Utility of three-dimensional echocardiography in assessing and predicting response to cardiac resynchronization therapy

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BACKGROUND: Cardiac resynchronization therapy (CRT) can be a valuable treatment for heart failure. However, there are high nonresponse rates using current CRT inclusion criteria.

OBJECTIVE: To assess the value of three-dimensional echocardiography (3DE) in predicting response to CRT.

METHODS: Functional assessments and 3DE were performed in heart failure patients pre-CRT, 24 h post-CRT and six to 12 months after CRT. The dyssynchrony index (DI) was calculated as the SD of the time to minimum volume in 16 left ventricle segments corrected by heart rate. Response to CRT was defined as functional improvement (alive at late follow-up with improvement by one New York Heart Association class) and a decrease in left ventricular end-systolic volume by 15% or greater at six to 12 months follow-up.

RESULTS: A total of 53 patients were enrolled. Average 3DE acquisition time was less than 5 min. Seventy-two per cent of patients showed functional improvement, while 43% showed functional and echocardiographic evidence of response. Baseline DI and the decrease in DI at 24 h were both correlated with reverse remodelling. Responders had higher baseline DI values compared with nonresponders (mean 16.8 versus 7.1, $P < 0.001$), and showed a greater decrease in DI values at 24 h (mean decrease 7.9 versus 0.7, $P < 0.001$). All responders had baseline DI values of greater than 10 (negative predictive value of 100%). A decrease in the DI value by more than 5 at 24 h in patients with a baseline DI of greater than 10 identified responders with a positive predictive value of 83%.

CONCLUSIONS: 3DE may be valuable in predicting response to CRT. A baseline DI cut-off of greater than 10 in our patients excluded reverse remodelling to CRT. In addition, the decrease in DI at 24 h had a high positive predictive value for long-term response to CRT.

Key Words: Biventricular pacing; Cardiac resynchronization therapy; Dyssynchrony; Heart failure; Three-dimensional echocardiography; Ventricular remodelling

Despite major advances in the treatment of cardiovascular disease, the burden of congestive heart failure (CHF) continues to increase in our society. There are over five million patients suffering from this syndrome in North America, and more than 600,000 new diagnoses are made annually (1). Projections suggest that by the year 2016, the number of people with CHF will increase from 1996 levels by more than 50% in the older than 65 years of age cohort (2). Cardiac resynchronization therapy (CRT) was introduced approximately 18 years previously (3) to reduce dyssynchrony in patients with advanced heart failure by providing coordinated biventricular pacing. Subsequent trials have shown that CRT is associated with

Utilité de l'échocardiographie 3D dans l'évaluation et la prédiction de la réponse au traitement de resynchronisation cardiaque

HISTORIQUE : Le traitement de resynchronisation cardiaque (TRC) peut être utile dans l'insuffisance cardiaque. Or, on constate des taux élevés de non-réponse lorsqu'on utilise les critères d'inclusion actuels du TRC.

OBJECTIF : Évaluer l'utilité de l'échocardiographie 3D à prédire la réponse au TRC.

MÉTHODES : On a soumis des patients atteints d'insuffisance cardiaque à des épreuves fonctionnelles et à des échocardiographies 3D avant un TRC, 24 heures après le TRC et de six à 12 mois après le TRC. L'indice de dyssynchronie (ID) a été calculé sous forme d'écart-type (É.-T.) de l'intervalle avant l'obtention du volume minimum dans 16 segments ventriculaires gauches, corrigé en fonction de la fréquence cardiaque. La réponse au TRC était définie par une amélioration fonctionnelle (patient en vie pour le suivi tardif, avec amélioration d'une classe de la NYHA) et une diminution de 15 % ou plus du volume téléstolique ventriculaire gauche après six à 12 mois de suivi.

RÉSULTATS : En tout, 53 patients ont été inscrits. Le temps d'acquisition de l'échographie 3D moyen a été de moins de cinq minutes. Soixante-douze pour cent des patients ont manifesté une amélioration fonctionnelle, tandis que 43 % ont présenté des signes de réponse fonctionnelle et échocardiographique. L'ID de départ et la diminution de l'ID à 24 heures étaient tous deux en corrélation avec le remodelage inverse. Les sujets qui ont répondu présentaient un ID plus élevé au départ comparativement à ceux qui n'ont pas répondu (moyenne 16,8 vs 7,1, $p < 0,001$) et ont manifesté une baisse plus marquée de leur ID à 24 heures (baisse moyenne de 7,9 vs 0,7, $p < 0,001$). Tous les sujets ayant répondu présentaient des ID de plus de 10 au départ (valeur prédictive négative 100 %). Une baisse de l'ID de plus de 5 après 24 heures chez les patients dont l'ID était supérieur à 10 au départ a permis de reconnaître ceux qui répondaient avec une valeur prédictive positive de 83 %.

CONCLUSIONS : L'échocardiographie 3D peut être utile pour prédire la réponse au TRC. Un ID seuil supérieur à 10 au départ chez nos patients a permis d'exclure le remodelage inverse au TRC. De plus, la baisse de l'ID à 24 heures s'accompagnait d'une forte valeur prédictive positive pour ce qui est de la réponse à long terme au TRC.

consistent reductions in all-cause mortality, as well as significant improvements in functional class and left ventricular (LV) function (4,5). Consequently, CRT is currently recommended for patients with advanced heart failure (New York Heart Association [NYHA] class 3 or 4), poor LV function (LV ejection fraction [LVEF] lower than 35%) and evidence of ventricular dyssynchrony in spite of maximal medical therapy (6).

The original trials used prolonged QRS duration as a major inclusion criterion for CRT (4,5,7). Accordingly, only patients with QRS durations of greater than 120 ms were recommended for the procedure. However, QRS duration was subsequently shown to be a

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poor predictor of CRT response, with nonresponse rates of up to 40% (4,7). There is also strong evidence that many patients with narrower QRS durations might benefit from CRT (8-11). Consequently, there is a need to establish novel criteria to define patients who are likely to benefit from CRT.

Echocardiography has emerged as a promising tool for quantifying dyssynchrony and predicting response in CRT candidates (12). However, none of the presently established echocardiographic methods for assessing dyssynchrony are accurate enough to be recommended for routine clinical use (13). Three-dimensional echocardiography (3DE) is a relatively new echocardiographic modality that permits assessment of all the individual LV segments in real time during one cardiac cycle (14). In the present report, we describe our experience with the use of 3DE in assessing and predicting patient response to CRT.

METHODS

Patients

All patients who underwent successful CRT implementation at Sunnybrook Health Sciences Centre (Toronto, Ontario) from 2005 to 2007 were included in the present study. Heart failure patients at the institution were considered for CRT if they had an LVEF of less than 35%, QRS duration of greater than 150 ms or QRS duration of greater than 100 ms plus echocardiographic evidence of dyssynchrony, and symptoms worse than NYHA class 2 in spite of optimal medical therapy for more than six months. Patients were excluded if they had a significant comorbidity that severely limited life expectancy or quality of life, had acute myocardial infarction within one month, or underwent coronary artery bypass graft surgery or percutaneous coronary intervention within three months. Clinical and device assessments were performed perioperatively, one week postoperatively and every three months thereafter. Conventional two-dimensional echocardiography (2DE) and 3DE were performed preoperatively, 24 h postoperatively, and six to 12 months later (late follow-up). Functional class by NYHA classification and 3DE acquisition time were also recorded with each assessment.

Echocardiography and 3DE

Echocardiography was performed with Sonos 7500 and iE33 echocardiographic imaging systems (Philips Medical Systems, USA). Standard parasternal apical four- and two-chamber views were used for two-dimensional, M-mode and Doppler assessments.

The methodology for 3DE has been detailed elsewhere (15). Briefly, an X4 matrix array transducer (Philips Medical Systems) was used to acquire full-volume data sets of the entire left ventricle at the apex. Each data set was obtained over four consecutive cardiac cycles and required a relatively stable RR interval. A minimum of two data sets were obtained during every study. Data sets for 3DE were digitally stored and analyzed using Philips integrated online software (QLAB version 5.0, 3DQ Advanced; Philips Medical Systems). The acquisition time for each 3DE was recorded.

The apical four- and two-chamber views through the pyramidal three-dimensional data set were considered to be the fundamental planes. End-diastolic and end-systolic frames, visually determined as the largest and smallest LV cavity volumes in the cardiac cycle, respectively, were selected for analysis. The endocardial border of each frame was traced using a semiautomated detection process, with subsequent manual adjustment of the endocardial border if needed. A three-dimensional model of the left ventricle was then generated and subdivided into 17 volumetric segments according to the American Society of Echocardiography 17-segment model (16). LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV) and LVEF were calculated.

The most apical segment was excluded due to its low contribution to overall dyssynchrony measures. Regional time-volume curves were derived for the 16 remaining segments. The SD of the time to the minimal systolic volume for all 16 segments (Tsmv-16-SD), expressed

as a percentage of the RR interval in seconds, was used to derive the dyssynchrony index (DI):

$$DI = Tsmv-16-SD \times 100/RR \text{ interval}$$

Higher DI values correspond to greater mechanical dyssynchrony.

Response to CRT

Patients were classified as clinical responders if they met the following criteria six to 12 months post-CRT:

- 1) Remained alive without needing cardiac transplantation; and
- 2) Functional class improvement by one or more NYHA class.

Patients were classified as showing reverse remodelling if they fulfilled the following criteria:

- 1) Remained alive without requiring cardiac transplantation six to 12 months post-CRT; and
- 2) Decrease of LVESV by at least 15% of the baseline value.

Echocardiographic evidence of reverse remodelling (rather than clinical improvement) was chosen as the primary measure of response to CRT due to its superior prognostic value in CRT recipients (17).

Statistical analysis

One-tailed, paired *t* tests were used to compare values of LVEF, LVEDV, LVESV and DI before and after CRT (acutely and at six to 12 months post-CRT). Two-tailed *t* tests assuming unequal variance were used to compare echocardiographic characteristics of responders and non-responders. Linear regression analysis was performed to determine the relationship between LV reverse remodelling with baseline DI and the change in DI 24 h post-CRT. The absolute change in LVEF at six to 12 months was also compared with the baseline DI and acute change in DI 24 h post-CRT. For all tests, a value of *P* < 0.05 was considered to be statistically significant.

RESULTS

Patient characteristics

Fifty-three consecutive patients underwent successful CRT implantation at the centre from 2005 to 2007. The patients' baseline characteristics are shown in Table 1. The mean age of patients was 68 years. There were 44 men (83%) and nine women (17%). Ischemic heart disease was the etiology of heart failure in 36 patients (68%). Five patients (9%) had NYHA class 2 heart failure symptoms, while the rest were in class 3 or 4. The average preprocedural LVEF was 25%. Eight patients with controlled atrial fibrillation and eight with a paced rhythm were included; the remaining patients were in sinus rhythm.

Procedure

All patients received CRT through the transvenous approach. Atrial leads were placed in the right atrial appendage in 42 patients. Right ventricle leads were placed in the right ventricular apex in all cases. LV leads were placed in either the posterior lateral or the lateral branch of the coronary vein in 51 patients and in the anterolateral branch in two patients. All of the implanted devices had defibrillator capabilities.

Clinical follow-up

Fifty-three patients were followed for an average of 9.2 months. Four patients died during that period. There were two heart failure-related deaths; one patient died as the result of a massive stroke. One patient received a cardiac transplantation because of progressive CHF. Two patients required lead repositioning. Five patients were transferred to another centre for follow-up and were consequently unavailable for late echocardiographic follow-up.

At the last visit, 38 patients (72%) reported NYHA class 2 functional capacity or clinical improvement of at least one class.

TABLE 1
Baseline characteristics of the cohort of recipients of cardiac resynchronization therapy (CRT) (n=53)

Characteristic	
Age, years, mean $\pm$ SD	68.0 $\pm$ 12
Male sex	44 (83)
Ischemic heart failure etiology	36 (68)
Duration of disease, months	
$\leq$ 24	5 (9.4)
>24	48 (90.6)
Rhythm	
Sinus	37 (70)
Atrial fibrillation	8 (15)
Paced	8 (15)
Left bundle branch block	23 (43)
Right bundle branch block	5 (9.4)
Nonspecific intraventricular conduction delay	17 (32)
QRS duration, ms, mean $\pm$ SD	166 $\pm$ 37
Pre-CRT medications	
ACE inhibitor/angiotensin receptor blocker	48 (90)
Beta-blocker	42 (79)
Digoxin	20 (38)
Loop diuretic*	50 (94)
Spironolactone	6 (11)

Data presented as n (%) unless otherwise indicated. *Three patients were dialysis dependent. ACE Angiotensin-converting enzyme

TABLE 2
Three-dimensional echocardiography-derived parameters of interest before cardiac resynchronization therapy (CRT), 24 h post-CRT and at late follow-up

Variable	Pre-CRT (n=50)	24 h post-CRT (n=50)	6 to 12 months post-CRT (n=40)
LVEF, %	25.0	28.2*	32.8*
LVEDV, mL	171.5	171.4 [†]	167.0 [†]
LVESV, mL	129.7	124.6*	115.0 [‡]
DI	10.6	8.1 [‡]	7.13 [‡]

* $P < 0.001$ for comparison with pre-CRT values, using one-tailed paired t test;

[†] $P < 0.05$ for comparison with pre-CRT values, using one-tailed paired t test;

[‡] $P < 0.01$ for comparison with pre-CRT values, using one-tailed paired t test. DI Dyssynchrony index; LVEDV Left ventricular end-diastolic volume; LVEF Left ventricular ejection fraction; LVESV Left ventricular end-systolic volume

3DE follow-up

Three patients had poor endocardial definition on initial echocardiographic assessment and were not included in the analyses of echocardiographic variables. Fifty patients had adequate pre-CRT and 24 h post-CRT 3DEs. Four patients died, one was transplanted and five were followed up at different centres. The 40 remaining patients had repeat 3DE at an average of 9.2 months after their successful CRT procedure. Each 3DE required an additional 5 min on average compared with standard 2DE.

Table 2 shows the values of DI, LVEF, LVESV and LVEDV at baseline (pre-CRT; 50 patients), 24 h post-CRT (50 patients) and at late echocardiographic follow-up (40 patients). The average DI decreased acutely from 10.6 to 8.1, and further decreased to 7.13 at late follow-up ($P < 0.01$ for both comparisons). LVEF showed a small but significant improvement within 24 h of CRT from 25.0% to 28.2%, and this value further increased to 32.8% at late follow-up in transplant-free survivors ($P < 0.001$ for both comparisons). The mean LVESV decreased acutely post-CRT from 129.7 mL to 124.6 mL ($P = 0.04$), and further decreased to 115 mL at late follow-up ($P = 0.0013$).

TABLE 3
Comparison of three-dimensional echocardiography-derived measures of interest between responders and nonresponders to cardiac resynchronization therapy

	Responders	Nonresponders	P
Baseline DI	16.8 $\pm$ 6	7.1 $\pm$ 4	<0.001
24 h change in DI	-7.9 $\pm$ 3	-0.7 $\pm$ 5	<0.001
Baseline LVEF, %	21.8 $\pm$ 7	27.5 $\pm$ 6	<0.01
Baseline LVESV, mL	126 $\pm$ 28	130 $\pm$ 50	0.72
Absolute change in LVEF, %	+16.5 $\pm$ 7	+1.22 $\pm$ 4	0.010
Relative change in LVESV, %	-30.6 $\pm$ 12	+3.3 $\pm$ 10	<0.001

Data presented as mean $\pm$ SD. P values are for two-tailed t tests comparing responders and nonresponders, assuming unequal variance of a given variable within the groups. Data are reported for 17 responders. The 24 h changes in dyssynchrony index (DI), baseline left ventricular ejection fraction (LVEF) and baseline left ventricular end-systolic volume (LVESV) data are reported for 28 nonresponders (alive and dead). Data on the absolute change in LVEF and relative change in LVESV are reported for 23 transplant-free living nonresponders

Figure 1 The distribution of dyssynchrony index (DI) values at baseline in cardiac resynchronization therapy (CRT) recipients, divided based on their response to CRT. All the responders to CRT had baseline DI values of greater than 10, while nonresponders had values above and below 10

Responders versus nonresponders

Table 3 shows differences in echocardiographic variables between responders and nonresponders. Using the defined criteria for echocardiographic response, there were 17 responders to CRT, with a mean decrease in LVESV by 30.6% of the baseline value. Echocardiographic nonresponders, on the other hand, had a 3.3% relative increase in LVESV. All patients meeting the criteria for reverse remodelling also showed an improvement in LVEF and reported clinical improvement. However, 21 of the patients who improved clinically did not meet the criteria for LV reverse remodelling.

The baseline DI in the responder group was significantly higher than in the nonresponder group (mean values 16.8 versus 7.1, $P < 0.001$). Figure 1, a plot of baseline DI values in responders and nonresponders, demonstrates that none of the responders had a baseline DI value of less than 10. Figure 2 displays a plot of 3DE-measured mechanical dyssynchrony (DI) at baseline against the change in LVESV, while Figure 3 plots baseline DI against LVEF at late follow-up. Both plots demonstrate the correlation of baseline DI with the magnitude of remodelling and improvement in ventricular function ($R^2 = 0.40$ and 0.51 , respectively).

Responders to CRT also showed a greater decrease in 3DE-measured dyssynchrony 24 h post-CRT compared with nonresponders (mean absolute decrease 7.9 versus 0.7, $P < 0.001$). Figure 4 represents the

Figure 2) Graph of baseline dyssynchrony index (DI) values versus relative change in left ventricular end-systolic volume (LVESV) at late follow-up. DI values at baseline correlated with the relative decrease in LVESV ($R^2=0.40$)

Figure 3) Graph of baseline dyssynchrony index (DI) values versus absolute change in left ventricular ejection fraction (LVEF) at late follow-up. DI values at baseline correlated with the absolute improvements in LVEF ($R^2=0.51$)

relationship between the acute (24 h) change in DI and the relative change in LVESV, while Figure 5 demonstrates the absolute change in LVEF. A good correlation was observed between the decrease in dyssynchrony at 24 h and the magnitude of improvement in LVESV and LVEF at late follow-up ($R^2 = 0.48$ and 0.53 , respectively).

Analysis of responders and nonresponders (Table 4) showed that an empirically derived cut-off at a baseline DI of greater than 10 allowed prediction of echocardiographic response to CRT with a sensitivity of 100% and a specificity of 75%, corresponding to a positive predictive value of 70.8% and a negative predictive value of 100%. When patients with a baseline DI of greater than 10 were observed to have a decrease in DI by more than 5 at 24 h post-CRT, the specificity increased to 89.3% and the positive predictive value rose to 83.3%.

Figure 4) Graph of absolute change in dyssynchrony index (DI) values 24 h postcardiac resynchronization therapy (CRT) versus the relative change in left ventricular end-systolic volume (LVESV) at late follow-up. The decrease in DI correlated with the reduction in LVESV ($R^2=0.48$)

Figure 5) Graph of absolute change in dyssynchrony index (DI) values 24 h postcardiac resynchronization therapy (CRT) versus the absolute change in left ventricular ejection fraction (LVEF) at late follow-up. The decrease in DI showed good correlation with the improvement in LVEF ($R^2=0.53$)

DISCUSSION

The present report describes our experience with real-time 3DE in a cohort of 53 CRT recipients. The cohort had an echocardiographic nonresponse rate of 62% and a clinical nonresponse rate of 38%, demonstrating the poor predictive value of present methods of selecting CRT candidates. We found that 3DE was easily integrated into our practice, with satisfactory images obtained in 94% of our cohort at an average additional time cost of 5 min. More importantly, we observed that measures of dyssynchrony in the form of the DI allowed accurate discrimination of nonresponders to CRT. Using an empirical cut-off at a DI of greater than 10, we were able to identify nonresponders with a

negative predictive value of 100%. Incorporation of measures of acute synchronization at 24 h allowed further distinction between responders and nonresponders. Using a combined cut-off at a baseline DI of greater than 10 and a decrease in DI by more than 5, responders to CRT were identified with a positive predictive value of 83%.

The principal mechanism of action of CRT is to reduce ventricular mechanical dyssynchrony (18), leading to increased cardiac work efficiency (19) and promoting reverse remodelling in the long term (17,20). The main Achilles heel continues to be the large proportion of nonresponders, as demonstrated in our cohort. In the recently published results of the Predictors of Response to CRT (PROSPECT) trial, Chung et al (21) reported an echocardiographic nonresponse rate of 44% and a clinical nonresponse rate of 31%. The large nonresponse rates have spurred a plethora of research to more accurately select patients for CRT. Bleeker et al (18) recently reported that reverse remodelling is dependent on mechanical resynchronization as measured by tissue Doppler imaging. However, none of the methods available today have been shown to predict response before patients undergo the implantation procedure. Electrocardiogram-based platforms, including QRS duration, have been unhelpful (11,22). M-mode-based variables such as septal-to-posterior wall motion delay have been shown to not be significantly different between responders and nonresponders (23,24). Several other studies have reported the poor predictive value of other variables derived from 2DE platforms (21,25,26). In particular, the recently published PROSPECT trial results highlighted the poor predictive value and significant variability in measuring mechanical dyssynchrony using 12 two-dimensional tissue Doppler-derived parameters (21).

Unlike 2DE-based platforms, the quantification of mechanical dyssynchrony with real-time 3DE simultaneously includes all myocardial segments by examining the composite effect of radial, circumferential and longitudinal asynchrony of regional contraction. Thus, 3DE theoretically allows a more complete analysis of dyssynchrony within the whole left ventricle compared with 2DE-based platforms. Kapetanakis et al (15) reported that 3DE-derived dyssynchrony measures were low in healthy subjects, and increased with worsening LV systolic function. They also showed that 3DE-derived dyssynchrony measures improved in 26 patients undergoing CRT. CRT responders had higher baseline dyssynchrony measures and showed greater reductions in dyssynchrony after CRT compared with nonresponders. Van Dijk et al (27) recently showed that the acute hemodynamic response in 17 patients undergoing CRT was significantly correlated with 3DE-derived dyssynchrony measures.

Our report confirms and expands on previous observations by reporting on our experience with a larger cohort of 53 patients. We found that the degrees of improvement in LVEF and reverse remodelling at six to 12 months were both correlated with the degree of baseline dyssynchrony measured by 3DE and with the degree of resynchronization at 24 h post-CRT. One of our important observations is that none of the patients showed echocardiographic remodelling in response to CRT if the baseline DI was 10 or lower (negative predictive value of 100%). In patients with a baseline DI of greater than 10, we were able to predict long-term response with a high level of accuracy (positive predictive value of 83%) at 24 h if we observed a decrease in 3DE-derived DI by more than 5.

These results will need further prospective validation, but they suggest that the 3DE-derived DI might provide a simple, noninvasive way to identify patients who would not benefit from CRT. The baseline DI value could be used to exclude candidates unlikely to benefit from CRT – thus, potentially saving many patients from an unnecessary invasive, expensive procedure with nonzero risk. Once the procedure is performed, the degree of synchronization at 24 h could be used to inform patients of their likelihood to respond to CRT in the long term and to direct further treatment.

Limitations

Our study was a single-centre, nonrandomized, nonblinded retrospective observational study with an inherent design bias. However, the data used to generate our conclusions were objective and were

TABLE 4

Operating characteristics of baseline dyssynchrony index (DI) of greater than 10 and a decrease in DI by greater than 5 as predictive tests of response to cardiac resynchronization therapy

Baseline DI>10*	Improvement (Δ LVESV < -15%)	No improvement (Δ LVESV $\geq$ -15%)	Total
DI>10?			
Yes (DI>10)	17	7	24
No (DI $\leq$ 10)	0	21	21
Total	17	28	45
Baseline DI>10 and decrease in DI by >5†			
Both values positive?			
Yes (DI>10 and decrease in DI>5)	15	3	18
No (DI $\leq$ 10 or decrease in DI $\leq$ 5)	2	25	27
Total	17	28	45

Data presented as n. *Sensitivity: 100%, specificity: 21/28=75%, positive predictive value: 17/24=70.8%, negative predictive value: 100%; †Sensitivity: 15/17=88.2%, specificity: 25/28=89.3%, positive predictive value: 15/18=83.3%, negative predictive value: 25/27=92.6%. LVESV Left ventricular end-systolic volume

collected prospectively. In addition, our sample size limited our ability to perform an assessment of interaction between different preoperative clinical parameters. It may also limit the generalizability of our results. Furthermore, our DI cut-off was not derived prospectively, and it would be premature to exclude present CRT candidates from treatment before these results are prospectively validated. Such prospective validation would ideally use hard end points such as mortality instead of the surrogate measure of echocardiographic remodelling that we used.

Another limitation is that we did not perform objective measurements of clinical response such as the 6 min walk test. This could confound our findings of clinical response because we have observed a possible placebo effect in patients who had no evidence of cardiac reverse remodelling. This discrepancy in rates of clinical response and echocardiographic improvement has been reported previously (17,21). As described above, we chose to primarily follow echocardiographic remodelling markers as evidence of therapeutic benefit given its objectivity and tighter correlation with patient outcome post-CRT.

The 3DE technology itself has several limitations. The full-volume loop was compiled using data from four consecutive cardiac cycles. Dyssynchrony assessments could be considerably compromised by significant variation of the RR interval during the four acquired cycles (as can occur in atrial fibrillation or premature contractions). In addition, recognition of the endocardial border is crucial in assessing segmental volume changes – we were unable to obtain adequate images for 3DE dyssynchrony analysis in three of our 53 patients. Furthermore, inter- and intraobserver variability were not systematically examined in our study. Because the 3DE analysis is mainly software driven, the semiautomated detection process of recognizing the endocardial border by an individual observer is the principal source of variability. In our experience, the newer machine (iE33) and software version (5.0) have improved imaging quality, which leads us to believe that further improvement of technological capabilities will further enhance 3DE capabilities.

CONCLUSION

We have described our single-centre experience with using real-time 3DE in the context of providing CRT to 53 patients. Analysis of our cohort demonstrates the tantalizing possibility of using

3DE-derived dyssynchrony measures in the assessment of CRT candidates. We found that a DI cut-off of greater than 10 may allow identification of CRT nonresponders with a negative predictive value of 100%. Subsequent observation of an absolute decrease in DI by more than 5 at 24 h post-CRT in patients with a baseline DI of greater than 10 predicted echocardiographic remodelling with a positive predictive value of 83%. We also observed strong correlations in the degree of remodelling and LVEF improvement at six to 12 months with both baseline DI and with a decrease in DI at 24 h post-CRT. Our data should encourage

further prospective assessments of the ability of 3DE to improve on current criteria for selection of CRT recipients.

DISCLOSURES: All authors had full access to and take responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

CONFLICTS OF INTEREST: None of the authors have any conflicts of interest to declare.

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