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Real-Time 3-Dimensional Echocardiographic Assessment of Left Ventricular Dyssynchrony

Pitfalls in Patients With Dilated Cardiomyopathy

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OBJECTIVES This study sought to establish normal values for real-time 3-dimensional echocardiography (RT3DE)–derived left ventricular (LV) dyssynchrony index (LVDI) and determine its age dependency, and to compare dyssynchrony in patients with normal LV function and patients with dilated cardiomyopathy (DCM), with and without left bundle branch block (LBBB).

BACKGROUND Cardiac resynchronization therapy is known to be ineffective in one-third of patients with heart failure, highlighting the need for alternative techniques to assess LV dyssynchrony.

METHODS Datasets from RT3DE were analyzed to calculate LVDI using 16- and 17-segment models. First, 135 normal subjects were studied to establish LVDI abnormality threshold (mean + 2 SD) and to study the relationship with age. Then, 3 groups of patients (N = 16 each: DCM with and without LBBB, normal LV function with LBBB) were compared with 50 age-matched normal control subjects.

RESULTS In normal subjects, the 16-segment model resulted in a lower LVDI abnormality threshold than the 17-segment model (4.0% vs. 4.5%). In patients with normal LV function, LVDI was significantly lower than in those with DCM, irrespective of LBBB. Although LBBB resulted in a nearly 2-fold increase in LVDI in patients with normal LV function, its effects were nonsignificant in DCM. All patients with DCM and ejection fraction <35% had abnormally high LVDI, likely as a result of low signal-to-noise ratio in low-amplitude regional volume curves hampering accurate determination of regional ejection time.

CONCLUSIONS Normal values established in this study resulted in indiscriminate diagnosis of abnormal dyssynchrony in all patients with reduced LV function. The value of RT3DE-derived LVDI in the evaluation of dyssynchrony in patients with reduced LV function needs to be critically reassessed because of the inability to accurately detect end-ejection in low-amplitude regional volume curves. Alternative indices of dyssynchrony need to be developed to address this limitation. (J Am Coll Cardiol Img 2009;2:802–12) © 2009 by the American College of Cardiology Foundation

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Although cardiac resynchronization therapy (CRT) is known to benefit most patients with heart failure (HF), the inability to show a positive response in up to one-third of the patients in whom CRT is indicated has highlighted the need for redefining the selection criteria for CRT (1) and triggered a search for alternative approaches. Currently, a prolonged QRS complex on 12-lead electrocardiogram (ECG) is a prerequisite to select patients for CRT, in addition to left ventricular (LV) ejection fraction (LVEF) under 35% and severe HF (New York Heart Association functional class III/IV) (2–5). However, several recent studies have shown that QRS width is a poor predictor of response to CRT (6–10). Importantly, because LV dyssynchrony was shown to be a predictor of severe cardiac events, independent of QRS width and LVEF (7), the search for alternative echocardiographic methods to evaluate mechanical LV dyssynchrony has gained increasing attention.

See page 813

Tissue Doppler imaging (TDI) assessment of LV dyssynchrony is considered the standard technique for selection of patients for CRT. Despite its excellent temporal resolution, this technique has several limitations, including the inability to assess multiple myocardial segments simultaneously, angle dependency that limits the evaluation of the timing of motion in the longitudinal direction only, and the inability to reliably quantify apical wall motion. In addition, no single echocardiographic measure of dyssynchrony is currently recommended to improve patient selection for CRT beyond current guidelines (11,12).

Real-time 3-dimensional echocardiography (RT3DE) is a simple and reproducible method for measuring LV dyssynchrony (6), free of the above limitations of TDI. This technique is capable of capturing the 3D dynamics of the entire LV, including the timing of wall motion, independent of its direction. Accordingly, it has been postulated that this technique may prove useful in the selection of patients for CRT. However, because a certain level of dyssynchrony is present even in normal ventricles, the RT3DE diagnosis of abnormally increased dyssynchrony in individual patients relies on the availability of normal values for quantitative indexes of dyssynchrony, which have yet to be established. Moreover, an important question in this regard is whether LV dyssynchrony is age dependent and whether its normal range needs to be age adjusted for individual patients.

Although it has been shown that RT3DE-derived LV dyssynchrony is inversely related to ejection fraction (EF), it is not known whether RT3DE-derived measures of LV dyssynchrony are sufficiently sensitive to quantify the impact of left bundle branch block (LBBB) or whether the effects of LBBB on LV dyssynchrony are different in patients with normal versus abnormal ventricular volumes and EF. This information is crucial as part of the evaluation of the RT3DE-based technique as an alternative method to improve the criteria for selection of patients for CRT.

In addition, in previous RT3DE studies (6,13–16), the LV dyssynchrony index (LVDI) was calculated using a 16-segment model that included 4 apical segments, each containing one-fourth of the apical cap. It is not known how the use of the current American Heart Association–recommended standard 17-segment model, in which the apical cap is treated as a separate segment, would affect LVDI.

Accordingly, the aims of this study were: 1) to establish normal values for LVDI, calculated using both the 16- and 17-segment models, and to determine whether this index is age- and/or sex-dependent; and 2) to compare the degree of LV dyssynchrony, as assessed by RT3DE in patients with normal LV function and dilated cardiomyopathy (DCM), and understand the effects of LBBB in these patients.

ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy
DCM = dilated cardiomyopathy
ECG = electrocardiogram/electrocardiography
EDV = end-diastolic volume
EF = ejection fraction
ESV = end-systolic volume
HF = heart failure
LBBB = left bundle branch block
LV = left ventricle/ventricular
LVDI = left ventricular dyssynchrony index
LVEF = left ventricular ejection fraction
RT3DE = real-time 3-dimensional echocardiography
TDI = Tissue Doppler imaging

METHODS

Study design and population. A total of 183 subjects were studied prospectively in 2 separate protocols. Protocol 1 was designed to address aim 1 and included 135 normal subjects over a wide range of ages who had normal blood pressure, no history of heart disease, were not taking any cardiac medications, and had no 2-dimensional echocardiographic evidence of cardiac abnormality. Protocol 2 was designed to address aim 2 listed previously and included 48 additional patients: 32 patients with DCM (group 1 with 16 consecutive patients with LBBB and group 2 with 16 consecutive patients without LBBB) and 16 consecutive patients with

normal LV function and LBBB (group 3). These patients were compared with a subgroup of 50 age-matched normal subjects (group 4: normal LV function and no LBBB) from protocol 1. All participants gave written informed consent, which was approved by the institutional review board.

ECG. All patients underwent a transthoracic 3D echocardiographic study. A 12-lead ECG was recorded at a speed of 25 mm/s in every patient to evaluate QRS width and to determine the presence of LBBB. The QRS duration was measured using the widest QRS complex in leads II, V_1, and V_6.

Real-time transthoracic 3D echocardiography. A Sonos 7500 scanner (Philips, Andover, Massachusetts) equipped with a fully sampled matrix array transducer (model X4) was used. Patients were studied by an experienced cardiac sonographer in the left lateral decubitus position with the transducer in the apical position. To ensure inclusion of the entire LV volume within the pyramidal scan volume, datasets were acquired using the wide-angled mode, thus acquiring 4 wedge-shaped subvolumes (93° × 21°) during a single 5- to 7-s breath-hold. The acquisition of the LV subvolumes was triggered by ECG at every other R-wave to ensure sufficient time for digital storage of data. Thus, acquisition of a single full-volume dataset required 8 cardiac cycles.

Data analysis. Images were analyzed using the 4-dimensional LV-analysis software (TomTec Imaging Systems, Unterschleissheim, Germany) for quantification of global ventricular function and regional mechanical dyssynchrony. Three apical views (4-, 3-, and 2-chamber) were identified, and the LV endocardial boundary was manually traced on the first frame of the sequence corresponding to end-diastole and a frame depicting the smallest LV cavity, roughly corresponding to end-systole. During tracing, the papillary muscles and endocardial trabeculae were included in the LV cavity. Then, the LV endocardial surface was automatically reconstructed frame-by-frame throughout the cardiac cycle and corrected manually if necessary. From these surfaces, a curve of LV volume over time was generated. From these volume–time curves, end-diastolic volume (EDV) and end-systolic volume (ESV) were derived as maximum and minimum values, and EF was calculated.

Quantification of LV mechanical dyssynchrony. Analysis was performed separately for the 16- and 17-segment models. A segmental volume–time curve was generated for each segment. The nadir of each segmental volume curve represented the timing of regional end of ejection, which was expressed in percent of the RR interval to take into account differences in heart rate between patients. The LVDI was calculated as the SD of the timing of regional end of ejection for all segments.

Reproducibility analysis. All measurements were performed by an investigator experienced in the interpretation of echocardiographic images who was blinded to the patient's diagnosis and prior test results. Two months later, the same investigator, blinded to the previous results, repeated the measurements in 12 randomly selected patients enrolled in protocol 2, including 3 patients in each group. In addition, measurements were also completed by a second blinded investigator. Intraobserver and interobserver variability of LVDI was calculated as the absolute difference between the corresponding 2 repeated measurements, divided by their mean.

Statistical analysis. Statistical analysis was performed using Microsoft Excel 2003 (Microsoft, Palo Alto, California). Data were expressed as mean ± SD. The Pearson correlation coefficient was used to compare continuous variables. Differences in EDV, ESV, EF, and LVDI values in protocol 2 were compared using unpaired, 2-tailed *t* tests between each pair of groups. A probability value of ≤ 0.05 was considered statistically significant.

RESULTS

The normal subjects enrolled in protocol 1 included 135 subjects (86 males, 49 females), age range 3 to 88 years, with body surface area ranging between 0.57 and 2.35 m^2 (mean 1.72 ± 0.23 m^2). Mean EDV was 102 ± 29 ml, ESV 44 ± 15 ml, and EF 57 ± 5%. Figure 1 shows an example of an RT3DE image obtained in a normal subject with the LV-cast with the superimposed 17-segment model segmentation and the corresponding 17 regional volume curves. Of note, the amplitude of the curve corresponding to the anteroseptal segment is relatively low, reflecting a reduced change in regional volume throughout the cardiac cycle, which, when combined with noise, may hamper the accurate determination of the regional ejection time. Importantly, excluding this segment from analysis reduced the calculated LVDI from 4.2% to 2.6%.

In protocol 1, mean LVDI in 135 normal subjects was 2.29 ± 1.12 when calculated for 17 segments and 2.22 ± 0.91 for 16 segments. Figure 2 shows LVDI values obtained in normal control subjects as a function of age. These data showed

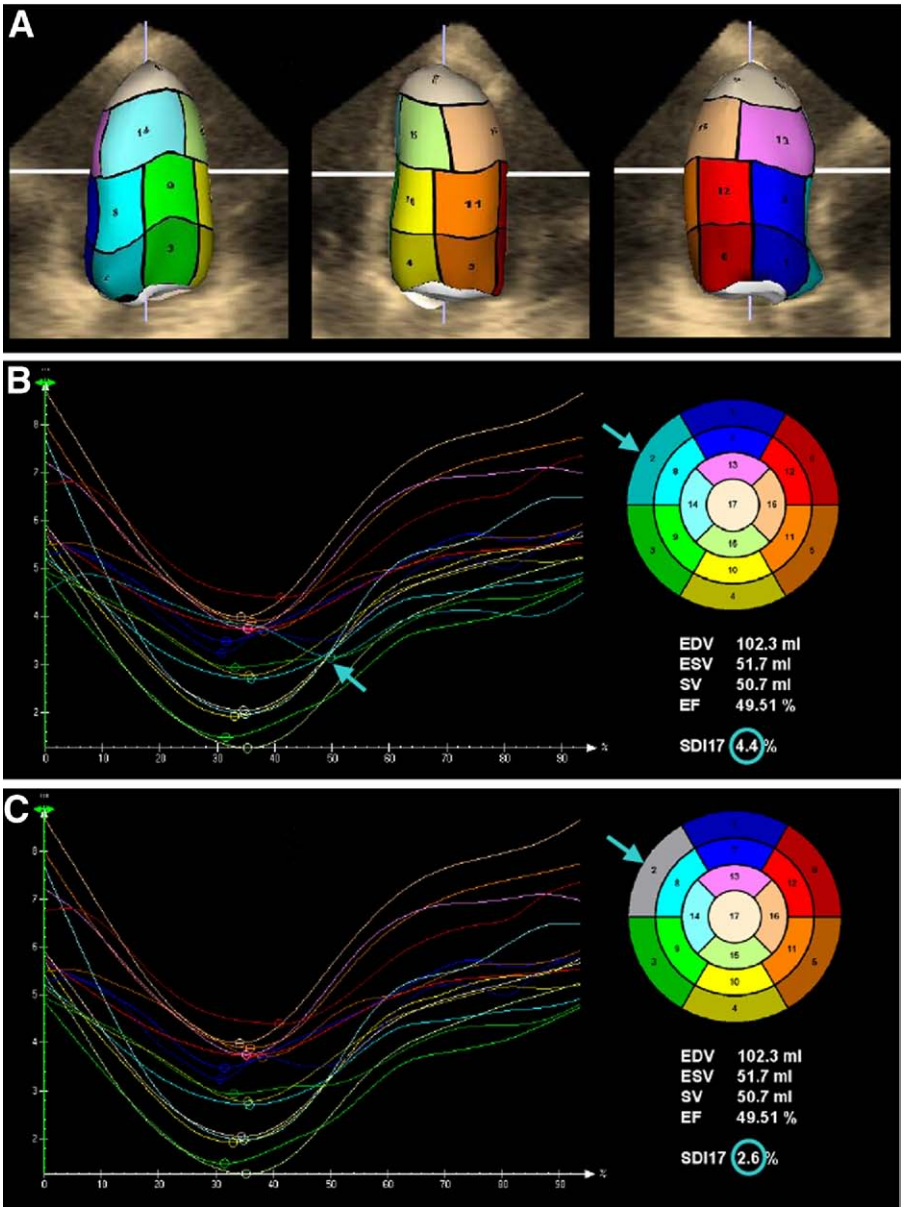

Figure 1. Effects of Outlier Segments on RT3DE-Derived LVDI

(A) The RT3DE images obtained in a normal subject shown with the LV-cast from 3 different perspectives (from left to right: septal, inferolateral, and anterolateral) and the segmentation using the 17-segment model. **(B)** The corresponding 17 regional volume curves showing relatively synchronized motion reaching end-ejection between 30% and 40% of the RR interval, with the exception of the basal anteroseptal segment **(arrows)**, which showed reduced amplitude of motion and seems to reach end-ejection at 50%. **(C)** Exclusion of this segment from analysis **(arrow)** reduced the calculated LVDI from 4.4% to 2.6% **(cyan circles)**. EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; LV = left ventricle; LVDI = left ventricular dyssynchrony index; RT3DE = real-time 3-dimensional echocardiography; SDI = systolic dyssynchrony index; SV = stroke volume.

that the 16-segment model resulted in less dyssynchrony in normal subjects (lower mean) and less normal variability (smaller SD). No significant gender-related differences were noted: 2.21 ± 0.87 for male subjects and 2.23 ± 0.99 for female subjects (not significant). No age-related differences were found (Fig. 2), with the exception of children younger than 10 years of age, whose LVDI values were lower compared with those of subjects age 10 to 19 years ($p = 0.054$, 2-tailed t test).

Patient characteristics in protocol 2 are shown in Table 1. Female and male subjects were evenly

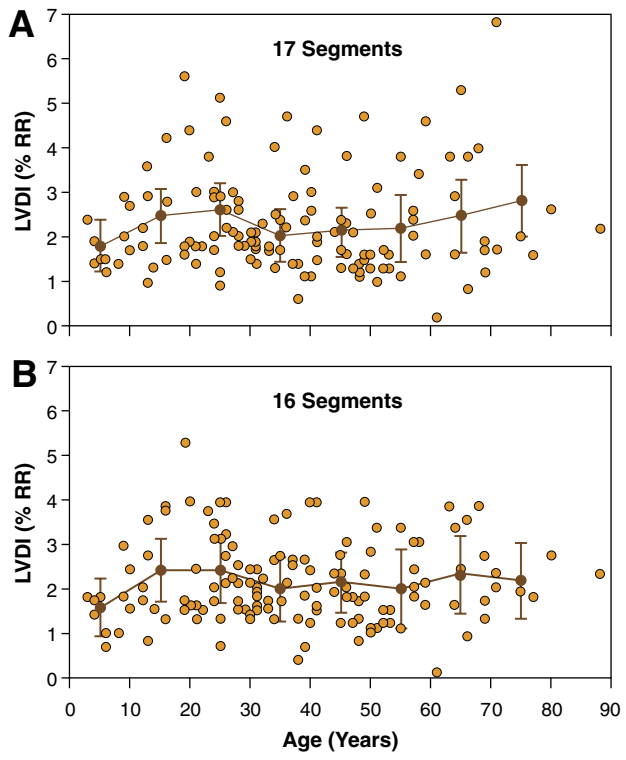

Figure 2. Age Dependency of Normal Values of RT3DE-Derived LVDI

The LVDI values (expressed in percent of RR interval) measured in 135 normal subjects **(orange circles)** over the wide range of ages, shown with mean ± SD values for different age decades **(brown circles with error bars)**, calculated for 17 **(A)** and 16 myocardial segments **(B)**. Abbreviations as in Figure 1.

distributed in groups 1 and 2. As expected, the mean QRS width was significantly wider in patients with LBBB in groups 1 and 3 than in patients with normal QRS widths in groups 2 and 4 (Table 1). Figure 3 shows examples of regional volume curves obtained in 1 patient from each group. Although the high amplitude is preserved in both subjects with normal EF (Fig. 3A and B), the different degrees of dyssynchrony are easy to identify, as evidenced by the greater dispersion of regional ejection times in the patient with LBBB (Fig. 3B, LVDI = 4.4%) compared with the patient without LBBB (Fig. 3A, LVDI = 0.1%). In contrast, in the patient with DCM (Fig. 3C), the amplitude of the curves is low and the ability to accurately detect the end of ejection in each segment is considerably affected by noise. Although the presence of LBBB can be detected by visualizing dyskinetic motion in some of the segments (Fig. 3D), the calculated LVDI is similar (16.1% and 14.6%), irrespective of LBBB.

Indeed, RT3DE-derived LV function parameters, including global EDV, ESV, and EF, summarized in Figure 4, showed that groups 1 and 2 of patients with DCM had significantly higher EDV and ESV and lower EF compared with groups 3 and 4 of patients with normal LV function. Compared with the normal control subjects, LVDI was significantly elevated in patients with DCM, irrespective of the presence of LBBB. The presence of LBBB resulted in smaller but significant differences, both in patients with DCM (between groups 1 and 2) and in those with normal LV function (between groups 3 and 4).

Figure 5 shows LVDI values obtained in individual patients in the 3 groups plotted together with those of the normal subjects studied in protocol 1 against age in the same format as in Figure 2. The abnormality threshold, defined as the mean + 2 SD of the normal population, was lower with the apical cap excluded: 4.04% for 16 segments compared with 4.53% for all 17 segments, without reaching statistical significance. The 135 normal subjects provided confidence between 90% and 95% in the above definition of the abnormality threshold.

The 16-segment analysis resulted in almost complete separation between patients with DCM (both groups 1 and 2), whose LVDI was above the abnormality threshold in 16 of 16 (100%) and 15 of 16 (94%) patients, respectively, from the normal control subjects (group 4). In this control group, the vast majority of patients (48 of 50 or 96%) had LVDI below the abnormality threshold. The 17-

Table 1. Demographics Data of the Patients Studied in Protocol 2

	Group 1	Group 2	Group 3	Group 4
Total, N	16	16	16	50
Male, n (%)	9 (56)	7 (44)	3 (19)	39 (78)
Age, yrs ± SD	63 ± 13	56 ± 17	67 ± 13	58 ± 10
QRS width, ms ± SD	165 ± 24*	98 ± 12†	148 ± 11‡	76 ± 23

Group 1: dilated cardiomyopathy (DCM) with left bundle branch block (LBBB), group 2: DCM without LBBB, group 3: normal left ventricular function with LBBB, group 4: normal control subjects. *Significant difference group 1 versus 2 ($p < 0.05$). †Significant difference group 2 versus 3 ($p < 0.05$). ‡Significant difference group 3 versus 4 ($p < 0.05$).

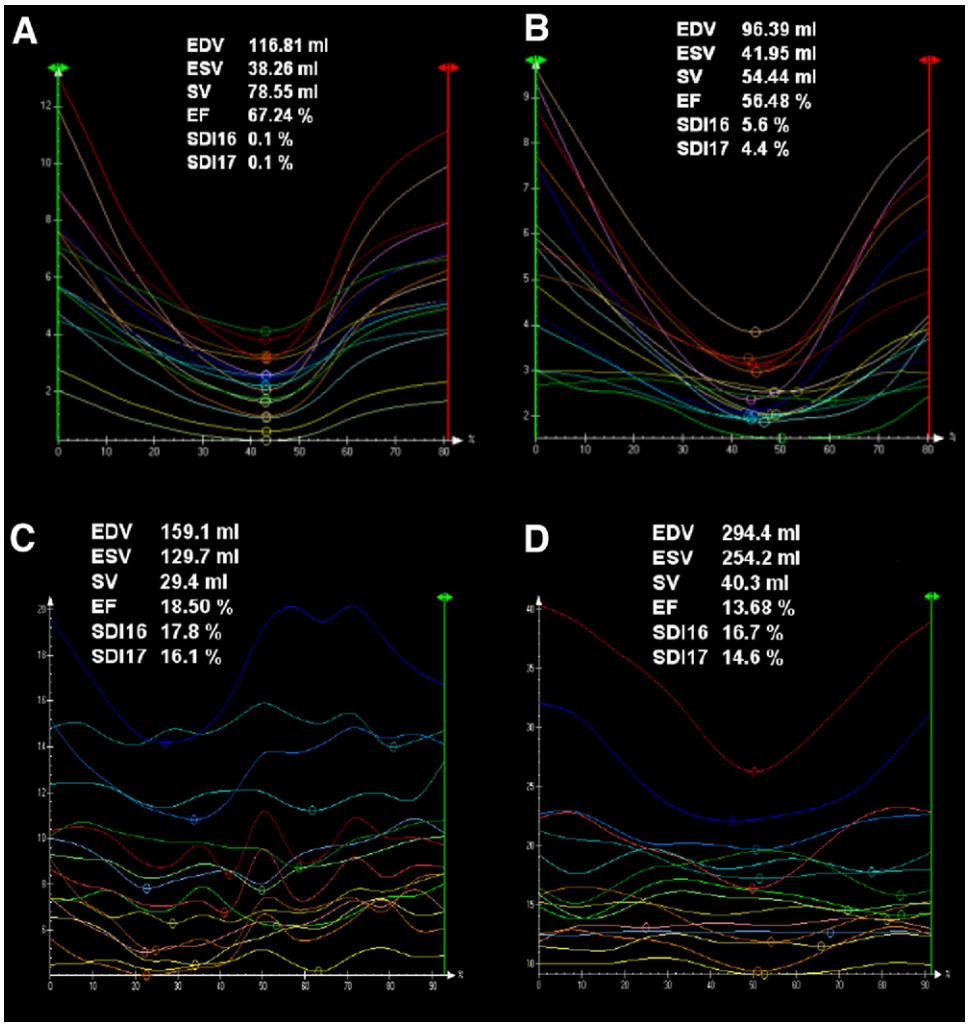

Figure 3. RT3DE-Derived Regional LV Volume Curves

Evaluation of LV dyssynchrony in 1 patient of each group, which shows the effects of reduced ejection fraction and LBBB in 4 patients with: **(A)** normal LV function without LBBB (group 4), **(B)** normal LV function and LBBB (group 3), **(C)** dilated cardiomyopathy (DCM) without LBBB (group 2), and **(D)** DCM with LBBB (group 1). See text for details. LBBB = left bundle branch block; other abbreviations as in Figure 1.

segment analysis resulted in a larger number of normal control subjects with LVDI above the abnormality threshold, and thus less clear separation between patients with DCM and normal control subjects. Patients with normal LV function and LBBB (group 3) were roughly equally distributed above (9 of 16 or 56%) and below (7 of 16 or 44%) the abnormality threshold for both 16- and 17-segment analyses.

When combining all patients studied in protocol 2, a high negative correlation ($r = -0.91$) was noted between LVDI and EF. Separate regression analysis of each group showed that LVDI correlated well only in groups 1 and 2 ($r = 0.80$ and $r = 0.78$, respectively), whereas normal subjects in groups 3 and 4 were clustered within a narrow EF range, not allowing a meaningful regression analysis. A plot of LVDI against EF showed that none of the patients with DCM and EF <35% had dyssynchrony within normal limits as defined in this study, irrespective of the presence of LBBB (Fig. 6). This indicated that LVDI could not differentiate between these 2 groups of patients and thus provided little if any useful additional information as far as potential indication for CRT. Intraobserver variability in measured LVDI was 9.2 ± 6.0%, and interobserver variability was higher: 15.2 ± 21%.

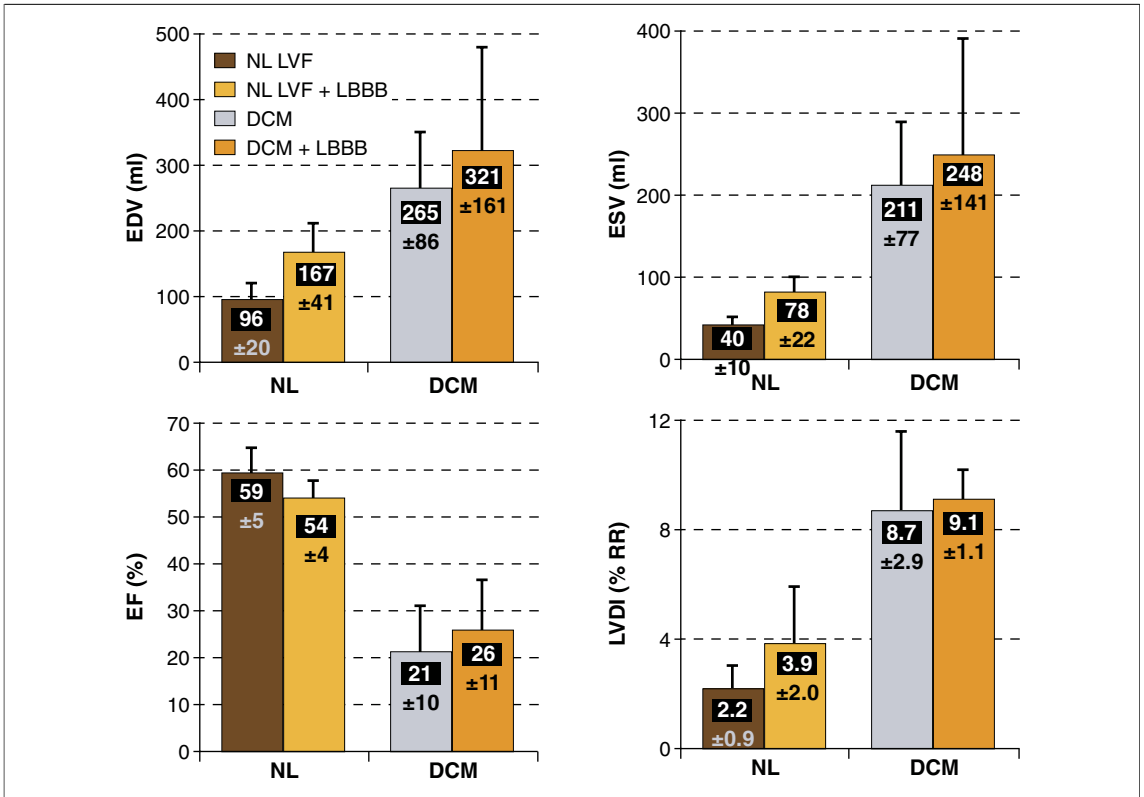

Figure 4. Intergroup Comparisons of Left Ventricular Volumes, Function, and Dyssynchrony

Mean + SD (error bars) of the left ventricular function (LVF) parameters (end-diastolic volume [EDV] and end-systolic volume [ESV]; ejection fraction [EF]) and left ventricular dyssynchrony index (LVDI) obtained in the 4 groups of patients (same as in Fig. 3) in protocol 2. All intergroup comparisons showed significant differences in EDV, ESV, and LVDI, whereas ejection fraction was significantly different only between normal (NL) and dilated cardiomyopathy, irrespective of left bundle branch block. Abbreviations as in Figure 3.

DISCUSSION

HF has a poor prognosis with a 5-year mortality of approximately 50% (17). Approximately 30% of patients with symptomatic HF have a prolonged QRS complex (≥120 ms) as a manifestation of conduction system disease (18,19). CRT has emerged as an effective treatment for patients with moderate to severe HF symptoms, LBBB, and significant LV dysfunction, in addition to optimal medical management with beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, diuretic agents, and digoxin. It has been shown that CRT not only improves the quality of life, symptoms, and functional capacity (2,3), but also reduces mortality (4,5) compared with optimized medical therapy. Nevertheless, 30% to 40% of patients do not respond to CRT (8–10,20). This might be because of the widely used selection criteria, which heavily rely on QRS duration; limitations of the techniques currently used to assess LV dyssynchrony, such as TDI; and the lack of guidance for optimal positioning of CRT leads (21).

This study was designed to study the RT3DE index of LV dyssynchrony using both the 16-segment model, as in the previous studies (6,13–16), as well as the 17-segment model currently recommended by the American Heart Association and the American Society of Echocardiography. First, normal values of LV dyssynchrony were established in protocol 1 in a large group of normal subjects over a wide age range and were found to be gender independent and age independent with the exception of children in the first decade of life, who had slightly less dyssynchrony than older subjects. This finding allowed us to establish an abnormality threshold for LVDI independent of age and gender. This abnormality threshold was tested in protocol 2 and yielded several important findings, including: 1) increased LV dyssynchrony in patients with DCM, irrespective of the presence of LBBB; 2) a smaller but significant increase in dyssynchrony in the presence of LBBB both in patients with DCM and

in those with normal LV function, despite LVDI below the abnormality threshold noted in 44% of the latter patients; and 3) significant negative correlations between LVDI and EF.

Although increased dyssynchrony in patients with DCM without LBBB may be counterintuitive, this finding confirmed those of several prior studies (22–25). The prevalence of LV dyssynchrony in patients with DCM and no LBBB in our study (94%) was considerably higher compared with prior studies that reported an incidence of LV dyssynchrony in a wide range between 27% and 56% of patients with narrow QRS, HF, and LV dysfunction. This difference is likely related not only to differences in study populations (mean EF of 31.3 ± 11.3% and 27.8 ± 7.0% [6,26] respectively, i.e., higher than in our patients), but also to methods of analysis. In particular, the definition of abnormality threshold for LVDI varied among studies, as well as the technique used for its detection (6,12,22–25). The abnormality threshold defined in our study was considerably lower (4.0%) than that previously obtained in smaller groups of subjects by Kapetanakis et al. (6) and more recently by Soliman et al. (16) (8.3%). This is probably because these investigators used an older version of the analysis software based on a less refined algorithm for endocardial surface detection, which was more likely to produce noisy regional volume curves that could artificially increase the calculated LVDI. On the other hand, our abnormality threshold was slightly higher than that recently reported by Gimenes et al. (14) (3.6%).

Our new abnormality threshold resulted in no patients with DCM and EF <35%, whose level of dyssynchrony would be considered to be within normal limits (Fig. 6). Importantly, all patients with conventional indications for CRT implantation (EF <35% and wide QRS) would still be selected using the new threshold. However, patients with DCM and narrow QRS, who would not qualify for CRT using the conventional criteria, would also be considered as candidates for CRT using the criterion for RT3DE-derived LVDI dyssynchrony. Thus, the use of the lower abnormality threshold defined in this study would increase the number of patients with DCM who would potentially qualify for CRT. Nonetheless, in view of the recent results of Beshai et al. (21), who showed that patients with DCM and narrow QRS did not clearly benefit from CRT, one might question whether this increase in referrals would result in a further increase in the number of nonresponders. However, assuming that the lack of response to CRT may be in part caused by incorrect lead placement, the use of RT3DE to identify the area of maximum activation delay to determine the feasibility of lead placement in the vicinity of this area is in fact likely to improve the effectiveness of the therapy.

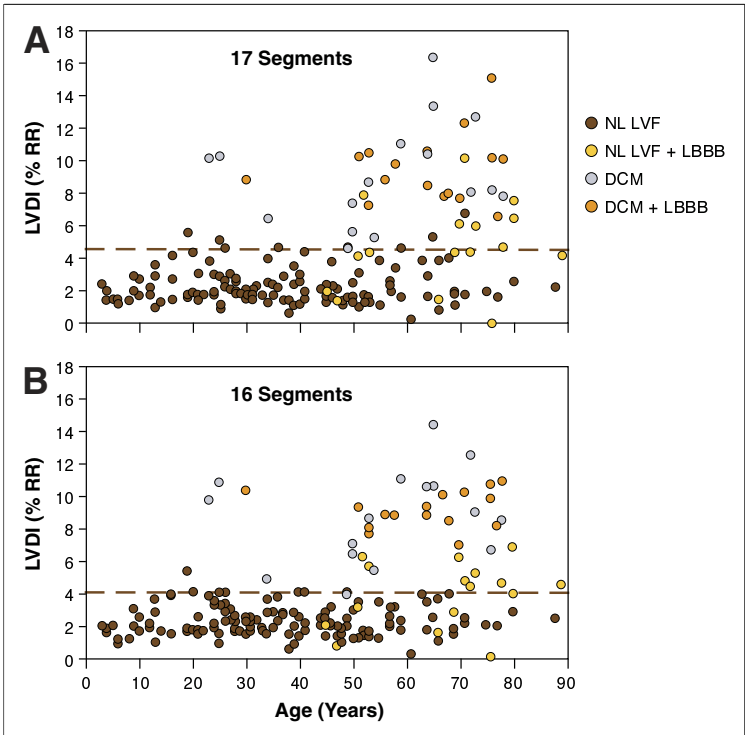

Figure 5. Scatter Plot of LVDI Values as a Function of Age

An LVDI obtained in individual patients in the 3 groups (same as in Fig. 3) in protocol 2, shown with those of all normal (NL) control subjects against age in the same format as in Figure 2. Data are shown for both 17-segment analysis **(A)** and 16-segment analysis **(B)**. The **dashed horizontal lines** represent the abnormality threshold defined as 2 SD above the mean of the normal control subjects. Abbreviations as in Figures 1, 3, and 4.

Nevertheless, an important question one must consider is whether RT3DE-derived increased LVDI measured in patients with DCM truly reflects increased LV dyssynchrony or alternatively is a result of inaccurate identification of regional ejection times from low-amplitude and frequently high-noise regional volume curves. In fact, the definition of LVDI as an SD per se makes this index prone to errors because it is expected that because of noise even a single outlier value measured in 1 segment would significantly affect the SD, that is, erroneously detect increased LV dyssynchrony (Fig. 1). Based on the results of this study, it seems that high LVDI directly reflects low EF rather than true dyssynchrony. This is in agreement with the results of Soliman et al. (16), who reported a correlation of $r^2 = 0.07$ between LVDI and QRS

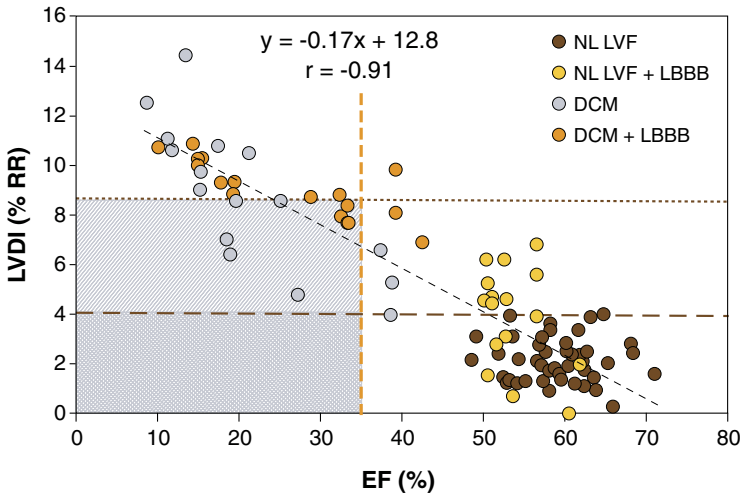

Figure 6. Scatter Plot of LVDI Values as a Function of LV EF

An LVDI obtained in individual patients in the 4 groups in protocol 2, shown against EF with the results of linear regression analysis. The **dashed horizontal line** represents the abnormality threshold defined as 2 SD above the mean of the 135 normal (NL) control subjects in protocol 1, with the nonpopulated cross-hatched rectangular area showing that none of the patients with DCM and EF <35% had dyssynchrony within normal limits as defined in this study. The **dotted line** represents the 8.3% threshold used by Kapetanakis et al. (6), with the **hatched rectangular area** showing that there are a considerable number of patients with DCM and EF <35% whose LVDI would be considered within normal limits (see text for details). DCM = dilated cardiomyopathy; EF = ejection fraction; other abbreviations as in Figure 1.

duration in patients with HF. As LV function worsens, the amplitude of the regional volume curves decreases, which, when combined with noise, results in erroneously widespread values of regional ejection times. Accordingly, algorithms for endocardial surface detection need to be improved to minimize noise in regional volume curves. Also, alternative approaches for estimating LV dyssynchrony from RT3DE images, such as the use of dyssynchrony indices capable of giving different weight to regional curves depending on their amplitude (27) or other sophisticated analysis techniques, such as cross-correlation analysis that does not rely on accurate identification of a single point on potentially regional volume curves (28), need to be further developed and tested in patients with LV dysfunction.

Although the intraobserver and interobserver variability levels in LVDI derived from RT3DE images in our patients are relatively high, they are similar (16) or even lower (11) than those reported in other studies in patients with DCM. Of note, reproducibility analysis in this study was performed in a mixed group of patients, including 6 of 12 patients with DCM. It is expected that in patients with preserved LV function, the intermeasurement variability would be lower.

Study limitations. The RT3DE echocardiographic assessment of LV dyssynchrony has several limitations. One limitation is the dependency on image quality for accurate tracking of the endocardial boundary in all 16 segments, because inadequate tracking in a single segment can directly affect the calculated LVDI. Of note, since the time when images were acquired for this study, newer equipment has become available that provides improved image quality at higher frame rates. Another limitation is that manual correction of the endocardial boundary in one segment may affect its tracking in adjacent segments. Also, the relatively low frame rate is a disadvantage compared with TDI. Finally, the relatively small size of groups 1, 2, and 3 in protocol 2 is a potential limitation of our study. However, this limitation does not affect the important finding that all patients with DCM in groups 1 and 2 (total of 32) were indiscriminately diagnosed with abnormally high LV dyssynchrony when compared with a threshold established in a large number of normal subjects (total of 135). Moreover, the differences in LVDI between the groups were found to be significant despite the small number of patients in each subgroup, thus eliminating the possibility of a statistically underpowered study.

CONCLUSIONS

RT3DE is a feasible, fast, noninvasive, and reproducible method of identifying and quantifying LV dyssynchrony in patients with preserved LV function. Age- and sex-independent normal values of LVDI established in this study redefined the threshold for abnormal dyssynchrony without the apical cap. The abnormally high LV dyssynchrony in all patients with EF <35% irrespective of QRS duration is likely a result of the inability of RT3DE to accurately determine regional ejection times in all LV segments because of the low signal-to-noise ratios of the regional volume curves. The consequent inability to differentiate between patients with and without true LV dyssynchrony in the presence of low EF renders RT3DE-derived LVDI not useful for either the selection of patients for CRT or the follow-up of its effects. Alternative approaches for estimating LV dyssynchrony from RT3DE images need to be designed to address this pitfall.

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JACC: CARDIOVASCULAR IMAGING, VOL. 2, NO. 7, 2009
JULY 2009:802–12

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