-P delay (130 ms) or RS-SD (76 ms).\textsuperscript{20,21,23}

**Statistical analysis**

Data were expressed as mean ± standard deviation for continuous variables and as absolute frequencies and relative percentages for categorical variables. An unpaired t-test was used to assess each paired comparison between patients with and without favourable characteristics. Categorical variables were compared using the $\chi^2$ tests. Person’s correlation coefficient was used to describe the relationship between two variables. Optimal cut-off values with regard to the prediction of reverse remodelling were determined by constructing the receiver operating characteristics (ROC) curves. The statistical significance of the difference between the areas under the ROC curve (AUC) was tested using the method proposed by Hanley and McNeil.\textsuperscript{24} Intra- and inter-observer variability for determining dyssynchrony and discoordination from the identical digital cineloops were assessed in 20 randomly selected patients. For all tests, a value of $P < 0.05$ was considered statistically significant. Statistical analysis was performed using the SPSS version 18.0 (SPSS, Inc., Chicago, IL, USA).

**Results**

Baseline characteristics of the study patients are listed in Table 1. The prevalence of female, an LBBB morphology, QRS ≥ 150 ms, and a non-ischaemic aetiology of heart failure were 41 (34%), 82 (68%), 67 (56%), and 60 (50%), respectively. Patients with one of the four favourable characteristics were more likely to have other favourable characteristics. Females were more likely to have an LBBB than males (90 vs. 57%, $P < 0.001$). Patients with an LBBB had a significantly longer mean QRS duration (163 ± 27 vs. 141 ± 17 ms, $P < 0.001$) and more likely to have a non-ischaemic aetiology than patients with non-LBBB (57 vs. 34%, $P = 0.018$). Patients with QRS ≥ 150 ms were more likely to exhibit an LBBB (84 vs. 49%, $P < 0.001$) and non-ischaemic aetiology than patients with QRS < 150 ms (58 vs. 40%, $P = 0.044$). Patients with non-ischaemic aetiology were younger, had a longer mean QRS duration, and were more likely to have an LBBB (all $P < 0.05$).

Table 2 summarizes discoordination and dysynchrony measures in patients with and without favourable characteristics. Patients with favourable characteristics had greater amounts of
myocardial thinning during ejection and RDI-M than those without (all $P < 0.05$). In contrast, dysynchrony indices failed to demonstrate significant differences between male and female and between ischaemic and non-ischaemic subjects. The prevalence of mechanical dysynchrony or discoordination based on the reported cut-off values is shown in Figure 2. There was a significant difference in any pairwise comparison of the prevalence of mechanical discoordination except between males and females. The prevalence of mechanical dysynchrony based on the AS-P delay $\geq 130$ ms did not differ between males and females ($P = 0.42$), between ischaemic and non-ischaemic aetiologies ($P = 0.85$) and between QRS $< 150$ ms and QRS $\geq 150$ ms ($P = 0.06$). Mechanical dysynchrony based on the RS-SD $\geq 76$ ms failed to demonstrate a significant difference in any pairwise comparison.

There was only weak correlations between the QRS duration and the AS-P delay ($r = 0.22, P = 0.016$) and between the QRS duration and the RDI-M ($r = 0.29, P = 0.001$). As shown in Figure 3, there was a moderate correlation between the RDI-M and the AS-P delay ($r = 0.50, P < 0.001$). Using the RDI-M cut-off of 38% and the AS-P delay cut-off of 130 ms, 33 (28%) patients had discrepant prediction of a favourable response to CRT. Among them, 28 (23%) patients had dysynchrony but no discoordination, and 5 (4%) patients had discoordination but no dysynchrony. In the 28 patients who showed dysynchrony but no discoordination, 19 patients (68%) exhibited the ischaemic aetiology, whereas among the 5 patients with significant discoordination but no dysynchrony, 4 patients (80%) exhibited the non-ischaemic aetiology. Figure 4 shows examples of patients who exhibited discrepant prediction results for a favourable response with mechanical dysynchrony and discoordination. Mechanical dysynchrony without discoordination was likely to occur in ischaemic patients who exhibited minimal opposite deformation during ejection (Figure 4A) or mainly post-systolic deformation (Figure 4B). Mechanical discoordination without dysynchrony could be observed in patients with severely impaired LV function and multi-phasic septal strain signals (Figure 4C).

The differences in regional myocardial thinning, myocardial thickening, and time to the peak strain of patients with ischaemic
Table 1  Baseline characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Gender</th>
<th>QRS morphology</th>
<th>QRS duration</th>
<th>Aetiology of heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Non-LBBB</td>
<td>LBBB</td>
</tr>
<tr>
<td></td>
<td>(n = 79)</td>
<td>(n = 41)</td>
<td>(n = 38)</td>
<td>(n = 82)</td>
</tr>
<tr>
<td>Age, years</td>
<td>68 ± 15</td>
<td>72 ± 10</td>
<td>66 ± 15</td>
<td>70 ± 13</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>0 (0)</td>
<td>41 (100)*</td>
<td>4 (11)</td>
<td>37 (45)**</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>25 ± 6</td>
<td>25 ± 8</td>
<td>26 ± 7</td>
<td>24 ± 7</td>
</tr>
<tr>
<td>NYHA class ≥3, n (%)</td>
<td>51 (65)</td>
<td>31 (76)</td>
<td>24 (63)</td>
<td>58 (63)</td>
</tr>
<tr>
<td>QRS duration, ms</td>
<td>156 ± 28</td>
<td>157 ± 25</td>
<td>141 ± 17</td>
<td>163 ± 27***</td>
</tr>
<tr>
<td>LBBB, n (%)</td>
<td>45 (57)</td>
<td>37 (90)*</td>
<td>0 (0)</td>
<td>82 (100)**</td>
</tr>
<tr>
<td>Ischaemic aetiology, n (%)</td>
<td>44 (56)</td>
<td>16 (39)</td>
<td>25 (66)</td>
<td>35 (43)**</td>
</tr>
</tbody>
</table>

EF, ejection fraction; LBBB, left bundle-branch block; LV, left ventricular; NYHA, New York Heart Association.

*p < 0.05 vs. male gender.
**p < 0.05 vs. non-LBBB.
***p < 0.05 vs. QRS < 150 ms.
****p < 0.05 vs. ischaemic aetiology.

and non-ischaemic aetiologies are summarized in Figure 5. An inhomogeneous pattern in regional myocardial thinning, myocardial thickening, and time to peak strain was observed, particularly in the non-ischaemic patients. The largest amount of myocardial thinning and conversely the smallest amount of myocardial thickening during ejection were mainly found at the early-activated septal and anteroseptal walls, whereas an inverse pattern was observed at the late-activated posterior and lateral walls. Compared with ischaemic patients, the amounts of myocardial thinning during ejection in the non-ischaemic subgroup were significantly greater in septal (P < 0.001), anteroseptal (P < 0.001), and anterior (P = 0.02) segments. The non-ischaemic subgroup also had smaller amounts of myocardial thickening in septal (P = 0.005), anteroseptal (P < 0.001), and anterior (P < 0.001) segments than the ischaemic subgroup. The time to peak strain of six mid-ventricular segments were similar between the ischaemic and non-ischaemic subgroups except the non-ischaemic patients had a shorter time to peak strain at the septal wall (P = 0.02).
Of 39 patients who had follow-up data 6 months after CRT, reverse remodelling was found in 22 patients (56%) (Table 3). There were no significant differences in age, gender, QRS duration, QRS morphology, New York Heart Association functional class, number of favourable characteristics, LV EF, and medications between responders and non-responders. Responders were more likely to exhibit non-ischaemic aetiology (86 vs. 47%, $P = 0.007$). The amounts of average myocardial thinning during ejection and RDI-M at the baseline were significantly greater in responders than in non-responders (6.6 ± 2.5 vs. 2.4 ± 2.9%, $P < 0.001$ for myocardial thinning; 67.9 ± 28.1 vs. 29.0 ± 28.9%, $P < 0.001$ for the RDI-M). No significant differences in dysynchrony indices were found between responders and non-responders (246 ± 112 vs. 193 ± 145 ms, $P = 0.20$ for the AS-P delay; 154 ± 55 vs. 129 ± 73 ms, $P = 0.24$). Baseline RDI-M ≥38% was able to predict reverse remodelling (sensitivity 96%, specificity 83%, AUC = 0.86, 95% CI: 0.74–1.0, $P < 0.001$). In contrast, the AS-P delay and favourable characteristics failed to predict reverse remodelling (AUC = 0.62, 95% CI: 0.42–0.8, $P = 0.22$ for the AS-P delay; AUC = 0.65, 95% CI: 0.48–0.83, $P = 0.11$ for favourable characteristics) (Figure 6A).

The ROC curves were generated to determine the predictive values of favourable characteristics alone (model 1), favourable characteristics combined with the presence of mechanical dysynchrony (model 2), and favourable characteristics combined with the presence of mechanical discoordination (model 3) with respect to reverse remodelling. As shown in Figure 6B, the presence of mechanical dysynchrony provides an incremental value over the favourable characteristics alone ($P = 0.034$ for model 1 vs. model 2). Favourable characteristics combined with the RDI-M (with ≥38% used as a cut-off value) provided the best ability to predict reverse remodelling (AUC = 0.85, 95% confidence interval 0.73–0.98, $P < 0.001$ vs. model 1, $P = 0.017$ vs. model 2).

As seen in Supplementary data online, Table, reproducibility was excellent for the RDI-M, AS-P delay, and RS-SD (intra-class correlations for intra-observer variability were 0.99, 0.95, and 0.94, respectively, and for inter-observer variability were 0.99, 0.89, and 0.87, respectively). Inter- and intra-observer variability of the RDI-M, AS-P delay, and RS-SD were similar.
**Discussion**

This study demonstrates that mechanical discoordination performed better than mechanical dyssynchrony in differentiating between patients with and without favourable characteristics for the CRT response and between responders and non-responders. CRT candidates with one of the four favourable characteristics including female, LBBB, QRS duration ≥ 150 ms, or non-ischaemic aetiology were more likely to have other favourable characteristics and to show mechanical discoordination than those without. Combining the favourable characteristics and RDI-M provides the best ability to predict reverse remodelling. These findings support the hypothesis that the RDI-M rather than pure time-delay measures specifically reflects the substrate amenable to CRT and thus may serve as a better tool for improving patient selection for CRT beyond the current guidelines.

The use of temporal delay in CRT has several limitations, regardless of which technique is used to derive a dyssynchrony index. First, many dyssynchrony indices rely on the identification of the peak value of regional motion or deformation for the analysis, which is not reliable in CRT candidates since the dysynchronous failureing heart, as opposed to the normal heart, often displays a complex and multi-phasic signal of motion or deformation. Compared with tissue Doppler velocity, speckle-tracking strain provides a more reliable assessment of dyssynchrony because the strain signal contains fewer peaks and is less noisy. However, in the present study, minimal or opposite-only strain was usually observed in akinetic or dyskinetic segments and multi-phasic signals were often found in the early-activated segments. Thus, the occurrence of minimal, multi-phasic, or opposite-only strain signal made it difficult to define peak mechanical events. Secondly, delayed contraction with a late peak of strain is not confined to delayed activation, but can also occur as a consequence of myocardial ischaemia or increased afterload. It is therefore difficult to distinguish these abnormalities from delayed activation using pure time-delay indices, particularly in ischaemic patients.

As opposed to pure time-delay indices, the RDI-M incorporates the information of the phase and strain amplitude. The rationale to use the RDI-M is that out-of-phase deformation in the early-activated segments reduces cardiac efficiency since part of the mechanical energy is wasted into internal work, instead of stroke work. This out-of-phase deformation depends on local elasticity as well as contractility; therefore the RDI-M indirectly reflects myocardial viability and contractility. It is interesting to note that CRT candidates with an ischaemic aetiology were more likely to show dyssynchrony without discoordination compared with non-ischaemic patients, and this can be classified into two patterns (Figures 4A and B). First, the early-activated segments were infarcted earlier and developed a minute amount of disordinated thinning during ejection. Considering only the time delay...
neglects the importance of the regional viability and contractility. Thus, although equal time delays between segments with different viability or contractility will result in the same dyssynchrony index, it is unreasonable to assume that they have a similar mechanical impact. Secondly, delayed contraction with a late peak of strain occurred in some segments while the timings of the peak strain in the other segments were close to the end-systole. Dyssynchrony analysis might characterize these patients as responders due to the presence of a significant time delay between segments, whereas discoordination analysis would reveal a lack of substrate amenable to CRT. On the other hand, discoordination without dyssynchrony could be observed in patients with severely impaired LV function

Figure 5 Regional distribution patterns of myocardial thinning during ejection (A), myocardial thickening during ejection (B), and time to peak strain (C) in CRT candidates with ischaemic and non-ischaemic aetiologies, respectively. The distribution patterns of myocardial thinning and thickening was highly polarized between the early- and late-activated segments especially in patients with a non-ischaemic aetiology. The time to peak strain of six mid-ventricular segments was similar between the ischaemic and non-ischaemic subgroups, except that non-ischaemic patients had a shorter time to peak strain at the septal wall.
The mechanical discoordination may have two origins: asynchrony of electrical activation and/or disparity in regional contractility as a result of ischaemia or infarction.30 The infarcted myocardium forms a scar, which is less compliant than the viable myocardium and therefore stretches less during ejection if it is early activated. The scar tissue cannot be recruited by CRT and myocardium forms a scar, which is less compliant than the viable myocardium and therefore stretches less during ejection if it is early activated.

Detailed evaluation of discoordinated deformation for the prediction of the response to CRT can be quantified by means of the RDI-M, systolic rebound stretch, or strain delay index.17–20,31,32 The systolic rebound stretch specifically measures the amounts of systolic stretching that occur after premature shortening by means of longitudinal strain analysis. De Boeck et al.19 found that the systolic rebound stretch was converted into additional shortening after CRT and that the majority of systolic rebound stretch and functional improvements occurred in the early-activated septum. Septal and total systolic rebound stretch were found to perform equally well in the prediction of reverse remodelling.15 In the present study also, the main part of the discoordinated thinning during ejection was observed in the septal walls and the amounts of septal and average myocardial thinning during ejection were significantly greater in non-ischaemic patients than in ischaemic patients. Further studies are needed to evaluate whether the discoordinated thinning during ejection will convert into additional thickening similarly to systolic rebound stretch, and whether septal or average thinning during ejection is useful in the evaluation of patients undergoing CRT. As opposed to systolic rebound stretch, which selectively measures systolic stretching, the strain delay index calculates the sum of differences between the peak and end-systolic strain and represents the wasted energy due to systolic stretching in the early-activated segments and post-systolic thinning in the late-activated segments.31,32 Lim et al. demonstrated that the baseline strain delay index was closely correlated with reverse remodelling in both

### Table 3  Comparisons between responders and non-responders

| Age (years) | 72 ± 9 | 73 ± 8 | 70 ± 11 |
| Female, n (%) | 22 (56) | 13 (59) | 9 (53) |
| Ischaemic aetiology, n (%) | 12 (31) | 3 (14) | 9 (53)* |
| QRS duration, ms | 161 ± 20 | 164 ± 26 | 159 ± 17 |
| Left bundle-branch block, n (%) | 39 (100) | 22 (100) | 17 (100) |
| Number of favourable characteristics | 3.0 ± 0.9 | 3.2 ± 0.8 | 2.7 ± 1.0 |
| NYHA class | 3.5 ± 0.4 | 3.5 ± 0.4 | 3.4 ± 0.3 |
| LV EF, % | 22 ± 7 | 23 ± 7 | 21 ± 7 |
| Average thinning, % | 4.8 ± 3.3 | 6.6 ± 2.5 | 2.4 ± 2.9*
| RDI-M, % | 50.3 ± 34.6 | 67.9 ± 28.1 | 29.0 ± 28.9*
| AS-P delay, ms | 223 ± 129 | 246 ± 112 | 193 ± 145 |
| RS-SD, ms | 143 ± 64 | 154 ± 55 | 129 ± 73 |
| Medications (%) | | | |
| ACEI or ARB | 33 (85) | 19 (86) | 14 (82) |
| Beta-blocker | 33 (85) | 18 (82) | 15 (88) |
| Spironolactone | 15 (38) | 9 (41) | 6 (35) |
| Loop diuretics | 34 (87) | 18 (82) | 16 (94) |

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; AS-P delay, antero-septal to posterior wall delay; LV EF, left ventricular ejection fraction; NYHA, New York Heart Association; RDI-M, mid-ventricular radial discoordination index; RS-SD, standard deviation of times to peak radial strain.

*P < 0.05 vs. responders.

and multi-phasic strain signals, as illustrated in Figure 4C. Peak strain was abnormally low in all segments, reflecting their underlying severe dysfunction. The presence of a multi-phasic peak and out-of-phase myocardial thinning in the early-activated segments and a minute amount of myocardial thickening in the late-activated segments resulted in discoordination without dyssynchrony.

The mechanical discoordination may have two origins: asynchrony of electrical activation and/or disparity in regional contractility as a result of ischaemia or infarction.30 The infarcted myocardium forms a scar, which is less compliant than the viable myocardium and therefore stretches less during ejection if it is early activated. The scar tissue cannot be recruited by CRT and does not contribute much to the discoordination value. It may explain why patients with an ischaemic aetiology had lower values of mechanical discoordination is concordant with two previous studies.18,20 In a study using magnetic resonance imaging, circumferential discoordination was calculated as the internal stretch fraction, defined as the ratio of stretch to shortening during ejection if it is early activated. They found that patients with non-ischaemic cardiomyopathy had a higher internal stretch fraction and were more likely to show reverse remodelling than those with ischaemic cardiomyopathy.18 In a multivariate analysis for the prediction of all-cause mortality after CRT, lack of mechanical discoordination (RDI-M < 38%) was often observed in patients with ischaemic cardiomyopathy and was independently associated with a worse outcome after adjusting ischaemic aetiology.20 Ischaemic aetiology was a significant predictor of mortality in univariate analysis, but was not associated with an increased risk of mortality when the RDI-M was included in the multivariate analysis.20

Detailed evaluation of discoordinated deformation for the prediction of the response to CRT can be quantified by means of the RDI-M, systolic rebound stretch, or strain delay index.17–20,31,32 The systolic rebound stretch specifically measures the amounts of systolic stretching that occurs after premature shortening by means of longitudinal strain analysis. De Boeck et al.19 found that the systolic rebound stretch was converted into additional shortening after CRT and that the majority of systolic rebound stretch and functional improvements occurred in the early-activated septum. Septal and total systolic rebound stretch were found to perform equally well in the prediction of reverse remodelling.15 In the present study also, the main part of the discoordinated thinning during ejection was observed in the septal walls and the amounts of septal and average myocardial thinning during ejection were significantly greater in non-ischaemic patients than in ischaemic patients. Further studies are needed to evaluate whether the discoordinated thinning during ejection will convert into additional thickening similarly to systolic rebound stretch, and whether septal or average thinning during ejection is useful in the evaluation of patients undergoing CRT. As opposed to systolic rebound stretch, which selectively measures systolic stretching, the strain delay index calculates the sum of differences between the peak and end-systolic strain and represents the wasted energy due to systolic stretching in the early-activated segments and post-systolic thinning in the late-activated segments.31,32 Lim et al. demonstrated that the baseline strain delay index was closely correlated with reverse remodelling in both
In the present study, patients with an ischaemic aetiology were more likely to show mechanical dyssynchrony without discoordination than non-ischaemic patients. This may be due to the fact that post-systolic deformation is not specific to asynchronous activation and could decrease the predictive power of dyssynchrony indices for the CRT response. Further studies are needed to evaluate whether the non-specific post-systolic deformation will influence the predictive value of the strain delay index, particularly in ischaemic patients.

The measurements of the RDI are still technically challenging, and have not been implemented in any commercially available software from a practical point of view. However, it is easy to identify significant discoordination by using the colour m-mode of the radial strain rate. The premature termination of septal contraction and discoordinated septal thinning during the ejection phase can be easily identified in a patient with reverse remodelling after CRT. The area coloured blue during the ejection period correlates with the amount of discoordination.

Although mechanical discoordination can be quantified from three deformation types, only the radial deformation was selected for the calculation of mechanical discoordination and dyssynchrony. In previous studies using speckle-tracking strain to identify potential responders to CRT, the radial strain constitutes the best method among the three types of deformation. Moreover, radial discoordination (myocardial thinning during ejection) reflects the combined effect of circumferential and longitudinal discoordination (myocardial stretching during ejection). As a result, the evaluation of LV discoordination by radial deformation may provide more information in a single assessment than longitudinal and circumferential deformation could provide individually. Although our study revealed that the discoordination indices performed significantly better than the dyssynchrony indices in the prediction of the response to CRT, only a small proportion of our study population received CRT implantation. Large studies are needed to confirm the incremental value of the RDI-M over clinical characteristics for the prediction of the response to CRT.

In conclusion, mechanical discoordination performs better than mechanical dyssynchrony in differentiating between CRT candidates with and without favourable characteristics. The high response rate seen in female and non-ischaemic patients could be explained by the RDI-M, but not by the dyssynchrony indices. In addition, the RDI-M provides significant incremental value over the favourable characteristics for the identification of CRT responders.

**Supplementary data**

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

**Funding**

This study was supported by grants CMRPG 370101 and CMRPG 3A0961 from the Chang Gung Memorial Hospital, Linkou, Taiwan.

**Conflict of interest:** none declared.

**References**


