Strain Rate Dispersion Index Can Predict Changes in Left Ventricular Volume and Adverse Cardiac Events Following Cardiac Resynchronization Therapy

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Background: We previously reported that the strain rate dispersion index (SRDI), an index of left ventricular (LV) contractility loss because of mechanical dyssynchrony, better predicted the acute response to cardiac resynchronization therapy (CRT) than time-delay indices. However, it remains unclear whether the SRDI can predict the chronic response. Additionally, the SRDI needs to be simplified for use in clinical practice.

Methods and Results: Echocardiography was performed in 40 heart failure patients who underwent CRT. The SRDI, the average of segmental peak systolic strain rates minus global peak systolic strain rate, was calculated, together with strain-derived time-delay indices (St-SD) in the longitudinal, circumferential and radial directions using a speckle-tracking method. As simplified indices, the longitudinal parameters were calculated from the apical 4-chamber view in addition to 3 apical views. LV end-systolic volume (ESV) significantly decreased 6 months after CRT. Although circumferential St-SD and all SRDIs correlated with the changes in ESV (ΔESV), multivariate analysis revealed that the circumferential SRDI was the single independent determinant of ΔESV. During the 20±14 months after CRT, cardiac events occurred in 14 patients. Kaplan-Meier analyses revealed that all SRDIs were significant predictors of cardiac events whereas none of St-SDs was.

Conclusions: The SRDI predicted the reduction in both LV volume and cardiac events after CRT better than time-delay indices. Additionally, a simplified SRDI could be as good a predictor of CRT response as the original. (Circ J 2013; 77: 2757–2765)

Key Words: Cardiac resynchronization therapy; Echocardiography; Heart failure; Left ventricular dyssynchrony
events after CRT remains to be elucidated. Additionally, although the SRDI can be calculated more easily than other indices of the amount of discoordination, its calculation from 3 apical views still remains somewhat complex and needs to be simplified in order to be used in routine clinical practice. The aims of this study were thus to determine whether the SRDI could predict the efficacy of CRT in chronic phase and whether a simplified SRDI obtained from a single apical view could be a useful alternative to the original.

**Methods**

**Study Subjects and Protocol**

We enrolled 54 consecutive HF patients who underwent implantation of a CRT device in Hokkaido University Hospital between May 2008 and July 2011. The criteria for CRT were essentially as follows: (1) symptomatic HF (New York Heart Association [NYHA] functional class III or IV), (2) depressed LV systolic function defined as LV ejection fraction (EF) \( \leq 35\% \), and (3) prolonged QRS duration \( \geq 120 \text{ ms} \). However, criterion 1 was extended to include NYHA class II on the basis of results of recent clinical trials. We excluded 10 patients with inadequate quality of echocardiographic images and 1 patient who underwent CRT immediately after cardiac valve surgery; 3 were lost to follow-up within 6 months after CRT. Accordingly, the study group consisted of 40 patients.

Transthoracic echocardiography, including tissue Doppler imaging (TDI) and 2-dimensional speckle-tracking method (2DST), were performed before and 2 weeks after the implantation of CRT device. Echocardiography was repeated 6 months after CRT to measure LV volumes. Responders in LV volumes to CRT were defined as having a reduction in LV end-systolic volume (ESV) \( \geq 15\% \) after 6 months. Cardiac events, including cardiac death and hospitalization for worsening HF, were recorded for 30±13 (range, 9–50) months after CRT. The study protocol was approved by Ethics Committee of the Hokkaido University, and all patients gave informed consent to participate in this study.

**Echocardiography**

All studies were performed with commercially available ultrasound systems (Aplio XG SSA-790A or Aplio Artida SSH 880CV, Toshiba Medical Systems, Tochigi, Japan). Digital 2D and color TDI cine-loops were obtained in the apical 4-chamber, 2-chamber, and long-axis views, and midventricular short-axis view. Care was taken to acquire the cine-loops that had close intervals of R to R wave for analysis of 2DST and TDI in patients with atrial fibrillation (AF). The frame rates were 53\( \pm 7\) s\(^{-1}\) for 2D imaging used for 2DST, and 58\( \pm 5\) s\(^{-1}\) for TDI.

LV end-diastolic and ESVs were measured from the apical 4- and 2-chamber images using the biplane method of disks, and the LVEF was calculated. In patients with AF, the LV volumes were measured over 5 consecutive beats, and the values were averaged.

**TDI Analysis**

The analysis of color TDI was performed using commercial software (Toshiba Medical Systems). Longitudinal tissue velocities of the LV wall were measured in the basal and mid segments in 3 apical views for a total of 12 segments. Time from the onset of QRS to peak systolic velocity during the ejection phase, which was determined by LV outflow Doppler imaging, was measured in each segment. The standard deviation of time to peak systolic velocity (TDI-SD) was then calculated within the 12 segments.\(^5\)

**Speckle-Tracking Analysis**

Myocardial strain and the strain rate (SR) were analyzed using 2DST software (Toshiba Medical Systems). The LV endocardial and epicardial borders were manually traced on an end-diastolic frame for the apical views and on an endsystolic frame for the midventricular short-axis view. The LV wall was divided and segmented into 16 segments. The segmentation was performed automatically by the software. Strain was defined as the fractional change in length or area, and strain rate was defined as the time derivative of strain. Strain and strain rate were calculated for each segment and averaged across all segments. The strain rate dispersion index (SRDI) was calculated by subtracting global peak systolic SR (white arrow) from the average of the 6 segmental peak systolic SRs (red arrow).

**Figure 1.** Demonstrable circumferential strain rate (SR) curves (Right) obtained from 6 segments in the midventricular short-axis view (Left). The 6 colored curves indicate segmental SRs and the white curve indicates global SR. The strain rate dispersion index (SRDI) was calculated by subtracting global peak systolic SR (white arrow) from the average of the 6 segmental peak systolic SRs (red arrow).
Figure 2. (A) Time-longitudinal strain rate (SR) curves (middle line) and corresponding images (left line). Upper panels show those obtained from apical 4-chamber view, middle panels from 2-chamber view, and lower panels from apical 3-chamber view. Right graph shows the time-global longitudinal SR curve obtained by averaging 18 segmental SRs. (B) Time-circumferential SR curves (right upper graph) and time-radial SR curves (right lower graph) obtained from midventricular short-axis images (left panels). L-SRDI, longitudinal strain rate dispersion index; L-SRDI_{4CV}, L-SRDI obtained from apical 4-chamber view; C-SRDI, circumferential strain rate dispersion index; R-SRDI, radial strain rate dispersion index.
Continuous variables are expressed as mean ± SD and compared using the 2-tailed Student’s t test for paired and unpaired data. Proportions were compared using chi-square analysis. Linear regression analysis was carried out to detect correlations between 2 continuous variables. Multiple linear regression analysis was used to identify the independent predictors of the reduction in LVESV after CRT. Receiver operating characteristic analyses were used to determine optimal cutoff values of continuous variables. The best cutoff value was defined as the point with the highest sum of sensitivity and specificity. Freedom from cardiac events was evaluated using Kaplan-Meier analysis, and the cumulative event rates were compared by log-rank test. For all tests, P < 0.05 was considered significant.

Results

Patients’ Baseline Characteristics

The baseline characteristics of the 40 study patients are summarized in Table 1. The mean age was 62 ± 12 years and males comprised 80% of the group. Ischemic etiology was 20% in total. QRS duration was 164 ± 27 ms with left bundle branch block in 48% and right ventricular pacing was performed in 25% of the patients. Mean LVEF was 28 ± 7%. Optimal medical therapy for HF had been administered, including angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, β-blocker, diuretics, and spironolactone.

Relationship Between Echocardiographic Indices and Reduction in LV Volume

Of the 40 patients, 2 died and 1 underwent LV reconstruction surgery within 6 months after CRT. Among the remaining 37 patients, the QRS duration shortened from 164 ± 27 to 145 ± 26 ms (P = 0.0006), LVEDV decreased from 211 ± 99 to 185 ± 106 ml (P = 0.002), LVESV decreased from 156 ± 88 to 131 ± 87 ml.

Table 1. Baseline Characteristics of the Study Patients

| Age (years) | All (n=40) | Responders (n=18) | Nonresponders (n=19) | P value |
|------------|-----------|-------------------|----------------------|--------|
| 62±12      | 59±14     | 65±11             |                      | 0.13   |
| Male, n (%)| 32 (80)   | 16 (89)           | 15 (79)              | 0.41   |
| NYHA class, n (%) |       |                   |                      |        |
| II         | 7 (18)    | 6 (33)            | 1 (5)                | 0.011  |
| III        | 29 (73)   | 9 (50)            | 17 (89)              |        |
| IV         | 4 (10)    | 3 (17)            | 1 (5)                |        |
| Ischemic cardiomyopathy, n (%) | 8 (20) | 2 (11)            | 6 (32)               | 0.12   |
| Atrial fibrillation, n (%) | 7 (18) | 3 (17)            | 4 (21)               | 0.73   |
| QRS duration (ms) | 164±27 | 171±27            | 157±28               | 0.15   |
| Left bundle branch block, n (%) | 19 (48) | 10 (56)           | 8 (42)               | 0.41   |
| Right ventricular pacing, n (%) | 10 (25) | 6 (33)            | 2 (11)               | 0.09   |
| LV end-diastolic volume (ml) | 211±99 | 211±125           | 216±77               | 0.91   |
| LV endsystolic volume (ml) | 156±88 | 158±115           | 157±63               | 0.97   |
| LV ejection fraction (%) | 28±7  | 28±7              | 28±7                 | 0.92   |
| Severe MR, n (%) | 15 (38) | 5 (28)            | 8 (42)               | 0.36   |
| Medication, n (%) |       |                   |                      |        |
| ACEI or ARB | 34 (85) | 15 (83)           | 16 (84)              | 0.94   |
| β-blocker   | 32 (80)   | 14 (78)           | 15 (79)              | 0.93   |
| Diuretic    | 38 (95)   | 16 (89)           | 19 (100)             | 0.083  |
| Spironolactone | 24 (60) | 7 (39)            | 15 (79)              | 0.012  |
| Amiodarone  | 20 (50)   | 9 (50)            | 8 (42)               | 0.63   |

Follow-up echocardiographic data could not be obtained for 3 of 40 patients: 2 patients died; 1 patient underwent cardiac surgery within 6 months after CRT. P values are for comparison between responders and nonresponders. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; LV, left ventricular; MR, mitral regurgitation; NYHA, New York Heart Association.
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Prediction of Response to CRT

Table 2. Echocardiographic Time-Delay Indices and SRDI Before and 2 Weeks After CRT in Volume Responders and Nonresponders

|                        | Responders | Nonresponders | P value |
|------------------------|------------|---------------|---------|
|                        | Before CRT | After CRT     |         |
| TDI-SD (ms)            | 50±12      | 39±11†        |         |
| LS-SD (ms)             | 142±44     | 93±35†        |         |
| LS-SD<sub>4ch</sub> (ms)| 152±64     | 90±32†        |         |
| L-SRDI (%)             | 0.28±0.16  | 0.14±0.08†    |         |
| CS-SD (ms)             | 118±60     | 69±42†        |         |
| C-SRDI (s–1)           | 0.23±0.15  | 0.11±0.08†    |         |
| RS-SD (ms)             | 150±55     | 81±42†        |         |
| R-SRDI (s–1)           | 0.46±0.24  | 0.26±0.16*    |         |

P values are for comparison between responders and nonresponders before CRT. *P<0.05 vs before CRT, †P<0.01 vs before CRT.

C, cardiac; CRT, cardiac resynchronization therapy; TDI-SD, standard deviation of time to segmental peak velocities by tissue Doppler imaging; LS-SD, standard deviation of time to segmental peak longitudinal strain; LS-SD<sub>4ch</sub>, LS-SD obtained from apical 4-chamber view; L-SRDI, longitudinal strain rate dispersion index; CS-SD, standard deviation of time to segmental peak circumferential strain; C-SRDI, circumferential strain rate dispersion index; RS-SD, standard deviation of time to segmental peak radial strain; R-SRDI, radial strain rate dispersion index.

Table 3. Univariate and Multivariate Predictors for Reduction in LVESV by CRT

|                        | Univariate | Multivariate |
|------------------------|------------|--------------|
|                        | R          | P value      | β          | P value      | β          | P value      |
| QRS duration           | 0.25       | 0.15         |            |              |
| TDI-SD                 | 0.32       | 0.028        | 0.19       | 0.138        | 0.19       | 0.138        |
| LS-SD                  | 0.22       | 0.18         |            |              |
| LS-SD<sub>4ch</sub>    | 0.30       | 0.07         |            |              |
| L-SRDI                 | 0.45       | 0.006        | 0.08       | 0.591        |            |              |
| L-SRDI<sub>4ch</sub>   | 0.44       | 0.006        | 0.12       | 0.402        |            |              |
| CS-SD                  | 0.41       | 0.007        | 0.18       | 0.185        | 0.18       | 0.185        |
| C-SRDI                 | 0.69       | <0.0001      | 0.69       | <0.0001      | 0.69       | <0.0001      |
| RS-SD                  | 0.09       | 0.57         |            |              |
| R-SRDI                 | 0.32       | 0.046        | -0.07      | 0.495        | -0.07      | 0.495        |

L-SRDI and L-SRDI<sub>4ch</sub> were respectively investigated for the multivariate analysis because they were closely interrelated. LVESV, left ventricular endsystolic volume. Other abbreviations as in Table 2.

(P=0.0005), and LVEF increased from 28±7 to 33±10% (P=0.0002) after CRT.

Of the 37 patients, 18 (49%) were classified as responders in LV volume, defined as a decrease in LVESV after CRT (ΔESV) ≥15%, and the remaining 19 patients (51%) as nonresponders (Table 1). As expected, responders showed a significant decrease in LVESV from 158±115 to 102±96 ml (P<0.0001) and an increase in LVEF from 28±7 to 38±11% (P<0.0001). In contrast, nonresponders showed no change in LVESV (157±63 to 159±71 ml, P=0.80) or LVEF (28±7 to 28±6%, P=0.69). Baseline clinical and echocardiographic parameters were comparable between responders and nonresponders except for the distribution of NYHA class and the use of spironoractone (Table 1). QRS duration at baseline tended to be longer in responders than in nonresponders (171±27 vs 157±28 ms, P=0.15).

Comparisons of time-delay indices and the SRDIs between responders and nonresponders are shown in Table 2. All of these indices, except for RS-SD and R-SRDI, were greater in responders than in nonresponders. All St-SDs and SRDIs significantly decreased 2 weeks after CRT in responders, suggesting that resynchronization could be brought by CRT. In contrast, they did not change after CRT in nonresponders except for a slight decrease in TDI-SD, L-SRDI<sub>4ch</sub>, C-SRDI, and RS-SD. Linear regression analyses between time-delay indices or SRDIs and ΔESV are shown in Table 3. The TDI-SD significantly correlated with ΔESV. For the longitudinal and radial indices, all of the SRDIs significantly correlated with ΔESV whereas the St-SDs did not. For the circumferential indices, both CS-SD and C-SRDI correlated with ΔESV. Multivariate analysis revealed that C-SRDI was the single independent determinant of ΔESV (Table 3).

Prediction of Long-Term Cardiac Events After CRT

The follow-up period was 20±14 (3–48) months. A shorter follow-up period was associated with the occurrence of cardiac events. During the follow-up period, 14 cardiac events occurred: 2 patients died from cardiac causes, and 12 patients were hospitalized for worsening HF. Baseline clinical and echocardiographic parameters were compared between patients with and without cardiac events (Table 4). All demographic and clinical parameters, including the prevalence of ischemic etiology and that of AF, were similar between groups. Echocardiographic LV volumes and EFs were also comparable. Echocardiographic
time-delay indices and SRDIs were compared between patients with and without cardiac events (Table 5). All SRDIs before CRT were significantly greater in patients without cardiac events than in those with events. In contrast, all of the time-delay indices were comparable between the groups. Patients with cardiac events showed a significant decrease in St-SDs and SRDIs after CRT whereas those with cardiac events did not, except for a slight decrease in LS-SD (122±45 to 91±34 ms, P=0.09) and a significant decrease in RS-SD. According to the Kaplan-Meier analysis, the event rate in responders in LV volume was significantly lower than in non-responders (Figure 3A). Regarding the longitudinal indices, patients with low L-SRDI experienced more cardiac events than those with high L-SRDI (Figure 3D). In contrast, the absence of a high TDI-SD or LS-SD was not predictive of cardiac events (Figures 3B, C). Similar trends were observed for both the circumferential indices (CS-SRDI: cutoff value 107.4 ms, P=0.05; C-SRDI: cutoff value 0.11 s⁻¹, P=0.0037) and radial indices (RS-SRDI: cutoff value 116.0 ms, P=0.32; R-SRDI: cutoff value 0.43 s⁻¹, P=0.026) (Figures 3E–H). Additionally, L-SRDI could also separate the patients with and without cardiac events as well as the L-SRDI obtained from 3 apical views, whereas LS-SD could not (LS-SD: cutoff value 155.5 ms, P=0.147; L-SRDI: cutoff value 0.14 s⁻¹, P=0.0004) (Figures 3I, J).

Reproducibility
We randomly selected 10 patients for the reproducibility analysis of the SRDI; 2 independent observers analyzed the same 2D cine-loops and 1 blinded observer repeated the analysis after an interval of 2 weeks. Bland-Altman plots for the St-SDs and SRDIs are shown in Figure S1. Respective intra- and interobserver interclass correlation coefficients were 0.98 and 0.94 for LS-SD, 0.98 and 0.94 for LS-SD 4CV, 0.86 and 0.81 for CS-SD, 0.76 and 0.77 for RS-SD, 0.96 and 0.94 for L-SRDI, 0.96 and 0.97 for L-SRDI 4CV, 0.97 and 0.96 for C-SRDI, and 0.91 and 0.84 for R-SRDI. The intra- and interobserver coefficients of variants were, respectively, 4.7% and 11.4% for LS-SD, 4.3% and 11.5% for LS-SD 4CV, 12.5% and 13.9% for CS-SD, 14.3% and 17.0% for RS-SD, 9.8% and 10.7% for L-SRDI, 9.6% and 9.8% for L-SRDI 4CV, 9.2% and 10.3% for C-SRDI, and 12.5% and 15.9% for R-SRDI.

Discussion
The findings of the current study can be summarized as follows: (1) a reduction in LV volume was better related to the SRDI than to the time-delay indices, (2) a low SRDI was an important risk factor for cardiac events after CRT, (3) longitudinal SRDI remained a useful marker of CRT response even if obtained from a single view. CRT is beneficial for HF patients with severe LV dysfunction and wide QRS duration. However, more than 30% of patients selected on the basis of QRS duration on surface ECG fail to obtain substantial benefit, suggesting that mechanical dys-

Table 4. Baseline Clinical and Echocardiographic Parameters of Patients With and Without Cardiac Events After CRT

|                      | No cardiac events (n=26) | Cardiac events (n=14) | P value |
|----------------------|-------------------------|-----------------------|---------|
| Age (years)          | 64±12                   | 59±13                 | 0.26    |
| Male, n (%)          | 21 (81)                 | 11 (79)               | 0.87    |
| NYHA class           | 2.9±0.5                 | 3.1±0.5               | 0.23    |
| Ischemic cardiomyopathy, n (%) | 6 (23) | 2 (14) | 0.50 |
| Atrial fibrillation, n (%) | 6 (23) | 2 (14) | 0.50 |
| QRS duration (ms)    | 169±29                  | 154±21                | 0.10    |
| Left bundle branch block, n (%) | 14 (54) | 5 (36) | 0.27 |
| Right ventricular pacing, n (%) | 7 (27) | 3 (21) | 0.70 |
| LV end-diastolic volume (ml) | 202±108 | 227±79 | 0.46  |
| LV endsystolic volume (ml) | 148±97 | 169±70 | 0.47  |
| LV ejection fraction (%) | 29±7    | 27±7     | 0.41    |
| Severe MR, n (%)      | 9 (35)                  | 6 (43)                | 0.61    |

P values are for comparison between cardiac events and no cardiac events. Abbreviations as in Table 1.

Table 5. Echocardiographic Time-Delay Indices and the SRDI Before and 2 Weeks After CRT in Patients With and Without Cardiac Events After CRT

|                      | No cardiac events | Cardiac events | P value |
|----------------------|-------------------|----------------|---------|
| TDI-SD (ms)          | 44±13             | 35±11†         | 0.27    |
| LS-SD (ms)           | 122±56            | 91±34†         | 0.29    |
| LS-SD 4CV (ms)       | 127±56            | 105±61         | 0.28    |
| L-SRDI (%)           | 0.24±0.15         | 0.15±0.10      | 0.037   |
| L-SRDI 4CV (%)       | 0.25±0.21         | 0.15±0.09      | 0.035   |
| CS-SD (ms)           | 112±60            | 79±50          | 0.087   |
| C-SRDI (s⁻¹)         | 0.20±0.14         | 0.11±0.07      | 0.019   |
| RS-SD (ms)           | 148±56            | 142±80         | 0.75    |
| R-SRDI (s⁻¹)         | 0.45±0.24         | 0.29±0.14      | 0.028   |

P values are for comparison between cardiac events and no cardiac events before CRT. *P<0.05 vs before CRT, †P<0.01 vs before CRT, ‡P<0.001 vs before CRT. Abbreviations as in Table 2.
improves global LV contractility through correcting the heterogeneity of myocardial shortening. Kirn et al demonstrated that the internal stretch fraction, an index of discoordination evaluated by magnetic resonance imaging, could better predict LV reverse remodeling after CRT than the time-delay indices. Lim et al also reported that the strain delay index, an index of wasted energy caused by dyssynchrony, predicted LV reverse remodeling by CRT better than the time-delay indices. The present results are consistent with these previous reports.

The concept of the SRDI is based on the following hypothesis. If LV contraction was synchronized, global LV systolic function will theoretically be equal to the average of segmental systolic function. Therefore, the average of the segmental peak SR, one part of the SRDI, represents the global LV systolic function when contraction is synchronized, whereas synchrony can better predict the response to CRT than electrical dyssynchrony. Nevertheless, in the Predictors of Responders to CRT (PROSPECT) trial, a multicenter study conducted to determine predictors of a response to CRT, the echocardiographic time-delay indices could not accurately predict a good result. One of the reasons is that the effects of CRT are related not only to mechanical dyssynchrony but also other factors such as myocardial scar burden or residual contractility. In the presence of conduction disturbance, asynchronous electrical activation causes dispersion of myocardial shortening and external work, resulting in a deterioration in LV global systolic function. Discoordination of contraction, which means the loss of LV systolic function caused by dyssynchrony, is more directly associated with improvement in LV systolic function by CRT than mechanical dyssynchrony itself because CRT improves global LV contractility through correcting the heterogeneity of myocardial shortening. Kim et al demonstrated that the internal stretch fraction, an index of discoordination evaluated by magnetic resonance imaging, could better predict LV reverse remodeling after CRT than the time-delay indices. Lim et al also reported that the strain delay index, an index of wasted energy caused by dyssynchrony, predicted LV reverse remodeling by CRT better than the time-delay indices. The present results are consistent with these previous reports.

The concept of the SRDI is based on the following hypothesis. If LV contraction was synchronized, global LV systolic function will theoretically be equal to the average of segmental systolic function. Thus, the average of the segmental peak systolic SR, one part of the SRDI, represents the global LV systolic function when contraction is synchronized, whereas glob-
al peak systolic SR, the other part of the index, represents that in the presence of dysynchrony. Therefore, the SRDI, which is the difference in the global LV systolic function between after and before resynchronization, can estimate the increase in global LV systolic function by the correction of dysynchrony. Patients with obvious mechanical dysynchrony, in which global SR becomes lower, should have a high SRDI. Patients with severely altered myocardial contractility, however, would have a low SRDI, even if significant dysynchrony exists, because segmental SRs are severely decreased. The SRDI thus can reflect not only the degree of dysynchrony but also the severity of impairment in myocardial contractility. Additionally, we considered that SR to be a suitable marker of myocardial contraction because myocardial SR is thought to be a less load-dependent index than strain. Indeed, we previously reported that the SRDI strongly correlated with changes in LV global contractility immediately after CRT. Moreover, the present study confirmed that the SRDI could predict LV reverse remodeling after CRT. However, although the SRDI gives an estimated increase in global LV systolic function by CRT, the estimation is based on the assumption that recoordination will be successfully achieved after CRT. Thus, it should be confirmed after CRT whether recoordination has been obtained or not. Our result showing volume responders had decreased St-SDs and SRDIs, as in Wang et al’s report, suggest the importance of recoordination in the beneficial effect of CRT.

In the present study, patients with a reduction in LV volume after CRT had a lower rate of long-term cardiac events than those without it, which is consistent with previous reports. Thus, low event rates in patients with a high SRDI could be related to favorable effects of CRT on LV systolic function. On the other hand, patients with severely altered LV systolic function have been reported to hardly respond to CRT. Kaspi et al demonstrated that not only mechanical dysynchrony but also residual LV contractility estimated by speckle-tracking strain was an important determinant of long-term events after CRT. High event rates in patients with a low SRDI might be caused by their severely altered LV contractility, because the SRDI decreases in concert with a decrease in segmental peak systolic SRs. On the other hand, the time-delay indices cannot reflect myocardial contractility, which might be a reason for their inadequate predictive value of cardiac events after CRT despite their relationship with reverse remodeling. Recently, Leenders et al demonstrated that the systolic rebound stretch in the septum, a marker of LV discoordination estimated by speckle-tracking longitudinal strain, was a stronger predictor of long-term prognosis after CRT than other clinical and echocardiographic parameters, including the septal to lateral wall shortening delay. Our result that the SRDI could relate to adverse events after CRT better than the time-delay indices supports their findings.

Although it is generally considered that the reproducibility of speckle-tracking-derived SR is somewhat low, our result showed an acceptable reproducibility of the SRDI. One of the reasons for the low reproducibility of the SRs is that they tended to have multiple peaks, which influences the reproducibility of time analyses. However, we measured the amplitude of segmental and global peak systolic SRs instead of duration, so that the number of peaks of the SR curves did not affect the value of the SRDI. In addition, we excluded patients with insufficient image quality from the analysis, which could improve the reproducibility of segmental SRs. In other words, the quality of 2D images limits the feasibility of the SRDI, but this is a major limitation of all speckle-tracking-derived indices. Indices that reflect the amount of wasted LV systolic function caused by mechanical dysynchrony have several advantages for predicting the response to CRT. However, they are not widely used in routine clinical practice because of the need for specific software and the complex calculations. In contrast, the SRDI can be calculated by only measuring the peak SR for each segmental SR curve and global SR curve. Moreover, when obtained from a single view, the SRDI can be calculated quite easily because most 2DST-software can automatically indicate the 2 factors of the SRDI: the values of the peak segmental SRs and global SR. Our study demonstrated that longitudinal SRDI obtained from the 4-chamber view could predict both reverse remodeling by CRT and long-term cardiac events after CRT. It has been suggested that the presence of posterolateral scar tissue can be one of the causes of a poor to no response to CRT. In addition, CRT corrects the mechanical dysynchrony mainly between the septal and lateral walls. For these reasons, the L-SRDI obtained from the 4-chamber view could be used as a predictor of the response to CRT as well as that obtained from 3 apical views. Thus, the SRDI could become a useful index that is easily calculated in clinical practice.

Study Limitations

First, in contrast to previous reports, the time-delay indices could not predict cardiac events after CRT, which might be partly related to the relatively small number of study patients. A study including a larger number of patients could demonstrate a statistically significant predictive value of time-delay indices. Second, in contrast to previous results, we could not demonstrate a predictive value of the radial indices. This might be related to the low reproducibility of radial indices in our software, which used automated tracking of both the endo- and epicardial borders obtained from a dilated LV, in which acquisition of adequate images including the entire epicardium was difficult. Third, the prevalence of nonresponders in this study was relatively higher than in previous reports. Although we could not detect the specific reason for this low rate of responders, different characteristics of our study patients might affect the responder rate. We thus have to confirm the value of the SRDI in a more balanced population. Fourth, although SR could be a more suitable marker of myocardial contractility than strain, our previous report showed similar predictive values between the SRDI and strain delay index, a strain-derived index of wasted energy by dysynchrony. We thus consider that the differences in load dependency between SR and strain would not strongly affect their predictive values. Fifth, although the frame rates of 2DST were comparable to those used in the previous report of 2DST-derived SR, those of TDI were considerably low, which could reduce the accuracy of TDI-SD.

Conclusions

The SRDI, an index of LV contractility loss caused by mechanical dysynchrony, could be an important predictor of LV reverse remodeling and long-term cardiac events after CRT. This index can be widely used in routine clinical practice to identify responders to CRT using a simplified calculation process.

Disclosures

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**Supplementary Files**

**Supplementary File 1**

Figure S1. Bland-Altman plots of St-SDs and strain rate dispersion index (SRDI) for intraobserver (A) and interobserver agreement (B). Please find supplementary file(s); [http://dx.doi.org/10.1253/circj.CJ-13-0483](http://dx.doi.org/10.1253/circj.CJ-13-0483)