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Echocardiography

New Equation for Prediction of Reverse Remodeling after Cardiac Resynchronization Therapy

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Objectives: To integrate data from two-dimensional echocardiography (2D ECHO), three-dimensional echocardiography (3D ECHO), and tissue Doppler imaging (TDI) for prediction of left ventricular (LV) reverse remodeling (LVRR) after cardiac resynchronization therapy (CRT). It was also compared the evaluation of cardiac dyssynchrony by TDI and 3D ECHO. Methods: Twenty-four consecutive patients with heart failure, sinus rhythm, QRS $\geq$ 120 msec, functional class III or IV and LV ejection fraction (LVEF) $\leq$ 0.35 underwent CRT. 2D ECHO, 3D ECHO with systolic dyssynchrony index (SDI) analysis, and TDI were performed before, 3 and 6 months after CRT. Cardiac dyssynchrony analyses by TDI and SDI were compared with the Pearson's correlation test. Before CRT, a univariate analysis of baseline characteristics was performed for the construction of a logistic regression model to identify the best predictors of LVRR. Results: After 3 months of CRT, there was a moderate correlation between TDI and SDI ($r = 0.52$). At other time points, there was no strong correlation. Nine of twenty-four (38%) patients presented with LVRR 6 months after CRT. After logistic regression analysis, SDI (SDI $>$ 11%) was the only independent factor in the prediction of LVRR 6 months of CRT (sensitivity = 0.89 and specificity = 0.73). After construction of receiver operator characteristic (ROC) curves, an equation was established to predict LVRR: LVRR $= -0.4$LVDD (mm) $+ 0.5$LVEF (%) $+ 1.1$SDI (%), with responders presenting values >0 (sensitivity = 0.67 and specificity = 0.87). Conclusions: In this study, there was no strong correlation between TDI and SDI. An equation is proposed for the prediction of LVRR after CRT. Although larger trials are needed to validate these findings, this equation may be useful to candidates for CRT. (Echocardiography 2012;29:678-687)

[Correction added on 30 March 2012, after first online publication: the values of sensitivity and specificity were placed wrongly in the abstract above and have now been corrected.]

Key words: cardiac resynchronization therapy, three-dimensional echocardiography, tissue Doppler imaging, left ventricular reverse remodeling.

Cardiac resynchronization therapy (CRT) has been shown to be an effective treatment for patients with advanced and refractory heart failure.[1,2] Despite careful selection and evaluation, however, up to 30% of patients do not benefit from CRT. This nonresponse rate reflects patients whose clinical symptoms do not improve after CRT. When evaluating left ventricular (LV) volumetric and functional responses after CRT, the nonresponder patient group may represent about 50% of the treated patients.[3–7]

Recent studies have demonstrated left ventricular reverse remodeling (LVRR) to be a useful marker of improved prognosis after CRT.[8–11] Therefore, the identification of patients who present with LVRR after CRT is important for evaluating the cost-effectiveness of this therapy for each individual patient. In the past decade, the identification of significant cardiac dyssynchrony has been associated with LVRR.

New methods have been developed for selecting and evaluating cardiac dyssynchrony.[12–15] Tissue Doppler imaging (TDI) and three-dimensional echocardiography (3D ECHO) have been used for this purpose with controversial results.[16–21] In this regard, 3D ECHO has been associated with excellent results in the detection of LVRR after CRT.[22] Recently, the value of the systolic dyssynchrony index (SDI) obtained from this technique as a marker for response to CRT has been demonstrated.[22–26]

The aim of this study was to devise an equation integrating data from conventional echocardiography, 3D ECHO, and TDI for predicting LVRR

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after CRT. The evaluation of cardiac dyssynchrony by TDI and 3D ECHO was compared before CRT and 3 and 6 months after CRT.

Methods:

Study Population and Protocol:

Thirty-five consecutive patients with nonischemic dilated cardiomyopathy who were referred for the implantation of a CRT device at the Heart Institute (InCor) of São Paulo University Medical School, São Paulo, Brazil were recruited from January 2007 to June 2009. Patients were selected for CRT based on the following criteria:

- 18–75 years old;
- LV ejection fraction (LVEF) ≤ 0.35, as evaluated by Simpson's rule;
- New York Heart Association (NYHA) functional class III or IV, despite optimal medical treatment;
- sinus rhythm;
- QRS duration ≥ 120 msec;
- left ventricular diastolic diameter > 55 mm.

Patients older than 40 years and with risk factors for coronary artery disease were referred for angiographic examination to exclude coronary artery disease. Before implantation of the CRT device, an EKG was performed, and quality of life was evaluated using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) with assessment of functional class (NYHA). Optimization of AV delay was performed 2 ± 1 days after the implantation of the CRT device using Doppler echocardiography and employing Ritter's formula.[27,28] After 3 and 6 months of CRT, patients were submitted to a reevaluation that consisted of a second EKG, the MLHFQ application, and a new echocardiographic examination.

After a 6-month follow-up period, patients were included in the responder group if there was clinical improvement (by at least one level of the NYHA functional class) and a reduction of $\geq 15\%$ of LV systolic end volume (LVESV). Responders and nonresponders were compared with respect to baseline characteristics, electrocardiographic patterns, and echocardiographic measurements. Anatomical and morphological variables and left ventricular dyssynchrony indexes were evaluated by TDI and 3D ECHO.

Tissue Doppler Imaging:

All patients were submitted to evaluation of electromechanical delay by TDI. All basal and mid-myocardial segments in the apical four-chamber, two-chamber, and long-axis views were evaluated according to the standard myocardial segmentation defined by the American Society of Echocardiography.[29] The electromechanical delay (QS interval) was defined by the time interval between the onset of the Q-wave on the electrocardiogram and the peak velocity of the systolic component on the TDI spectral curves. The difference between the largest and shortest QS interval was considered significant if larger than 65 msec.[30–32] The evaluation of cardiac dyssynchrony was performed using TDI to analyze four (4S), six (6S), and twelve (12S) myocardial segments.

Real Time Transthoracic 3D Echocardiography:

3D ECHO was performed before, and 3 and 6 months after CRT device implantation. A full volume dataset was acquired during a breath-holding period (15–20 sec). Images were considered inadequate for study inclusion when two or more myocardial segments could not be analyzed. For the quantification of the left ventricular volumes, appropriate software (Phillips Medical Systems, Andover, MA, USA, Qlab, versions 5.0 and 6.0) was used. Before the quantification, an alignment between the left ventricular apex and the tip of the mitral valve leaflets was performed in the coronal, sagittal, and transverse planes. Next, five predefined reference points were identified (mitral valve annulus in the inferior septal, lateral, inferior, and anterior walls and LV apex), and a semiautomated endocardial border recognition was performed by the software. When necessary, the endocardial border limits were edited during offline processing.

3D ECHO provides the percentage of cardiac dyssynchrony by evaluation of the SDI. SDI is defined as the standard deviation (SD) of the time taken to reach the minimum regional volume for each segment as a percentage of the cardiac cycle. Higher SDI values denote an increasing degree of intraventricular dyssynchrony.[33] In a recent study by Gimenes et al., the SDI standard values in a normal population were defined as normal when $<5\%$.[34]

The full-volume datasets were interpreted by two independent observers to account for interobserver variability. To account for intraobserver variability, the same reader analyzed the same full volume datasets a second time 1 month after the first occasion.

The research protocol was approved by the Heart Institute (InCor) of São Paulo University Medical School's ethics committee, and informed consent was provided by each patient.

Statistical Analysis:

The data analyses were performed with SPSS 13 software for Windows. Nominal data were expressed in frequency distributions and percentages, while comparisons were performed using the chi-square test or Fisher's exact test.

Continuous variables were tested for normality, and means and standard deviations (SDs) were calculated. Comparison between continuous variables at baseline and 6 months after CRT were performed with the Student's *t*-test. Comparisons between SDI and TDI, as well as 2D and 3D data, were performed with Pearson's correlation analysis. A univariate analysis of clinical, electrocardiographic, and echocardiographic baseline characteristics was performed to construct a logistic regression model to predict CRT response. Receiver operator characteristic (ROC) curves were generated to determine cutoff values for SDI, LVDD, LVEDV, and LVEF that were most closely associated with the CRT response.

Intra- and interobserver analyses of the LVEDV, LVESV, LVEF, and SDI, as evaluated by 3D ECHO, were performed using the intraclass correlation coefficient.

Results:

Thirty-five consecutive patients with dilated cardiomyopathy of nonischemic etiology were recruited for CRT from January 2007 to June 2009. Eight patients died before the 6-month reevaluation, one patient refused to participate during the follow-up period, and two patients were excluded because of inadequate echocardiographic imaging. Upon final analysis, 24 patients were included.

At baseline, the mean age of the patients was 59 ± 10 years, 10 (37%) patients were male, 21 (78%) had systemic arterial hypertension, and all of them were under optimized pharmacological treatment for heart failure. After CRT, the same medication was maintained with no significant difference in the dosage during follow-up period. Six months after CRT implantation, patients were divided into two groups according to CRT response, as follows: Group I (GI), i.e., responder patients (clinical improvement and reduction of $\geq$15% in LVESV), and Group II (GII), i.e., nonresponder patients. Both groups were similar regarding mean age, gender distribution, functional class (NYHA), quality of life assessed by the MLHFQ, medical treatment, and electrocardiographic findings at baseline (Table I).

The electrocardiographic and echocardiographic variables of GI and GII at baseline and 6 months after CRT are shown in Table II. Three months after CRT, functional class (NYHA) improved in 18/24 (75%) patients ($P < 0.001$) and remained unchanged in 6/24 (25%) patients. Six months after CRT, 19/24 (79%) patients improved in functional class, and 5/24 (21%) patients remained unchanged ($P < 0.001$). The quality of life also improved, as assessed by the Minnesota Living with Heart Failure Questionnaire (MLHFQ) in 21/24 (88%) patients 3 months after CRT ($P < 0.001$), and in 20/24 (83%) patients 6 months after CRT ($P < 0.001$). Nevertheless, only 9 (38%) patients demonstrated a decreased LVESV and were considered responders 3 and 6 months after CRT.

Six months after CRT, the functional class (NYHA) improved in GI ($P = 0.004$) and GII ($P = 0.012$). The quality of life assessed using the MLHFQ also improved in GI ($P = 0.002$) and GII ($P = 0.004$) (Fig. 1; Table II), but only 9 (38%) experienced a decreased LVESV and were considered responders. Regarding electrocardiographic parameters, after CRT, the PR interval was reduced in both groups (GI, $P < 0.001$; GII, $P = 0.004$), but the QRS duration reduced only in the responder group (GI, $P = 0.013$; GII, $P = 0.602$) (Fig. 2; Table II).

In GI, LVEDV ($P = 0.007$) and LVESV ($P = 0.002$) (3D ECHO) decreased after CRT, and in GII, LVEDV ($P = 0.291$) and LVESV ($P = 0.126$) increased (Fig. 3; Table II). After CRT, LVEF (3D ECHO) increased in GI ($P = 0.008$), and there was no change in LVEF in GII ($P = 0.326$ (Fig. 4; Table II).

The patients in GI had smaller left ventricular volumes, as estimated by Simpson's rule (LVEDV: 230 ± 35 mL vs. 316 ± 10 mL, $P = 0.045$; LVESV: 178 ± 30 mL vs. 238 ± 10 mL, $P = 0.047$) and greater cardiac dyssynchrony as detected by 3D ECHO (SDI: 13 ± 3% vs. 9 ± 3%, $P = 0.005$) and TDI in twelve segments (138 ± 31 msec vs. 102 ± 37 msec, $P = 0.026$). After CRT, only the patients in GI presented reduced SDI values (Fig. 5). ROC curve analysis yielded cutoff values for SDI $>$ 11%, which were associated with LVRR and symptomatic improvement.

After logistic regression analysis, SDI was the only independent predictor for LVRR after CRT. Patients with SDI $>$ 11%, LVEDV $\leq$ 335 mL, LVEF $\geq$ 0.22 estimated by 3D ECHO, and a left ventricular diastolic diameter (LVDD) $<$ 72 mm before CRT were more likely to present with LVRR 6 months after CRT. Cardiac dyssynchrony, as evaluated by 3D ECHO (SDI $>$ 11%) was the only independent factor in the prediction of LVRR 6 months after CRT (with sensitivity of 0.89 and specificity of 0.73; area under the curve was 0.82) (Fig. 6).

After logistic regression analysis, an equation balancing the three most relevant variables related to LVRR was constructed:

$$\text{LVRR} = -0.4\ \text{LVDD (mm)} + 0.5\ \text{LVEF (\%)} + 1.1\ \text{SDI (\%)}.$$

Output values that were greater than zero identified the responders. The positive and predictive values of this equation were estimated at

TABLE I

Baseline Characteristics

Variable	GI (9)	GII (15)	P
Age (years) (mean ± SD)	60 ± 9	59 ± 10	0.714
Male patients (N%)	2/9 (22%)	7/15 (46%)	0.225
Arterial systemic hypertension (N%)	7/9 (78%)	11/15 (73%)	0.603
Diabetes mellitus (N%)	3/9 (33%)	2/15 (33%)	0.255
Idiopathic etiology (N%)	9/9 (100%)	13/15 (87%)	0.225
New York Heart Association (NYHA) (N%)			
Functional class III	8/9 (89%)	14/15 (93%)	0.620
Functional class IV	1/9 (11%)	1/15 (7%)	
MLHFQ (mean ± SD)	62 ± 17	60 ± 25	0.859
Medical treatment (N%)			
ACE inhibitors/ARBs	9/9 (100%)	14/15 (93%)	0.625
Beta-blockers	9/9 (100%)	14/15 (93%)	0.620
Spironolactone	9/9 (100%)	13/15 (87%)	0.380
Diuretics	9/9 (100%)	14/15 (93%)	0.620
Digitalis	6/9 (67%)	10/15 (69%)	0.668
QRS duration (msec) (mean ± SD)	163 ± 16	161 ± 26	0.763
PR interval (msec) (mean ± SD)	200 ± 19	212 ± 49	0.305
LVDD (mm) (mean ± SD)	70 ± 5	75 ± 11	0.193
LA (mm) (mean ± SD)	48 ± 4	47 ± 6	0.644
LVEDV (Simpson) (mL) (mean ± SD)	230 ± 35	316 ± 14	**0.045**
LVESV (Simpson) (mL) (mean ± SD)	178 ± 30	238 ± 10	**0.047**
LVEF (Simpson) (mean ± SD)	0.24 ± 0.04	0.22 ± 0.04	0.178
LVDV (3D ECHO) (mL) (mean ± SD)	219 ± 37	268 ± 122	0.171
LVSV (3D ECHO) (mL) (mean ± SD)	166 ± 26	209 ± 101	0.135
LVEF (3D ECHO) (mean ± SD)	0.24 ± 0.05	0.23 ± 0.05	0.475
SDI (%) (mean ± SD)	13 ± 3	9 ± 3	**0.005**
LV mass (g) (mean ± SD)	238 ± 38	260 ± 79	0.462
Sphericity index (mean ± SD)	0.47 ± 0.04	0.48 ± 0.08	0.395
TDI (msec)			
4S	74 ± 31	68 ± 37	0.672
6S	89 ± 34	86 ± 38	0.858
12S	138 ± 31	102 ± 37	**0.026**

*Values are expressed as the mean ± standard deviation (SD). Bold values demonstrate statistically significant differences. MLHFQ = Minnesota Living with Heart Failure Questionnaire; LVDD = left ventricular diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; SD: systolic dyssynchrony index; TDI = tissue Doppler imaging.

0.75 and 0.81, respectively, with an accuracy of 0.79. The sensitivity of this equation for predicting LVRR was calculated at 0.67, and the specificity was calculated at 0.87. The best results were obtained when the values of LVDD, LVEF, and SDI were contained in the following intervals:

Echocardiographic Parameters	Minimum	Maximum
LVDD (mm)	63	95
LVEF (%)	13	34
SDI (%)	3	17

An example of M-mode echocardiogram and SDI analysis from a responder patient is demonstrated in Figure 7.

Eight full-volume datasets of different patients were analyzed with respect to inter- and intraobserver variability. For the intraobserver analysis, the quantification of LVEDV, LVESV, LVEF, and SDI was performed for a second time with a 30-day interval between the first and second analyses. The intraclass correlation coefficient (ICC) was 0.95 for both intra- and interobserver variability for the analysis of LVEDV.

The analysis of LVESV yielded an ICC of 0.97 and 0.95 for intraobserver and interobserver variability, respectively. The ICC for the LVEF analysis was 0.97 for intraobserver variability and 0.92 for interobserver variability. For the SDI, the ICC for intra- and interobserver variation was 0.86 and 0.85, respectively.

TDI and 3D ECHO were compared before and 3 and 6 months after CRT. Comparisons were carried out between TDI 4S and 3D ECHO, TDI 6S and 3D ECHO, and TDI 12S and 3D ECHO. After 3 months of the CRT implant, there was a moderate correlation between TDI 4S and SDI (r = 0.51) and TDI 6S (r = 0.52) and SDI. At baseline and after CRT, there was no strong correlation between TDI 4S, 6S, and 12S and 3D ECHO in the evaluation of cardiac dyssynchrony.

TABLE II

Pre- and Post-CRT Parameters in GI and GII

Variable	GI (9) Pre-CRT	GI (9) Post-CRT	P	GII (15) Pre-CRT	GII (15) Post-CRT	P
NYHA (N %)						
Functional class I	0 CF I	3 CF I	**0.004**	0 CF I	6 CF I	**0.012**
Functional class II	0 CF II	6 CF II		0 CF II	4 CF II	
Functional class III	8 CF III	0 CF III		14 CF III	4 CF III	
Functional class IV	1 CF IV	0 CF IV		1 CF IV	1 CF IV	
MLHFQ (mean ± SD)	62 ± 17	31 ± 22	**0.002**	60 ± 25	34 ± 26	**0.004**
QRS duration (msec) (mean ± SD)	166 ± 14	147 ± 24	**0.013**	161 ± 26	155 ± 53	0.602
PR interval (msec) (mean ± SD)	200 ± 19	146 ± 14	<**0.001**	215 ± 49	161 ± 21	**0.004**
LVEDV (3D ECHO) (mL) (mean ± SD)	219 ± 37	166 ± 138	**0.007**	268 ± 122	282 ± 145	0.291
LVESV (3D ECHO) (mL) (mean ± SD)	166 ± 25	109 ± 35	**0.002**	209 ± 100	228 ± 125	0.126
LVEF (3D ECHO) (mean ± SD)	0.24 ± 0.05	0.36 ± 0.10	**0.008**	0.23 ± 0.05	0.23 ± 0.06	0.326
SDI (%) (mean ± SD)	13 ± 3	8 ± 5	**0.014**	9 ± 3	11 ± 5	0.257
LV mass (g) (mean ± SD)	238 ± 38	213 ± 51	0.059	260 ± 79	293 ± 123	0.082
Sphericity index (mean ± SD)	0.47 ± 0.04	0.42 ± 0.06	0.098	0.48 ± 0.08	0.48 ± 0.09	0.763
TDI (msec)						
4S	74 ± 31	65 ± 33	0.505	68 ± 37	52 ± 34	0.256
6S	89 ± 34	88 ± 43	0.960	86 ± 37	66 ± 35	0.229
12S	138 ± 31	97 ± 52	**0.020**	102 ± 37	84 ± 32	0.211

[*] Values are expressed as the mean ± standard deviation (SD). Bold values demonstrate statistically significant differences. MLHFQ = Minnesota Living with Heart Failure Questionnaire; LVDD = left ventricular diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; SD = systolic dyssynchrony index; TDI = tissue Doppler imaging.

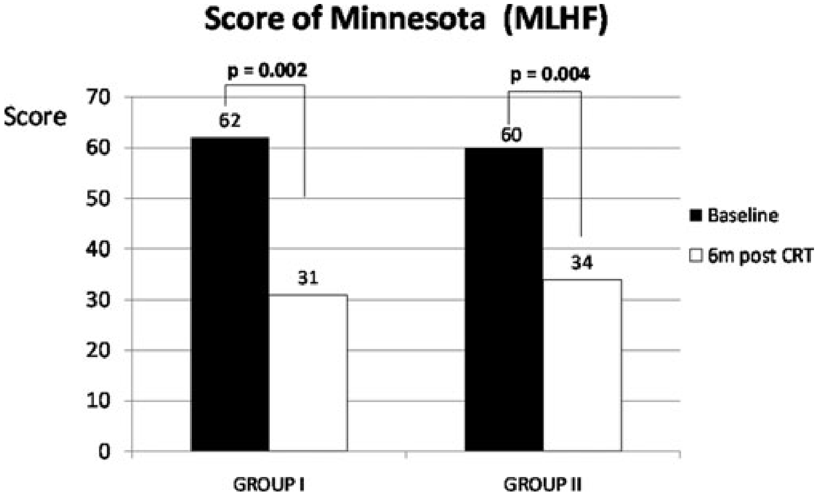


Figure 1. Scores from the Minnesota Living with Heart Failure Questionnaire (MLHFQ) for groups GI (responders) and GII (nonresponders). After 6 months of CRT, the quality of life improved for both groups, as evaluated by MLHFQ.

Discussion:

The correlation between TDI and 3D ECHO for the assessment of cardiac dyssynchrony has been extensively evaluated in recent studies with controversial results.[16–21] In this study, a strong correlation was not found between the TDI and 3D ECHO for evaluating cardiac dyssynchrony.

The discrepancies between TDI and 3D ECHO for evaluating cardiac dyssynchrony may be explained by the fact that these techniques provide distinct information concerning different aspects of cardiac motion. Both methods have advantages and limitations. While TDI evaluates longitudinal contractility, corresponding to only 15% of all cardiac fibers, 3D ECHO integrates the evaluation of radial, circumferential, and longitudinal myocardial contractility. In addition, TDI excludes the analysis of apical segments, evaluates each segment in different cardiac cycles, and is affected by the angle of incidence of the ultrasonic beam.[35]

On the other hand, 3D ECHO evaluates longitudinal, radial and circumferential contraction simultaneously, which provides a better agreement with the anatomic pattern of myocardial fibers. In addition, 3D ECHO evaluates the apical segments, which provides a more complete, robust and accurate measure of the intraventricular mechanical dyssynchrony. At present, the main limitations of 3D ECHO are associated with

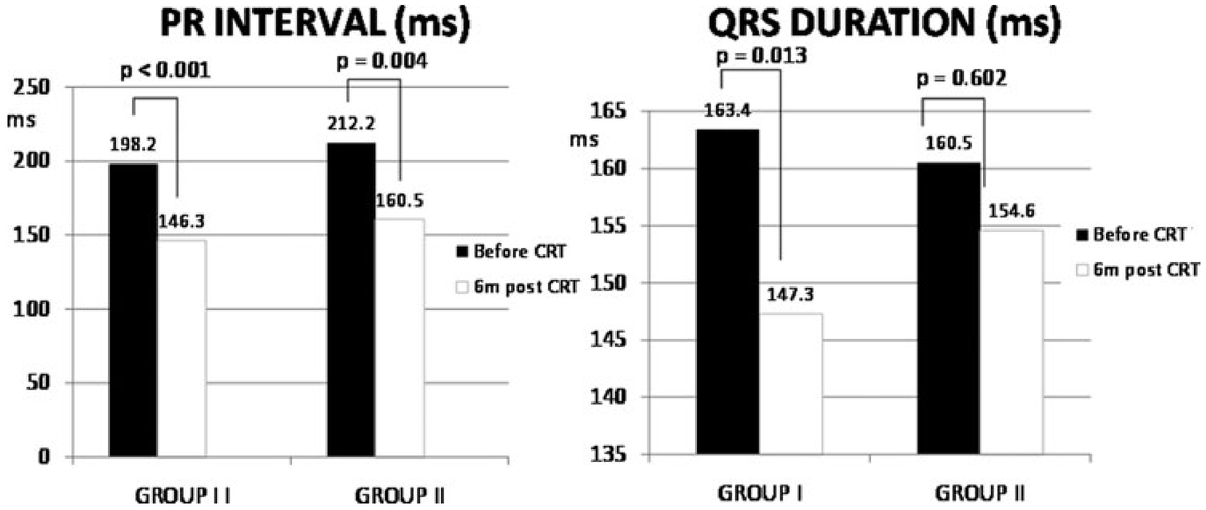


Figure 2. (Left) The mean PR interval duration (msec) before and after CRT in GI (responders) and GII (nonresponders). (Right) The mean QRS complex duration (msec) before and after CRT in GI (responders) and GII (nonresponders).

restricted temporal resolution (15–35 volumes/sec), and dependency on image quality. With the perspective of technological development, the limitation of the temporal resolution of 3D ECHO may be overcome in the near future.

To the best of our knowledge, this is the second study comparing TDI and SDI during CRT follow-up, but it is the first to be restricted to nonischemic cardiomyopathy patients.[21] This study is also the first to evaluate TDI and SDI in a setting of patients with larger left ventricular volumes and smaller LVEF and, probably, patients with more severe cardiac disease. In the study by Klein et al.,[21] cardiac dyssynchrony by TDI and 3D ECHO was evaluated in patients with different left ventricular systolic functions and different etiologies of cardiomyopathy (including ischemic etiology). Klein et al. concluded that marked differences between the techniques were observed for the presence of mechanical dyssynchrony when current cutoff values were applied, making the interchangeability of these techniques uncertain. The authors still suggested that the assessment of mechanical dyssynchrony by 3D ECHO might be an appropriate alternative to TDI for accurate prediction of response to CRT.

In other studies addressing the comparison of cardiac dyssynchrony by TDI and 3D ECHO,[16–21] a single comparison of the two techniques was performed with no follow-up. Additionally, in the present study, after logistic regression analysis, SDI derived from 3D ECHO was the only echocardiographic variable able to predict LV reverse remodeling 6 months after CRT. The sensitivity and specificity of SDI ($>$11% before CRT device implant) were calculated at 0.89 and 0.73, respectively, with an accuracy of 0.78.

At present, a clear cutoff value of 3D ECHO-derived mechanical dyssynchrony for the prediction of response to CRT is lacking. According to recent studies by Soliman et al.,[23,26] an SDI $>$ 10% predicted CRT response (defined as a $>$15% decrease in LVEDV on 3D ECHO) with good

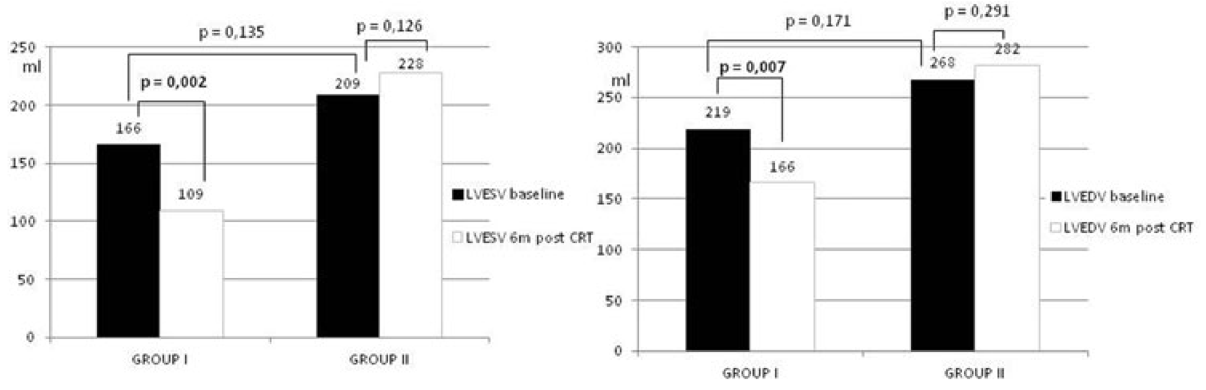


Figure 3. Baseline left ventricular diastolic volumes (LVEDV) (right) and left ventricular systolic volumes (LVESV) (left) between the responder (Group I) and nonresponder (Group II) patients are compared with levels obtained 6 months post-CRT.

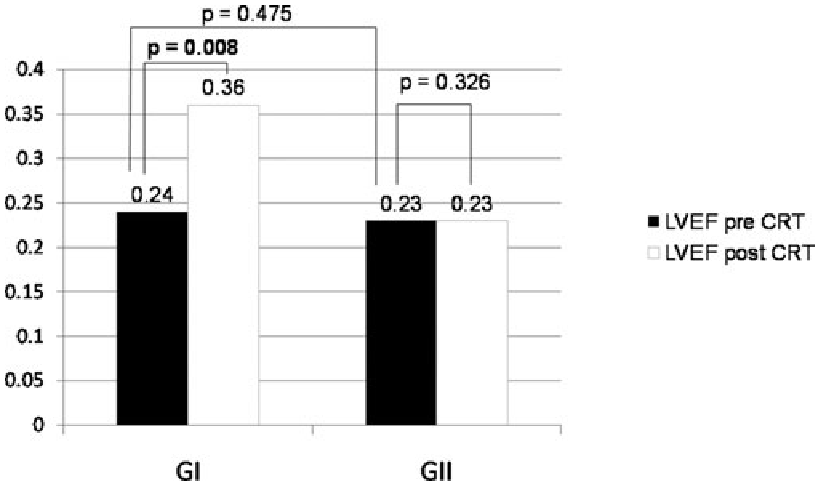


Figure 4. Variation of the mean left ventricular ejection fraction (LVEF), as evaluated by three-dimensional echocardiography before and 6 months after CRT in GI (responders) and GII (nonresponders).

sensitivity (96%) and specificity (88%). Thus, the results of the present study support other recent publications in reinforcing the role of 3D ECHO in the accurate identification of reverse volumetric LV remodeling after CRT, and providing a more intuitive assessment of dyssynchrony and response to CRT via a simple, reproducible, and rapid technique.

In this study, SDI was the only independent factor that could predict LVRR after CRT. 3D ECHO provided important information (SDI, LVEDV, and LVEF) that, coupled with LVDD diameter, was sufficient to determine the probability of CRT response.

Several studies have previously evaluated predictors for the response after CRT.[30–32] It is known that patients with smaller left ventricular diameters and volumes and relatively less severe left ventricular systolic dysfunction, are more prone to present with LVRR. However, this is the first study to establish cutoff values for these variables and to integrate them to estimate the probability of response after CRT. The association of smaller left ventricle volumes and less severe left ventricular systolic dysfunction with a greater probability of LVRR suggests the importance of timing for CRT implantation.

All of the variables included in the equation can be easily and rapidly measured by a trained physician. The indices derived from 3D ECHO can be estimated in approximately 6–10 minutes, and this information, integrated with clinical and

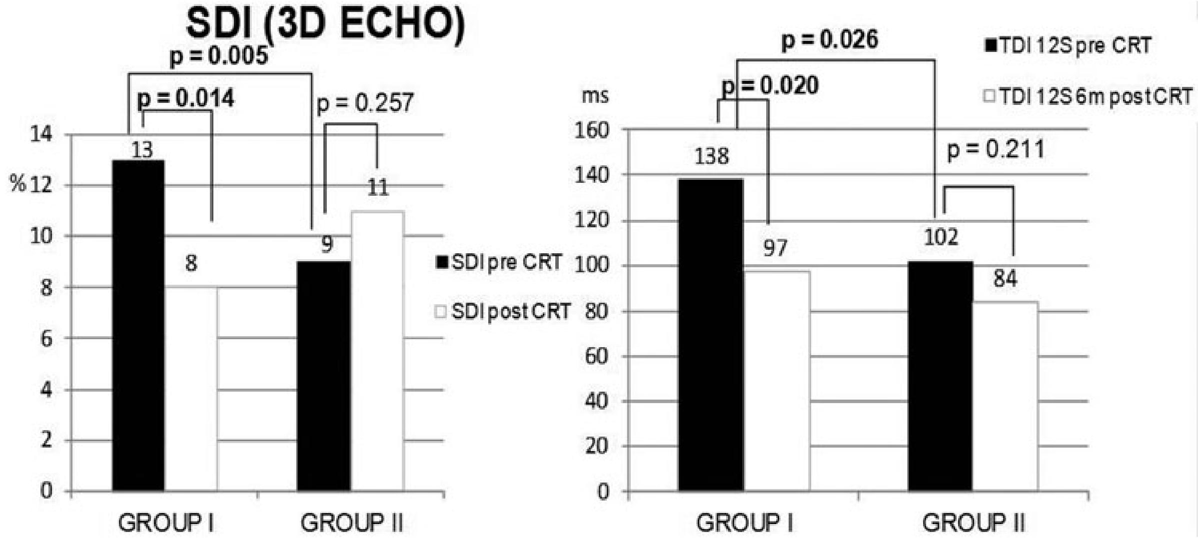


Figure 5. (Left) Variation of the mean SDI (systolic dyssynchrony index) (3D ECHO) before and 6 months post-CRT in GI (responders) and GII (nonresponders). (Right) Mean values of TDI 12S (msec) pre- and post-CRT in GI and GII. GI had more cardiac dyssynchrony, as evaluated by SDI and TDI 12S at baseline. Only the patients in GI demonstrated a reduction in cardiac dyssynchrony after CRT, as evaluated by both methods.

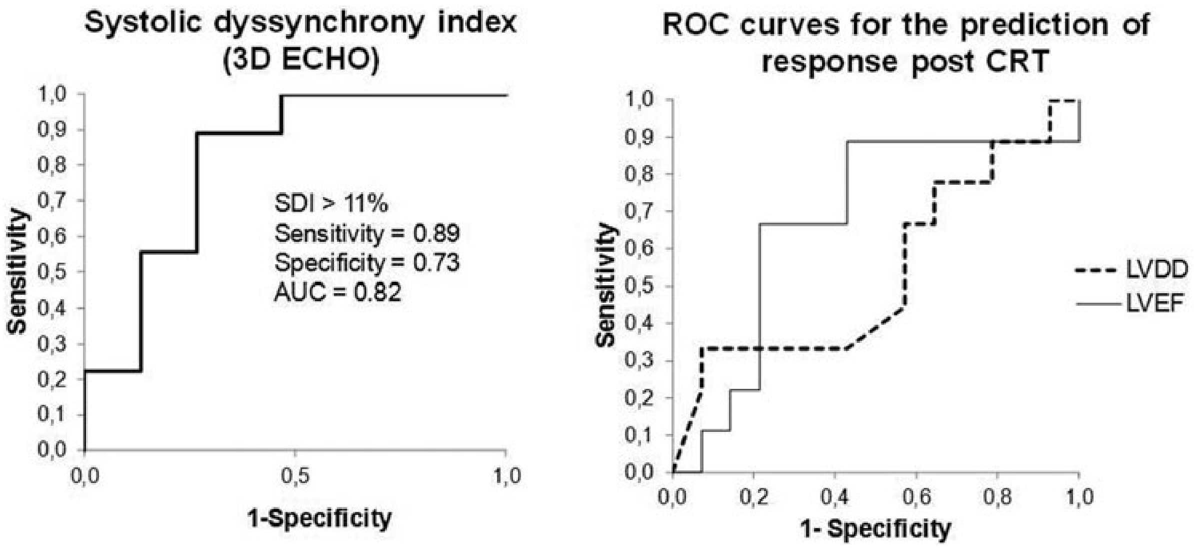
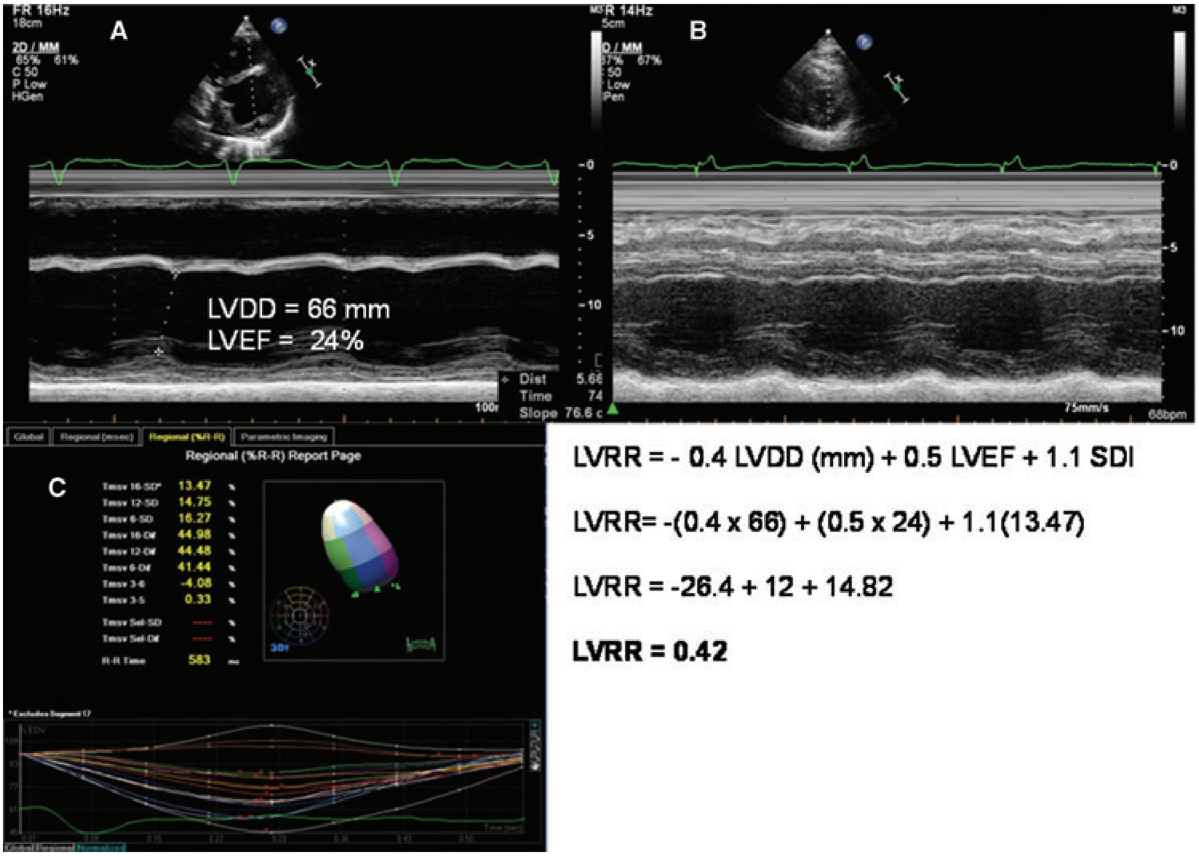


Figure 6. (Left) An SDI > 11% at baseline before CRT yielded a sensitivity of 0.89, a specificity of 0.73, and an area under the curve (AUC) of 0.82 for predicting left ventricular reverse remodeling (LVRR). (Right) ROC curves of left ventricular diastolic diameter (LVDD) and left ventricular ejection fraction (LVEF) at baseline for predicting LVRR after CRT. SDI = systolic dyssynchrony index.



LVRR = - 0.4 LVDD (mm) + 0.5 LVEF + 1.1 SDI

LVRR= -(0.4 x 66) + (0.5 x 24) + 1.1(13.47)

LVRR = -26.4 + 12 + 14.82

LVRR = 0.42

Figure 7. M-mode echocardiogram from a responder patient pre-CRT **A.** and post-CRT **B**. SDI before CRT was estimated in 13.47% **C**. After CRT, the patient presented with reductions of left ventricular volumes and increases in left ventricular ejection fraction (LVEF). LVEDD = left ventricular end diastolic diameter.

electrocardiographic data, can provide more accurate probabilities for assessing the response to CRT. Thus, the selection of patients for this procedure can be more precise, and many patients with a low chance of a positive CRT response can be evaluated for other treatments without being subjected to a risky and ineffective treatment.

Until a "gold standard" method in the evaluation of cardiac dyssynchrony is established, currently available echocardiographic methods must be used in an integrated and complementary manner, coupled with electrocardiographic and clinical data, for guiding clinical decisions.

The formula proposed in this study allows the association of anatomical and functional aspects with left ventricle global dyssynchrony analysis, which integrates information regarding electromechanical coupling, left ventricle anatomy, and function. This stronger association will shed more light on the complex clinical application of CRT.

Despite the lack of a "gold standard" method in the evaluation of cardiac dyssynchrony, echocardiography still remains a promising and useful technique in the selection of candidates to CRT.[36–39] Despite the necessity for improvement in the currently available methods for evaluation of cardiac dyssynchrony, 3D ECHO represents an interesting alternative for this purpose.

More modern methods derived from TDI and new techniques, such as three-dimensional speckle-tracking, can provide novel insights into the effects of CRT on LV performance while permitting the characterization of subendocardial and subepicardial LV twist. These methods may correlate better with SDI derived from 3D ECHO because they are less dependent on the ultrasonic beam incidence angle than are the currently available techniques.[14,15,40–42]

Study Limitations:

The main limitation of this study relates to the number of patients included in the follow-up period. The study population consisted of patients with severe cases of heart failure, which are associated with high rates of mortality. Otherwise, the inclusion criteria were notably strict, and this was a single-center study. Regarding technical aspects, currently available machines provide datasets with low temporal resolution.[42]

Conclusions:

In this study, there was no strong correlation between TDI and 3D ECHO in the evaluation of cardiac dyssynchrony before and after CRT. In this preliminary study, we propose an equation that uses variables from conventional echocardiography (LVDD) and 3D ECHO (LVEF and SDI) to predict LVRR after CRT. Although larger trials are needed to validate these findings, this equation can be of value to patient candidates for CRT in the clinical setting.

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