Novel Strain Rate Index of Contractility Loss Caused by Mechanical Dyssynchrony

– A Predictor of Response to Cardiac Resynchronization Therapy –

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Background: Time-delay indexes are limited in predicting the response to cardiac resynchronization therapy (CRT), partly because they do not reflect the residual left ventricular (LV) contractility. We computed a novel index of LV contractility loss due to dyssynchrony (the strain rate (SR) dispersion index: SRDI) by using the speckle-tracking SR and compared the efficacy of the SRDI, time-delay indexes, and strain delay index (SDI), the previously reported index of wasted energy due to dyssynchrony, for predicting the acute response to CRT.

Methods and Results: Echocardiography was performed in 19 heart failure patients (LV ejection fraction (EF) $25 \pm 6\%$) before and 2 weeks after CRT. The standard deviation of time to peak velocity, or strain, was calculated as time-delay indexes. The SRDI was calculated as the average of segmental peak systolic SR minus global peak systolic SR. Longitudinal SDI (L-SDI), longitudinal SRDI (L-SRDI), and circumferential SRDI (C-SRDI) significantly correlated with the change in global longitudinal strain (Δ global LSt), whereas the time-delay indexes did not. Although the time-delay indexes were comparable between responders (Δ global LSt $\geq 0.3\%$) and nonresponders, the L-SDI, L-SRDI, and C-SRDI were greater in responders. The area under the receiver operating characteristic curve of the L-SRDI, L-SDI, and C-SRDI for predicting responders was 0.89, 0.81, and 0.78, respectively.

Conclusions: The SRDI correlated fairly well with an improvement in global LV systolic function after CRT. (*Circ J* 2011; **75**: 2167–2175)

Key Words: Cardiac resynchronization therapy; Echocardiography; Heart failure; Left ventricular dyssynchrony; Left ventricular systolic function

Cardiac resynchronization therapy (CRT) has been shown to improve left ventricular (LV) function and mortality in patients with advanced heart failure.^{1–5} However, 30–40% of the patients who meet the standard selection criteria of widened QRS complex and low LV ejection fraction (EF) do not respond to CRT.^{2,6} Thus, it has been emphasized that LV mechanical dyssynchrony should be evaluated to predict the response to CRT, which has been estimated by time-delay indexes derived from the time-delay measurement of regional wall motion using velocity data acquired with tissue Doppler imaging (TDI).^{7–9} However, in the multicenter Predictors of Responders to CRT (PROSPECT) trial, the time-delay indexes assessed by TDI could not accurately predict the responses to CRT.¹⁰

One of the reasons for these disappointing results was thought to be the high variability of the time-delay indexes.¹⁰ In addition, because conduction disturbance, such as left bundle branch block, causes redistribution of myocardial shortening and external work, resulting a reduction in LV global systolic function,^{11–13} the amount of wasted contractility related to LV dyssynchrony should be taken into account in the prediction of CRT response.^{14–17}

Lim et al proposed a strain delay index (SDI), using myocardial strain assessed by the 2-dimensional speckle tracking method (2DST), to estimate the potential for incremental contractility gain after CRT.¹⁸ This index could reflect not only the time-delay of regional wall motion but also the amount of wasted energy related to LV dyssynchrony. In

Received October 29, 2010; revised manuscript received April 13, 2011; accepted April 28, 2011; released online July 14, 2011
Time for primary review: 68 days

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ISSN-1346-9843 doi:10.1253/circj.CJ-10-1099

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Figure 1. Demonstrable circumferential strain rate (SR) curves (Right) obtained from 6 segments (Left). The 6 colored curves indicate segmental SRs and the white, dashed curve indicates global SR. The strain rate dispersion index (SRDI) was calculated by subtracting the global peak systolic SR (white arrow) from the averaged segmental peak systolic SR (yellow arrow).

fact, they demonstrated that the SDI predicted LV reverse remodeling after CRT better than Doppler- or 2DST-derived time-delay indexes.¹⁸ However, the myocardial strain rate (SR) may be more suitable for the evaluation of LV contractility because it is thought to be less load-dependent than strain.¹⁹ We thus constructed an index to estimate the amount of LV contractility loss caused by dyssynchrony by using the 2DST-derived SR. The aim of the present study was to determine whether our new index, the SR dispersion index (SRDI), correlates better with the change in LV systolic function by CRT than either the time-delay indexes or the SDI.

Methods

Study Subjects and Protocol

Our study group comprised 26 consecutive patients with heart failure referred for CRT device implantation in Hokkaido University Hospital. The criteria for CRT were: (1) the presence of drug-refractory symptomatic heart failure (New York Heart Association (NYHA) functional class III or IV), (2) depressed LV systolic function defined as $EF \leq 35\%$, and (3) prolonged QRS duration (≥ 120 ms).²⁰ Transthoracic echocardiography including TDI and 2DST was performed before and 2 weeks after implantation of the CRT device. The study protocol was approved by the Ethics Committee of the Hokkaido University, and all patients gave informed consent before participation in the study.

CRT Device Implantation

The LV lead of the CRT device was inserted through the coronary sinus and positioned into the lateral or posterolateral cardiac vein with the help of a venogram. The right atrial and ventricular leads were positioned conventionally, and all leads were connected to the device. A dual-chamber biventricular implantable cardioverter-defibrillator (Concerto, Medtronic or Contak Renewal 4, Guidant Corporation) was implanted in all patients, except one in whom a CRT without defibrillator was implanted.

Echocardiography

All studies were performed with a commercially available ultrasound system (Aplio SSA-770A, Toshiba Medical Systems, Tochigi, Japan) with a 2.5-MHz phased array transducer. Digital 2D and color TDI cine loops were obtained in the apical 4-, 2-, and 3-chamber, and midventricular short-axis views. Care was taken to acquire the cine loops that have close intervals of the R to R wave for analysis of 2DST and TDI in patients with atrial fibrillation. The frame rates were 44–62/s (57 ± 8) for 2D imaging used for 2DST, and 54–69/s (58 ± 5) for TDI. The velocity range for TDI was ± 15 cm/s.

LV end-diastolic and end-systolic volumes were measured from the apical 4- and 2-chamber images using the biplane method of disks, and EF was calculated.²¹ In patients with atrial fibrillation, LV volumes were measured over 5 consecutive beats, and these values were averaged. The mitral regurgitation was graded as severe when the volume measured by the proximal isovelocity surface area method was more than 60 mL.²²

TDI Analysis

The color TDI cine loops were analyzed off-line using commercial software (TDI-Q, Toshiba Medical Systems, Tochigi, Japan). 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 was measured in each segment. Next, the standard deviation of time to peak systolic velocity (TDI-SD) was calculated within the 12 segments.⁸ The ejection phase was defined as the period from aortic valve opening to closure as determined by LV outflow using the pulsed Doppler method.

Speckle-Tracking Strain Analysis

Myocardial strain and SR were analyzed using 2DST software (Toshiba Medical Systems, Tochigi, Japan). The LV endocardial and epicardial borders were manually traced on an end-diastolic frame for the 3 apical views and on an end-

Table 1. Baseline Characteristics of the Study Patients

	All (n=19)	Responders (n=10)	Nonresponders (n=9)	P value
Age (year)	57±12	52±12	62±10	0.067
Male, n (%)	13 (84)	7 (70)	6 (67)	0.88
NYHA class, n (%)				
III	15 (79)	8 (80)	7 (78)	0.91
IV	4 (21)	2 (20)	2 (22)	0.91
Ischemic cardiomyopathy, n (%)	4 (21)	1 (10)	3 (33)	0.21
Electrocardiographic findings				
Atrial fibrillation, n (%)	2 (11)	0 (0)	2 (22)	0.13
QRS duration (ms)	164±24	167±27	161±22	0.63
Left bundle branch block, n (%)	11 (58)	6 (60)	5 (56)	0.84
Right ventricular pacing, n (%)	4 (21)	3 (30)	1 (11)	0.31
Echocardiographic findings				
LV end-diastolic volume (ml)	226±125	196±81	260±159	0.28
LV end-systolic volume (ml)	172±111	148±63	199±147	0.33
LV ejection fraction (%)	25±6	25±4	26±8	0.65
Global longitudinal strain (%)	−4.9±1.8	−4.6±1.9	−5.1±1.9	0.56
Severe MR, n (%)	6 (32)	2 (20)	4 (44)	0.25
Medication, n (%)				
ACEI or ARB	16 (84)	8 (80)	8 (89)	0.60
β-blocker	16 (84)	9 (90)	7 (78)	0.47
Diuretic	19 (100)	10 (100)	9 (100)	
Spironolactone	11 (58)	3 (30)	8 (89)	0.009
Amiodarone	9 (47)	5 (50)	4 (44)	0.81

P values are for comparison between responders and nonresponders.

NYHA, New York Heart Association; LV, left ventricular; MR, mitral regurgitation; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

Table 2. Echocardiographic and Electrocardiographic Parameters at Baseline and After CRT

	Overall (n=19)		Responders (n=10)		Nonresponders (n=9)		P value
	Baseline	After CRT	Baseline	After CRT	Baseline	After CRT	
LV end-diastolic volume (ml)	226±125	212±116*	196±81	186±84	260±159	242±142	0.650
LV end-systolic volume (ml)	172±111	154±95†	148±63	130±61*	199±147	180±122	0.276
LV ejection fraction (%)	25±6	29±6‡	25±4	30±4‡	26±8	27±7	0.331
Global longitudinal strain (%)	−4.9±1.8	−5.3±1.9	−4.6±1.9	−6.0±1.8†	−5.1±1.9	−4.5±1.7*	0.555
Global longitudinal SR (s ^{−1})	−0.24±0.09	−0.25±0.09	−0.24±0.10	−0.29±0.09*	−0.24±0.09	−0.22±0.73	0.996
Global circumferential SR (s ^{−1})	−0.38±0.18	−0.43±0.22	−0.41±0.18	−0.52±0.25†	−0.34±0.19	−0.33±0.16	0.455
Global radial SR (s ^{−1})	0.55±0.28	0.63±0.34	0.61±0.32	0.79±0.36	0.52±0.20	0.44±0.19	0.358
QRS duration (ms)	164±24	145±25†	167±27	147±24†	161±22	143±27	0.629
TDI-SD (ms)	48±10	38±13†	47±9	35±14†	48±11	41±13	0.832
LS-SD (ms)	125±51	103±30	128±53	105±32	123±51	100±30	0.819
CS-SD (ms)	91±42	75±38	80±43	61±28	102±41	89±43	0.261
RS-SD (ms)	142±54	85±47†	148±63	58±28†	135±42	132±48	0.693
L-SDI (%)	17.4±9.5	14.4±2.7	22.2±8.8	14.1±2.8*	12.2±7.6	14.7±2.7	0.017
C-SDI (%)	5.9±2.9	3.1±1.6†	6.9±3.2	2.9±1.9†	4.8±2.3	3.3±1.2	0.128
R-SDI (%)	15.7±7.8	9.2±4.7†	18.5±8.4	6.9±3.7†	12.2±6.4	12.1±4.4	0.100
L-SRDI (s ^{−1})	0.19±0.09	0.17±0.05	0.25±0.08	0.16±0.05*	0.13±0.07	0.16±0.05	0.004
C-SRDI (s ^{−1})	0.15±0.10	0.09±0.05†	0.19±0.10	0.10±0.05*	0.10±0.08	0.07±0.05	0.049
R-SRDI (s ^{−1})	0.41±0.21	0.29±0.14	0.48±0.26	0.26±0.08*	0.32±0.10	0.34±0.19	0.130

P values are for comparison of responders and nonresponders at baseline. *P<0.05 vs. baseline, †P<0.01 vs. baseline, ‡P<0.001 vs. baseline. CRT, cardiac resynchronization therapy; LV, left ventricular; SR, strain rate; 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; CS-SD, standard deviation of time to segmental peak circumferential strain; RS-SD, standard deviation of time to segmental peak radial strain; L-SDI, longitudinal strain delay index; C-SDI, circumferential strain delay index; R-SDI, radial strain delay index; L-SRDI, longitudinal strain rate dispersion index; C-SRDI, circumferential strain rate dispersion index; R-SRDI, radial strain rate dispersion index.

Figure 2. Time–circumferential strain rate curve obtained from a responder before (A) and 2 weeks after CRT (B). Note that the value of global peak systolic strain rate (white arrow in B) increased by CRT up to the level of average of 6 segmental peak systolic SRs at baseline (yellow arrow in A). SR, strain rate; SRDI, strain rate dispersion index.

systolic frame for the midventricular short-axis view. LV wall was divided into 6 segments within each view, and the time-strain and time-SR curves for each segment were extracted by automated tracking of the endocardial border for the longitudinal and circumferential indexes and that of both the endocardial and epicardial borders for the radial indexes. Longitudinal strain/SR curves were obtained from 3 apical views, and circumferential and radial strain/SR from the short-axis view. The standard deviation of time from the onset of QRS to segmental peak strain was calculated for the longitudinal, circumferential, and radial strains (LS-SD, CS-SD, and RS-SD, respectively).

The time-global strain curve was also extracted as reported by Lim et al, determining end-systole as the time point of peak global strain.¹⁸ Briefly, to correct the differences of the

R to R intervals among the apical images, strain values of all segments were averaged at every 2.5% of the R to R interval for the calculation of global longitudinal strain. Global circumferential and radial strains were obtained by averaging 6 segmental strains at each frame in the short-axis view. Peak strain (ϵ_{peak}) and strain at end-systole (ϵ_{ES}) were measured in each segment. Next, the longitudinal SDI (L-SDI) was measured as the sum of ($\epsilon_{\text{peak}} - \epsilon_{\text{ES}}$) from the 16 segments in the 3 apical views. The circumferential SDI (C-SDI) and radial SDI (R-SDI) were calculated from 6 segments in the short-axis view. In the segments that showed the strain in the stretching direction or biphasic strain with the absolute value of the stretching strain greater than the shortening strain, ($\epsilon_{\text{peak}} - \epsilon_{\text{ES}}$) were counted as zero.¹⁸

The SRDI was calculated as a new index of global LV

contractility loss caused by dyssynchrony. Peak systolic SRs were measured in all segments within each view. We also extracted the time–global SR curve by averaging all segmental SRs at every 2% of the R to R interval and measured global peak systolic SR. The SRDI was then calculated as the average of the segmental peak systolic SRs minus global peak systolic SR (Figure 1). The longitudinal SRDI (L-SRDI) was derived from the 3 apical views, and the circumferential SRDI (C-SRDI) and radial SRDI (R-SRDI) were derived from the short-axis view.

The accuracy of speckle tracking for each myocardial segment was visually judged by 2 independent observers. Patients who had 2 or more segments judged as having inadequate tracking quality in at least one view were excluded.

Estimation of LV Systolic Function

LV systolic function was estimated by global longitudinal strain and EF before and 2 weeks after CRT. Response to CRT were defined as an improvement of $\geq 0.3\%$ in global longitudinal strain at follow-up.

Statistical Analysis

Continuous variables are expressed as mean $\pm$ SD and compared with 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 for the detection of correlation between 2 continuous variables. Receiver-operating characteristic (ROC) curves were determined to evaluate the diagnostic performance of the time-delay indexes and indexes of LV contractility loss to detect responders to CRT. For all tests, $P < 0.05$ was considered significant.

Results

Patients' Baseline Characteristics

Of the 26 patients, 7 were excluded because of inadequate tracking quality of 2DST. Thus, the final study group consisted of 19 patients, whose baseline characteristics are summarized in Table 1. All patients had heart failure symptoms (NYHA class III or IV) with severe LV dysfunction and wide QRS duration; 15 patients had left bundle branch block (58%) or right ventricular pacing rhythm (21%) and the other causes of prolonged QRS duration were intraventricular conduction disturbance in 3 patients and right bundle branch block in 1 patient. Etiology was ischemic for 21% of all patients. Medications were optimal for heart failure, including angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, β -blockers, diuretics, and spironolactone.

Acute Responses to CRT

A CRT device was successfully implanted in all patients without any complications. None of the patients died or underwent heart transplantation during the follow-up. Two weeks after the implantation of the CRT device, NYHA functional class was significantly reduced from 3.2 ± 0.4 to 2.8 ± 0.4 ($P < 0.05$). The QRS duration decreased. EF significantly increased and global longitudinal strain tended to increase after CRT, but did not reach statistical significance (Table 2). Global longitudinal, circumferential, and radial SRs did not change after CRT in the overall patient group. There was a significant correlation between EF and global longitudinal strain ($R = -0.57$, $P < 0.001$).

The time-delay indexes, such as TDI-SD and RS-SD, and indexes of LV contractility loss, including the C-SDI, R-SDI, and C-SRDI, significantly decreased from baseline

Table 3. Correlation Between Echocardiographic Parameters and the Change in LV Systolic Function by CRT

	Δ global longitudinal strain		Δ EF	
	R	P value	R	P value
QRS duration	−0.31	0.204	0.41	0.09
TDI-SD	−0.09	0.712	0.05	0.83
LS-SD	−0.40	0.090	0.27	0.26
CS-SD	−0.02	0.941	−0.09	0.73
RS-SD	−0.31	0.198	0.14	0.56
L-SDI	−0.59	0.008	0.64	0.003
C-SDI	−0.30	0.220	0.29	0.23
R-SDI	−0.26	0.279	0.23	0.34
L-SRDI	−0.69	0.001	0.76	<0.001
C-SRDI	−0.47	0.045	0.34	0.15
R-SRDI	−0.36	0.13	0.28	0.24

Abbreviations see in Tables 1, 2.

values after CRT, whereas the LS-SD, CS-SD, L-SDI, L-SRDI, and R-SRDI did not change (Table 2).

Acute Responses in Responders vs. Nonresponders

Among the 19 patients, there were 10 acute responders (53%) defined as an increase in global longitudinal strain after CRT (Δ global LSt) $\geq 0.3\%$. The remaining 9 patients (47%) were classified as nonresponders. Responders showed a significant increase in EF and a slightly but significant decrease in LV end-systolic volume (Table 2). In contrast, nonresponders showed no changes in either of these parameters. Moreover, responders showed significantly improved global longitudinal strain, global longitudinal SR, and global circumferential SR whereas nonresponders did not. Global radial SR tended to increase in responders, but did not reach statistical significance (Table 2). Among the responders, QRS duration decreased (Table 2). RS-SD significantly decreased with CRT in the responders but not LS-SD and CS-SD (Table 2). The L-SDI, C-SDI, R-SDI, L-SRDI, C-SRDI, and R-SRDI all decreased with CRT in the responders (Table 2, Figure 2). In contrast, none of these parameters changed in the nonresponders (Table 2).

Prediction of Response to CRT

Baseline clinical and echocardiographic parameters were comparable between responders and nonresponders, except for spironolactone use (Table 1). The L-SDI, L-SRDI and C-SRDI at baseline were significantly higher in responders than in nonresponders (Table 2).

Linear regression analyses showed that neither QRS duration nor the TDI-SD at baseline correlated with Δ global LSt (Table 3). The LS-SD, CS-SD, RS-SD, C-SDI, R-SDI, and R-SRDI did not correlate with Δ global LSt (Table 3, Figure 3). In contrast, the L-SDI, L-SRDI and C-SRDI significantly correlated with Δ global LSt (Table 3, Figure 3). Similar trend was observed when LV systolic function was estimated by EF (Table 3).

ROC analyses for predicting the responders showed that, among these parameters, the L-SRDI had the largest area under the ROC curve. The L-SDI, L-SRDI, and C-SRDI could significantly discriminate between responders and nonresponders (Table 4).

Figure 3. Correlations between Δ global LSt and LS-SD (A), CS-SD (B), RS-SD (C), L-SDI (D), C-SDI (E), R-SDI (F), L-SRDI (G), C-SRDI (H), and R-SRDI (I). Δ global LSt, changes in global longitudinal strain before and after CRT. LS-SD, standard deviation of time to peak longitudinal strain; CS-SD, standard deviation of time to peak circumferential strain; RS-SD, standard deviation of time to peak radial strain; L-SDI, longitudinal strain delay index; C-SDI, circumferential strain delay index; R-SDI, radial strain delay index; L-SRDI, longitudinal strain rate dispersion index; C-SRDI, circumferential strain rate dispersion index; R-SRDI, radial strain rate dispersion index.

Table 4. AUC for Predicting Responders to CRT

	AUC	95% CI	P value
TDI-SD	0.49	0.21–0.77	0.94
LS-SD	0.57	0.30–0.84	0.62
CS-SD	0.34	0.09–0.60	0.25
RS-SD	0.54	0.28–0.81	0.74
L-SDI	0.81	0.62–1.00	0.02
C-SDI	0.70	0.50–0.97	0.14
R-SDI	0.73	0.49–0.98	0.09
L-SRDI	0.89	0.70–1.00	0.006
C-SRDI	0.78	0.55–1.00	0.04
R-SRDI	0.68	0.43–0.92	0.19

P values are for AUCs vs. the null hypothesis of a true area of 0.5. AUC, area under the receiver-operating curve; CI, confidence interval. Other abbreviations see in Table 2.

Reproducibility

Intra- and interobserver variabilities of EF were both 7% in our laboratory. Reproducibility of strain and SR measurements were assessed in 10 randomly selected patients. Analyses of global longitudinal strain, LS-SD, CS-SD, RS-SD, L-SDI, C-SDI, R-SDI, L-SRDI, C-SRDI, and R-SRDI were performed by 2 independent observers using the same 2D cine loop and the same cardiac cycle. A single blinded observer repeated the analyses after an interval of 2 weeks. The respective intra- and interobserver variabilities were 0.5% (9%) and 0.5% (10%) for global longitudinal strain, 12 ms (10%) and 20 ms (16%) for LS-SD, 17 ms (18%) and 19 ms (19%) for CS-SD, 26 ms (20%) and 31 ms (24%) for RS-SD, 1.9% (12%) and 3.0% (17%) for L-SDI, 0.9% (16%) and 0.9% (17%) for C-SDI, 2.9% (19%) and 3.9% (25%) for R-SDI, 0.02 s^{-1} (10%) and 0.03 s^{-1} (17%) for L-SRDI, 0.02 s^{-1}

(13%) and 0.02 s^{-1} (15%) for C-SRDI, and 0.07 s^{-1} (18%) and 0.09 s^{-1} (22%) for R-SRDI.

Discussion

This is the first study to demonstrate that a novel index of LV contractility loss because of dyssynchrony, the SRDI, could predict acute responders to CRT. Furthermore, the SRDI correlated well with the improvement in LV systolic function.

CRT has been shown to improve LV function and survival in NYHA III–IV patients with severe LV dysfunction and a wide QRS.^{1–5} However, more than 30% of patients selected on the basis of QRS duration do not respond to CRT,^{2,6} suggesting that mechanical rather than electrical dyssynchrony can better predict the response to CRT. Measurement of regional peak-systolic velocities with TDI has been shown to be highly predictive for the response to CRT and prognosis.^{7–9} However, limitations of the time-delay indexes measured by TDI to assess LV mechanical dyssynchrony for the prediction of response to CRT have been reported.^{10,23} The limited accuracy of the TDI parameters to predict the response to CRT might have several reasons. First, the accuracy of measurement of regional myocardial velocities by TDI is limited by ultrasound angle dependency and tethering effects, which are especially prominent in the dilated LV commonly seen in patients with severe heart failure who require CRT.^{24,25} Second and more importantly, the time-delay indexes do not take regional myocardial contractility into account. In the presence of a conduction disturbance, especially in left bundle branch block or right ventricular pacing, asynchronous electrical activation causes redistribution of myocardial shortening and external work, which is associated with a reduction in LV global systolic function.^{11–13} CRT improves the heterogeneity of myocardial shortening by activation of the latest activated site, resulting in augmentation of global LV contractility.²⁶ Therefore, dyscoordination of contraction can more directly associate with the improvement of LV systolic function by CRT than the dispersion of the timing of regional contraction. In fact, the present study demonstrated that the time-delay indexes derived from TDI and 2DST could not predict the changes in LV systolic function (Tables 3, 4).

The indexes of dyssynchronization, which measure the amount of both myocardial stretch and shortening during systole, were recently reported to better correlate with the immediate¹⁵ and chronic responses to CRT^{14,16,17} than the time-delay indexes. The SDI, an index of wasted energy caused by dyssynchrony, has been also reported as a strong predictor of the response to CRT.¹⁸ This index can account for the difference between ϵ_{peak} and ϵ_{ES} , which represents wasted energy caused by dyssynchrony per segment and sums these values in all LV segments. The SDI can be regarded as a dyscoordination index, but is somewhat different because it does not measure the amount of stretch. Therefore, we consider that our new index, the SRDI, is a logical extension of SDI. The concept of the SRDI is based on the idea that the wasted contractility from mechanical dyssynchrony can be the acute gain of contractility expected to be obtained by CRT. The average of the segmental peak systolic SR was estimated as global LV systolic function when the contraction is synchronized and global peak systolic SR was measured as the actual global LV systolic function in the presence of mechanical dyssynchrony. Therefore, the SRDI, the difference between the estimated and actual global LV systolic function, can estimate the increase of global LV

systolic function by the correction of dyssynchrony. Indeed, the present results demonstrated that the SRDI correlated better than the time-delay indexes with the changes in LV systolic function by CRT.

The present results support previous findings that indexes of LV systolic function wasted by mechanical dyssynchrony correlate better with the CRT response than the time-delay indexes.^{14–18} Our study, as well as that by Lim et al, demonstrated that both the SDI and SRDI correlated with the changes in LV systolic function after CRT. We thus consider that our index, the SRDI, is suitable for predicting the acute response to CRT for several reasons. First, although myocardial strain substantially depends on the afterload, the myocardial SR is less load-dependent.¹⁹ Therefore, SR can more accurately reflect regional systolic function than strain. Second, the segment that shows biphasic strain with myocardial stretching, ($\epsilon_{\text{peak}} - \epsilon_{\text{ES}}$) is estimated as zero for the calculation of SDI, which is acceptable in a segment with predominantly scarred myocardium. On the contrary, in the segment with viable myocardium remaining, the SDI may underestimate regional systolic function. In contrast, the SRDI can detect the decreased contractility of residual viable myocardium by measuring segmental peak systolic SR. Third, for the calculation of the SDI, the strain values need to be measured at 2 time points for each segment, whereas the SRDI can be calculated by measuring only the peak SR for each segment and the peak SR on the global SR curve. In addition, the 2DST-software can automatically measure the peak SR on a time–SR curve. Hence, the SRDI is a simpler than the SDI and can be used more easily in routine clinical practice.

It is generally considered that the reproducibility of the SR is substantially lower than that of strain when derived from 2DST. In the present study, however, the reproducibilities of the SDI and SRDI were similar. The calculation of the SDI needs 2 time points to be measured for each segmental strain curve, whereas the SRDI can be calculated by measuring peak SR alone for each segment. This difference in the number of measurement points could be a reason why the reproducibility of the SRDI was not worse than that of the SDI. In addition, the image quality was relatively good in our study population, resulting in less noisy SR curves being obtained in most of the patients.

Study Limitations

First, the results were obtained from a relatively small number of patients in a single center. Therefore, we have to acknowledge that this study is preliminary and further study with a larger number of patients is necessary to confirm the efficacy of the SRDI. Second, the SRDI cannot be applied to the patients for whom optimal echocardiographic images are not available. We excluded 7 of the original 26 patients (27%) because of inadequate image quality, which is similar to the 30% excluded by Lim et al.¹⁸ Third, we have to acknowledge that the follow-up period was short. We analyzed only the immediate changes in LV systolic function by CRT whereas the response to CRT is usually a combination of both immediate changes in systolic function and short-term reduction of LV volumes.²⁷ Thus, it must be determined whether the SRDI is effective in predicting the longer term beneficial response to CRT. In addition, we evaluated LV systolic function by global longitudinal strain, because it is generally considered to be a more sensitive marker of systolic function than EF. Even though the cut-off values of global longitudinal strain were somewhat arbitrary, it was significantly correlated with EF in our study patients.

Moreover, the parallel behavior between global strain and EF has been confirmed by the previous study by Brown et al.²⁸ Fourth, although the frame rates of 2DST were comparable to those used in a previous report of the 2DST-derived SR,²⁹ those of the TDI were considerably low, which could reduce the accuracy of the TDI-SD. Fifth, contrary to previously reported results,^{16,30,31} none of the radial indexes correlated with the changes in LV systolic function after CRT in the present study. The automated tracking of both the endo- and epicardial borders obtained from the dilated LV, in which adequate images including the entire epicardium were difficult to obtain, might deteriorate the reproducibility of radial indexes. We consider this lead to the radial indexes being ineffective in predicting the response to CRT. Sixth, because the dispersion of the timing of the peak SRs was not analyzed, we could not demonstrate a uniform comparison of timing vs. amplitude parameters for both strain and SR in the present study. Seventh, the L-SDI and L-SRDI strongly correlated with the changes in LV systolic function after CRT in the present study, whereas the C-SDI and C-SRDI had a weak correlation. Lim et al also reported that longitudinal strain better reflected regional or global wall motion than circumferential or radial strain.¹⁸ On the other hand, studies using magnetic resonance imaging reported the utility of circumferential strain for the evaluation of mechanical dyssynchrony.^{32,33} Therefore, it remains to be determined which direction of strain/SR can better predict functional improvement after CRT and further investigations are needed to clarify this issue.

Conclusions

SRDI, a novel index of LV contractility loss because of mechanical dyssynchrony, correlated fairly well with an improvement of global LV systolic function after CRT. This new index is expected to be predictive of the long-term beneficial effects of CRT.

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