Indian Heart Journal 71 (2019) 256–262

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Comparison of three-dimensional echocardiography and speckle tracking echocardiography in quantification and mapping of intraventricular mechanical dyssynchrony

Anupam Bhambhani*, Amalu Mathew

Department of Cardiology, Vydehi Institute of Medical Sciences and Research Centre, Whitefield, Bangalore 560066, India

ARTICLE INFO

Article history:
Received 23 February 2019
Accepted 26 April 2019
Available online 2 May 2019

Keywords:
Intraventricular mechanical dyssynchrony
Speckle tracking
Three-dimensional echocardiography

ABSTRACT

Objectives: The aim of the study is to compare two advanced methods of evaluation of left ventricular mechanical dyssynchrony (LVMD), the speckle tracking echocardiography (STE) and the three-dimensional echocardiography (3DE).

Methods: One hundred thirty-six subjects, with or without LV dysfunction and with or without bundle branch block (BBB), were included in this study, designed to investigate agreement between magnitude and spatial pattern of LVMD as assessed by 3DE and STE. The frequency and severity of LVMD and localization of most asynchronous segments were compared.

Results: Both 3DE and STE revealed progressive rise in frequency and magnitude of LVMD with increasing disease severity. Dyssynchrony was dependent on left ventricle ejection fraction rather than the QRS duration. The frequency and magnitude of dyssynchrony were maximum in patients having LV dysfunction with left BBB. Compared with STE, 3DE diagnosed LVMD more frequently in patients having LV dysfunction with narrow QRS (17.6% vs 60.3%, respectively; $P < 0.001$). When the two methods were compared for localization of most asynchronous segments, the results matched only in about 50% cases.

Conclusions: Both 3DE and STE provided consistent results with progressive rise in magnitude of LVMD, correlating with disease severity. 3DE diagnosed more patients as having LVMD in those having LV dysfunction with narrow QRS. The most delayed segment assessed by two methods matched only in about half the cases. Correlation with clinical CRT responsiveness is needed to conclude which method is more accurate in dyssynchrony mapping for targeted lead placement.

1. Introduction

This study compares two advanced methods of evaluation of left ventricular mechanical dyssynchrony (LVMD), the speckle tracking echocardiography (STE) and the three-dimensional echocardiography (3DE).

It is well known that a significant proportion of patients with advanced heart failure, who are apparently eligible for cardiac resynchronization therapy (CRT), do not derive significant benefit from the procedure[1] despite having left ventricle (LV) ejection fraction (EF) and electrocardiographic (ECG) findings comparable with those observed in responders. Among many other factors, two important ones suggested for this differential responsiveness are selection of the appropriate patient having significant LVMD and identification of the most delayed LV segment for targeted LV lead positioning. These factors can be improved with the help of sophisticated imaging techniques such as STE,[2] 3DE,[3] and tissue Doppler imaging[4] (TDI). Efficiency of TDI in LVMD evaluation has been questioned by some investigators[5] because of their observation that a significant number of normal subjects have TDI-derived LVMD indices that were higher than the proposed cutoffs for predicting benefit from CRT. Yet, another study comparing the LVMD parameters obtained from different strain imaging methods have reported poorer efficiency of STE than cardiac magnetic resonance myocardial tagging (CMR-TAG) in predicting post-CRT reverse remodeling.[6] Two-dimensional and Doppler imaging–based techniques have their inherent limitations because of the inability to image the whole LV simultaneously and possibility of imperfect alignment of the Doppler signal to the ventricular wall. In this

* Corresponding author. Department of Cardiology, Vydehi Institute of Medical Sciences & Research Centre, #82 EPIP Area, Whitefield, Bangalore 560066, India.
E-mail address: anupam.bhambhani@yahoo.in (A. Bhambhani).

https://doi.org/10.1016/j.ihj.2019.04.006

context, by its ability to interrogate the entire LV simultaneously, 3DE has the potential to overcome the limitations of two-dimensional echocardiography (2DE)–based techniques. However, the agreement between the dyssynchrony parameters obtained using STE and 3DE is unknown. This study compares the magnitude and spatial distribution of dyssynchrony obtained from STE or 3DE imaging, in a diverse group of subjects including, normal subjects, subjects having normal LVEF with either left bundle branch block (LBBB) or right BBB (RBBB), patients having LVEF ≤35% with narrow QRS; and those having LVEF ≤35% with complete LBBB.

2. Methods

2.1. Study design and subjects

This was a single-center, prospective, nonrandomized, cross-sectional study designed to investigate agreement between magnitude and spatial pattern of LVMD as assessed by two different advanced echocardiographic methods, the STE and 3DE. Patients aged ≥18 years, referred to our noninvasive cardiology division from January 2018 to May 2018, having moderate to severe LV dysfunction, with either normal QRS duration or ECG criteria of complete LBBB, or those with either RBBB or LBBB in combination with normal LVEF, were eligible for this study. In addition, 30 controls (>18 years in age and free of overt heart disease and/or hypertension) were also included in the study. Patients with decompensated heart failure, acute coronary syndrome, ventricular pacing, atrial fibrillation, or any other persistent arrhythmia likely to interfere with 3DE or STE recording, suboptimal echocardiographic window, and those with primary valvular or structural heart disease were excluded. In this way, a total of 160 subjects were screened; of whom, 24 were excluded either because of suboptimal 3DE images or inability to track more than one LV segment during STE analysis. The remaining 136 subjects, classified into the following 4 groups, were included in the final analysis: group 1 consisted of 30 controls; group 2 comprised 21 subjects having either complete LBBB or RBBB with structurally normal heart on 2D echocardiography and LVEF >50%; group 3 included 68 patients having LVEF ≤35% with narrow QRS; and group 4 consisted of 17 patients having LVEF ≤35% with complete LBBB.

Baseline characters including age, gender, New York Heart Association (NYHA) class, heart rate (HR), QRS duration, etiology of LV dysfunction (ischemic or nonischemic), LVEF as obtained by 3DE (3DE-LVEF), LVEF as obtained by STE (STE-LVEF), global longitudinal strain (GLS), volume rate (in case of 3DE), and frame rate (in case of STE imaging) were noted in eligible subjects, and consent was obtained. All subjects underwent 3DE recording and longitudinal strain imaging as described in the following section. Off-line 3DE and STE analyses were performed later using Q-lab 10.5 software.

2.2. ECG criteria used for diagnosing BBBs

American Heart Association criteria[7] were followed for ECG characterization. LBBB was diagnosed by the presence of QRS duration ≥120 msec, QS or rS in lead V1, absent Q waves in I, V5–V6, R peak time >60 msec in V5–V6, monophasic R wave with no Q wave in lead V6, broad and notched R wave in lead I, aVL, V5, and V6, or occasionally RS pattern in V5 and V6. RBBB was diagnosed by the presence of QRS duration ≥120 msec, broad and notched R wave with rSR′, rsR′, or rsr′ pattern in leads V1, V2 (R′ wider than initial r), S wave in leads I and V6, greater in duration than R wave or of >40 msec, or R wave peak time >50 msec in lead V1.

2.3. 3D echocardiography

LV full-volume loops were recorded by ECG-gated 3DE imaging in apical 4-chamber view on commercially available iE33 equipment (Philips Medical Systems, Andover, MA, USA), using the X5-1 matrix-array transducer. The sector width, speed, and depth were optimized to obtain maximum possible volume rate. The lateral width was adjusted to include whole LV. Gain settings were adjusted to obtain best possible endocardial border–cavity differentiation. To minimize stitch artifacts while still maintaining optimal lateral resolution, 2-beat RT3DE setting was used for recording full-volume loops in all patients. These data were digitally transferred to another computer having Q-lab software. For off-line analysis, end diastolic and end systolic frames were selected and appropriate points, namely, anterior, inferior, septal, lateral, and apical, were marked. The software automatically tracked the endocardium–LV cavity interface which was confirmed in short-axis view and edited manually by adding tracking points wherever appropriate. On initiating "sequence analysis," the software provided 3DE-LVEF. To study the magnitude and spatial pattern of intraventricular dyssynchrony, sixteen LV segments (all basal, mid, and apical segments) were selected. The Q-lab software automatically quantifies dyssynchrony as systolic dyssynchrony index (3DE-SDI) for the selected LV segments, which indicates standard deviation (SD) of time to attain minimum systolic volume (Tmsv) of the selected LV segments, expressed as percentage of cardiac cycle length (16-segment Tmsv-%R-R). Both the absolute value of Tmsv and 3DE-SDI were noted. 3DE-SDI >10% was considered indicative of significant dyssynchrony based on previously published validation.[3] Following this, the most dyssynchronous LV segment was identified from regional time–volume curves and color-coded bull's eye parametric images, and its location and segmental Tmsv value were noted.

2.4. Speckle tracking echocardiography

2DE recording of apical 4-chamber (AP4), apical 2-chamber (AP2), and apical 3-chamber (AP3) views was performed while focusing and zooming the LV to its maximum, keeping the depth shallowest while maintaining best possible frame rates and image resolution. The images were digitally exported in the digital imaging and communications in medicine (DICOM) format for off-line GLS analysis using cardiac motion quantification (CMQ) in Q-lab 10.0 software. This software automatically marks aortic valve closure time and assesses global myocardial peak systolic strain values (unlike midmyocardial, endocardial, or epicardial values). Appropriate region of interest was selected for each image which was followed by automatic tracking. Manual adjustments were done in the tracking points whenever the automatic tracking was found suboptimally corresponding to myocardial borders. Subjects with suboptimal postprocessing images or with inability to track ≥2 segments were excluded from the study. The basic strain parameters studied were peak systolic GLS and STE-LVEF. Magnitude of LVMD obtained by STE was labeled as STE-derived SDI (STE-SDI) and was quantified as SD of the time to attain peak systolic strain (TTP) by 16 LV segments, QRS onset being the reference point for timing analysis. Based on previously reported cutoff values, >60 msec was considered indicative for positive CRT responsiveness.[8] The most delayed LV segment (most dyssynchronous) was located from the bull's eye map of TTP analysis. We did not test circumferential or radial strain because longitudinal strain is more reproducible and standardization of STE algorithms has been done using longitudinal strain.[9] Moreover, radial strain evaluates anteroseptal-to-posterior wall delay, usually at mid-LV level, making it logically incomparable with 3DE because the latter evaluates the chamber in entirety.

Table 1
Baseline characteristics.

Variables	Group 1	Group 2	Group 3	Group 4
	($n = 30$)	($n = 21$)	($n = 68$)	($n = 17$)
Age	40.3 ± 14.2	56.5 ± 10.3	53.2 ± 12.3	61.4 ± 8.5
Gender				
Female	8 (26.7%)	4 (19%)	11 (16.2%)	6 (35.3%)
Male	22 (73.3%)	17 (81%)	57 (83.8%)	11 (64.7)
NYHA class				
I	30 (100%)	21 (100%)	–	–
II	–	–	5 (7.4%)	1 (5.9%)
III	–	–	60 (88.2%)	14 (82.4%)
IV	–	–	3 (4.4%)	2 (11.8%)
Heart rate	76.5 ± 16.2	80.3 ± 11.5	89.5 ± 16.1	85.0 ± 13.0
QRS duration	80.3 ± 4.2	132.5 ± 14.7	85.5 ± 11.1	147.7 ± 19.2
Etiology of LV dysfunction				
No LV dysfunction	30 (100%)	21 (100%)	–	–
Nonischemic	–	–	32 (47.1%)	10 (58.8%)
Ischemic	–	–	36 (52.9%)	7 (41.2%)
3DE-LVEF	63.29 ± 6.95	54.20 ± 8.43	26.70 ± 8.01	26.70 ± 8.02
STE-LVEF	60.59 ± 5.50	57.68 ± 6.60	35.71 ± 6.6	34.69 ± 8.28
Global longitudinal strain	−20.39 ± 2.36	−18.18 ± 2.22	−10.55 ± 2.78	−8.80 ± 3.23

3DE, three-dimensional echocardiography; 3DE-LVEF, LVEF as obtained by 3DE; LV, left ventricle; LVEF, left ventricle ejection fraction; STE, speckle tracking echocardiography; NYHA, New York Heart Association; STE-LVEF, LVEF as obtained by STE.

2.5. Statistical methods

Statistical analysis was performed with the SPSS software package for Windows version 15.0 (SPSS Inc., Chicago, IL, USA) and R Statistical Software version 3.5.1 (The R foundation for statistical computing). All categorical variables were expressed as percentages, and all continuous variables, as mean ± SD. The differences between categorical variables were analyzed by Chi-squared and McNemar's tests. Dyssynchrony indices were summarized using median and the 25th and 75th percentiles because they were not normally distributed. Comparisons among the four groups were performed using the Kruskal–Wallis test, followed by Dunn's test to correct for multiple comparisons, and the Bonferroni correction was applied for the adjustment of the significance level. The intraobserver reproducibility was evaluated using the Pearson correlation coefficient, and Bland–Altman plots were generated to assess the agreement between modalities. The mean difference and limits of agreement (±1.96 SD) of the Bland–Altman plots were used as reference of agreement. For all the analyses, P value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Demographic data; clinical and ECG parameters, mean LVEF, and etiology of LV dysfunction are shown in Table 1. The baseline ECG and echocardiographic parameters were as expected for each predecided group. Because every patient underwent both STE and 3DE evaluation for comparison and recordings for 3DE and STE analyses were performed in the same sitting, there was no question of difference in baseline characteristics of the subjects. The mean volume rate during 3DE recordings was 19.75 ± 1.59; the mean frame rate during 2DE recording for STE was 54.32 ± 6.38.

3.2. Dyssynchrony indices obtained by 3DE

On assessing the frequency of LVMD (Table 2), dyssynchrony was completely absent in the normal subject; only 9.5% subjects having normal LVEF with BBB had significant LVMD, while about 60% subjects having LV dysfunction without or with LBBB (60.3% and 64.7% respectively) were found to have significant LVMD (Fig. 1).

The comparative analysis of magnitude of LVMD in the four groups (Table 3, Fig. 2) revealed that there was no significant difference in LVMD indices between groups 1 and 2; however, there was significant and progressive rise in both the studied 3DE-derived LVMD indices between groups 2 and 3, as well as between groups 3 and 4.

3.3. Dyssynchrony indices obtained by STE

Assessment of frequency of dyssynchrony by STE (Table 2) revealed absence of dyssynchrony in controls; while 9.5% subjects having normal LVEF with BBB had significant LVMD. Among those with LV dysfunction, 17.6% with narrow QRS and 52.9% with LBBB had significant dyssynchrony (Fig. 1). When frequency of observed LVMD was compared between 3DE and STE, there was no

Table 2
Prevalence of mechanical dyssynchrony in various groups as assessed by 3D echocardiography (3DE-SDI) and speckle tracking echocardiography (STE-SDI).

Groups	3DE-SDI		STE-SDI		P value
	<10 msec (normal)	≥10 msec (abnormal)	<60 msec (normal)	≥60 msec (abnormal)	
Group 1	30 (100%)	0 (0%)	30 (100%)	0 (0%)	NS
Group 2	19 (90.5%)	2 (9.5%)	19 (90.5%)	2 (9.5%)	NS
Group 3	27 (40.7%)	41 (60.3%)	56 (82.4%)	12 (17.6%)	<0.001[a]
Group 4	6 (35.3%)	11 (64.7%)	8 (47.1%)	9 (52.9%)	NS

3DE, three-dimensional echocardiography; 3DE-SDI, 3DE-derived SDI; STE, speckle tracking echocardiography; STE-SDI, STE-derived SDI.
[a] McNemar's test.

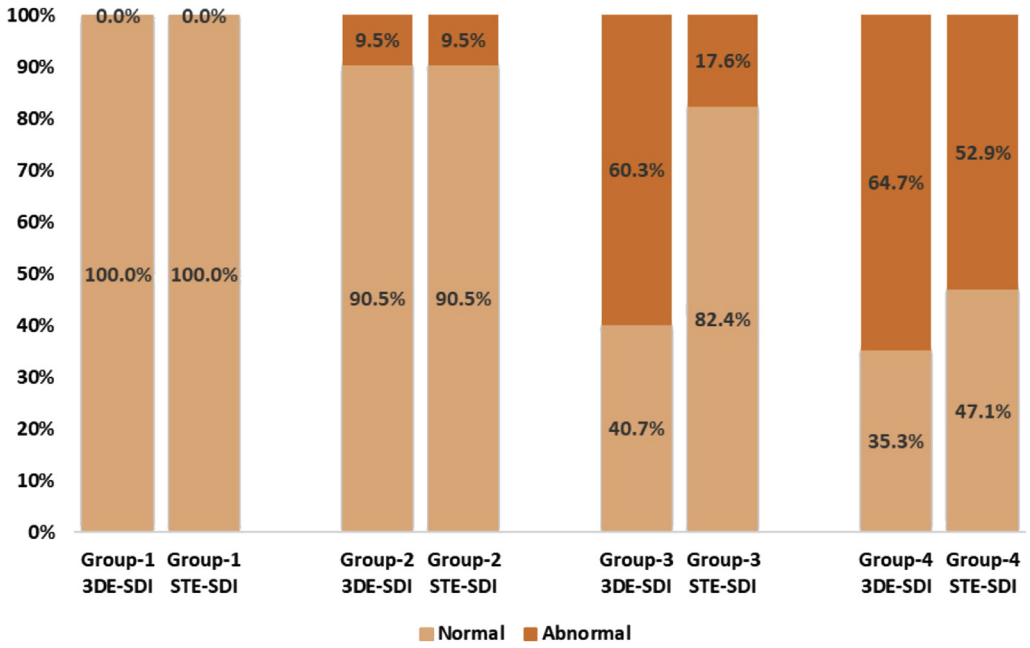

Fig. 1. Frequency of intraventricular dyssynchrony in different groups as assessed by 3D echocardiography (3DE-SDI) and speckle tracking echocardiography (STE-SDI). 3DE, three-dimensional echocardiography; 3DE-SDI, 3DE-derived SDI; SDI, systolic dyssynchrony index; STE-SDI, STE-derived SDI.

significant difference between groups 1, 2, and 4, while frequency of LVMD was significantly higher in group 3 when assessed by 3DE (Table 2).

There was no significant difference in STE-determined LVMD indices between groups 1 and 2; however, there was significant and progressive rise in the dyssynchrony indices between groups 2 and 3, as well as between groups 3 and 4 (Table 3, Fig. 2).

3.4. Mapping of the most dyssynchronous segment

The most dyssynchronous segment in each case was identified from bull's eye parametric images in both 3DE and STE (Fig. 3), which also quantified the delay of each segment. We compared the location of the most dyssynchronous segments identified by 3DE and STE in patients with significant LVMD, that is, groups 3 and 4 ($N = 85$). Absolute segment match or adjacent segment match of the most delayed segment was observed only in 47.05% cases (45.58% in group 3 and 52.9% in group 4). However, the most dyssynchronous segment identified by 3DE was also significantly delayed in 80.00% patients when assessed by STE, while the most dyssynchronous segment identified by STE was significantly delayed in 55.29% cases on 3DE analysis also. For assessing whether the delay of a particular segment was significant or not, we quantified the intersegmental delay between the earliest contracting segment and the segment in question, considering ≥130 msec as significant delay.[10]

3.5. Intraobserver variability

Both the Pearson correlation coefficient and Bland–Altman analysis showed high intraobserver agreement on dyssynchrony indices (Table 4).

4. Discussion

A study conducted about a decade before on CRT non-responders revealed that 9% of such patients had lack of baseline dyssynchrony and that another 21% had suboptimal lead position.[11] Around the same time, TDI-based techniques emerged as efficient tools for predicting CRT responsiveness[4]; but it was soon followed by several investigators raising suspicion about their reliability,[5,12,13] while at the same time, finding STE-based methods correlating more closely to LVMD in different groups of patients.[5] However, when correlation of LVMD parameters obtained from different strain imaging–based methods was compared, relatively poorer efficiency of STE was observed compared with CMR-TAG in predicting post-CRT reverse remodeling.[6] Moreover, STE-based evaluations have shown vendor variability also.[14,15] By their ability to simultaneously interrogate the entire chamber, the techniques based on 3DE are expected to be more accurate in diagnosing and quantifying LVMD, as well as in predicting CRT responsiveness. 3DE and STE have never been compared before for dyssynchrony assessment.

Table 3
Mechanical dyssynchrony indices obtained by 3D echocardiography (3DE-SDI) and speckle tracking echocardiography (STE-SDI).

Dyssynchrony indices	Group 1	Group 2	Group 3	Group 4	*P* value	Pairwise comparisons
3DE-SDI	1.4 (1.1, 2.3)	1.8 (1.0, 4.5)	11.2 (7.0, 16.0)	12.5 (8.2, 17.1)	<0.001	BCDE
STE-SDI	27.4 (13.9, 34.6)	39.0 (25.0, 52.9)	40.7 (30.3, 51.4)	72.9 (51.9, 81.6)	<0.001	BCEF

3DE, three-dimensional echocardiography; 3DE-SDI, 3DE-derived SDI; STE, speckle tracking echocardiography; STE-SDI, STE-derived SDI.
Data are expressed as median (first and third quartiles). Bonferroni-corrected $P < 0.05$ assessed for the following intergroup comparisons: A, groups 1 and 2; B, groups 1 and 3; C, groups 1 and 4; D, groups 2 and 3; E, groups 2 and 4; F, groups 3 and 4.

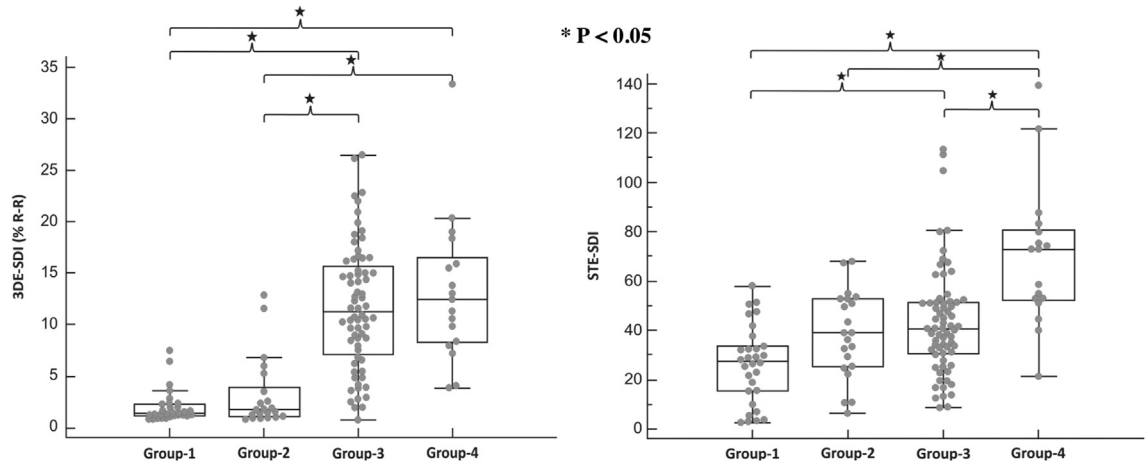

Fig. 2. Magnitude of intraventricular dyssynchrony in different groups as assessed by 3D echocardiography (3DE-SDI) and speckle tracking echocardiography (STE-SDI). 3DE, three-dimensional echocardiography; 3DE-SDI, 3DE-derived SDI; SDI, systolic dyssynchrony index; STE-SDI, STE-derived SDI.

Our study found that both 3DE and STE methods indicated a clear difference in the magnitude of dyssynchrony between subjects with and without LV systolic dysfunction, and there was significant difference in the severity of LVMD between patients with LV dysfunction with or without LBBB. These observations indicate accuracy of both the methods in discriminating patients with and without dyssynchrony, as well as in assessing severity of LVMD. We found the following similarities and dissimilarities when the two methods were compared.

A. **Similarities**: Both 3DE and STE revealed complete absence of dyssynchrony in the control group and a progressive rise in prevalence as well as magnitude of LVMD in the order as follows: group 1 < group 2 < group 3 < group 4 (Tables 2 and 3). Dyssynchrony was clearly dependant on LVEF rather than QRS duration. There was no significant difference in magnitude of LVMD between controls and those having BBB with normal LVEF when assessed using either of the two methods, and the frequency and magnitude of dyssynchrony were maximum in patients having LV dysfunction with LBBB. Magnitude of LVMD increased significantly from group 2 to group 3 and from group 3 to group 4 (Table 3). Dyssynchrony was observed by both 3DE and STE with comparable frequency in groups 1, 2, and 4; in fact, both 3DE and STE showed exactly matching figures for frequency of dyssynchrony in group 1 (0% each) and group 2 (9.5% each). However; in group 3, LVMD was diagnosed in significantly more patients by 3DE than by STE (60.3% vs 17.6%; $P < 0.001$).
B. **Differences**: Compared with STE, 3DE characterized more patients as having significant dyssynchrony in patients having narrow QRS with LV dysfunction (17.6% vs 60.3%, respectively; $P < 0.001$). In addition, when the two methods were compared for localization of most dyssynchronous segments, the results matched only in about 50% cases.

Because both STE and 3DE depend on timing the mechanical events, they are likely to assess LVMD efficiently. We used analogous methods for comparing the two modalities in the sense that both peak strain and Tmsv indicate the end of shortening. However; each method has its inherent, albeit different, advantage in

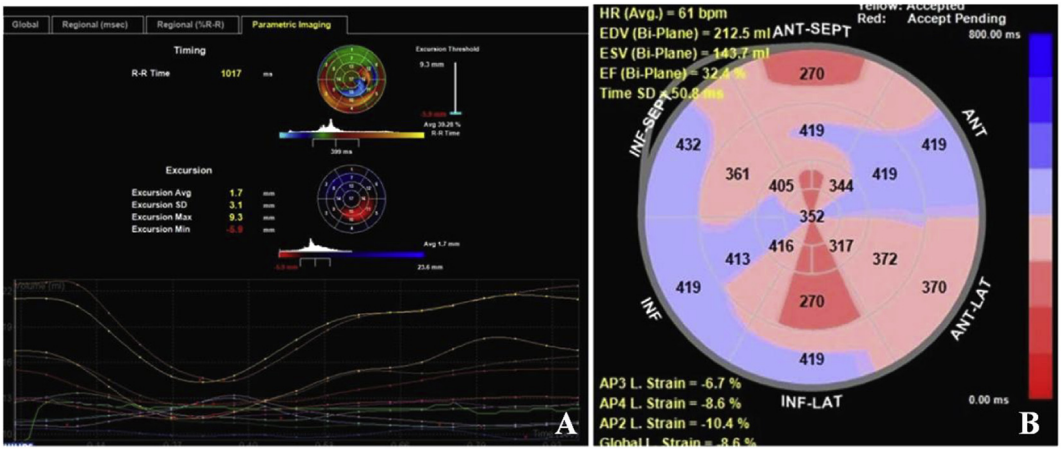

Fig. 3. Dyssynchrony assessment by 3DE (A) and STE (B) using color-coded bull's eye maps in a group 3 patient. This patient did not have significant dyssynchrony by both the methods. (A) shows time to achieve minimum systolic volumes for 17 LV segments (upper polar maps). Blue color indicates the earliest contracting segment; red color indicates the latest contracting (most asynchronous) segment. The lower part of the figure A shows regional time–volume curves for the earliest and most delayed segments; red arrow heads indicate minimum systolic volume for each segment. (B) shows time to achieve peak systolic strain for different LV segments. The basal inferior septal segment was found the most asynchronous by both the methods (compare A and B). 3DE, three-dimensional echocardiography; AP2, apical 2-chamber; AP3, apical 3-chamber; AP4, apical 4-chamber; EF, ejection fraction; HR, heart rate; LV, left ventricle; SD, standard deviation; STE, speckle tracking echocardiography.; ESV, end systolic volume.

Table 4
Reproducibility of dyssynchrony parameters (intraobserver variability).

Parameter	Correlation coefficients	Mean bias ± SD[b]
STE-SDI	0.95	−3.1 ± 8.67
3DE-SDI	0.96	−0.11 ± 0.34

3DE, three-dimensional echocardiography; 3DE-SDI, 3DE-derived SDI; SD, standard deviation; STE, speckle tracking echocardiography; STE-SDI, STE-derived SDI.
[a]Pearson correlation coefficients (all correlations are significant at the 0.001 level.)
[b] Bland–Altman analysis.

assessing LVMD; 3DE can examine the entire chamber geometry simultaneously, while STE precisely assesses segmental function through deformation and therefore can avoid the effect of tethering on observations,[16] thereby discerning contraction from passive movement.

4.1. Mapping of the latest mechanical activation

The concept of targeted lead positioning is supported by many observations; when studied using coronary vein electroanatomic mapping, the electrical activation sequence of LV is heterogeneous in presence of LBBB related to myocardial disease compared with that seen in right ventricular pacing.[17] Similar observations were reported by other investigators too.[18] Hence, morphologically similar ECGs may not be associated with similar activation and contraction sequences of different LV regions and emphasize the importance of identifying the appropriate LV segment for stationing the LV lead for effective CRT. There is strong evidence suggesting that the CRT results can be improved by positioning the LV lead in the area of the latest LV activation or latest mechanical contraction.[19–22] Longer term mortality benefit has also been observed in patients treated by targeted lead approach.[23] Logically, this concept may be even more relevant while considering CRT in patients with heart failure having LVMD with narrow QRS because they do not have predictable electrical activation sequence as there is no specific conduction abnormality.

Although invasive mapping methods such as CARTO, NOGA, or EnSite are most precise for identifying activation sequence,[24] these are not available everywhere because of logistic reasons, cost, and lack of expertise; moreover, the catheter-based method can interrogate a limited number of recording sites.[25] In addition, a preprocedure decision on whether or not a mechanical substrate is present in a patient justifying CRT is necessary; therefore, a less expensive, easy, but accurate noninvasive method in this context may be more practical for routine use.

In our study, despite strong agreement between quantitative parameters of LVMD, the attempt to localize the most delayed segment revealed disappointing results as the agreement between the two methods was low.

The disagreements observed between the two methods may be attributed to the following facts: (i) STE uses 2D planes, which may be partly oblique and therefore may affect the exact localization of the dyssynchronous segment, a factor minimized in 3DE; (ii) the apex identified for STE may not be the true apex, whereas the identified apex is more likely to be the true apex in 3DE because of the use of the X-plane feature; (iii) most importantly, the segments may be different in terms of maximum delay in peak myocardial motion and peak deformation because STE identifies the asynchronous segment by deformation analysis and therefore discriminates the tethering effect, whereas 3DE observations chiefly depend on the mechanical delay. However, we found that the 3DE-identified most dyssynchronous segments were also significantly delayed in 80.00% patients when assessed by STE; (iv) 3DE-SDI is corrected for R-R interval, whereas STE-SDI is not corrected.

5. Strengths and limitations

Our observations were consistent in a variety of subjects while comparing the two methods. The image recording for strain and 3DE analysis was done at the same sitting, ruling out the possibility of differences in HR, loading conditions, or any other physiological factor likely to influence observations. In addition, this ensured the same position of ECG electrodes which may influence the parameters because ECG triggering is used in both the imaging modalities studied here.

The limitations of this study are as follows: first, the results were not clinically validated by CRT responsiveness; second, the two methods studied here were not compared with other methods such as CMR-TAG; third, we could not assess interobserver variability because it is a single-operator study, although this was partially offset by the fact that the investigator was experienced in the two echocardiographic methods and the intraobserver variability was within acceptable limits; and fourth, the number of subjects in each group should have been larger, especially group 4. In view of these limitations, this study can be considered a hypothesis-generating pilot study with observations that need to be confirmed in a larger multicenter trial.

6. Conclusions

In this investigation, a variety of subjects were evaluated by two advanced echocardiographic methods, both of which provided consistent results in all four groups with progressive rise in magnitude of LVMD correlating with the disease severity. 3DE diagnosed more patients as having LVMD in the group having LV dysfunction with narrow QRS. Both the methods clearly discerned different groups in terms of severity of dyssynchrony. Because the most delayed segment assessed by two methods matched only in about half the cases, correlation with clinical CRT responsiveness is needed to conclude which method is more accurate in dyssynchrony mapping for targeted lead placement. Although various conventional and tissue Doppler–based dyssynchrony parameters have been compared earlier,[26] to the best of our knowledge, this is the first study comparing 3DE and STE for quantitative and qualitative assessment of LVMD.

Conflict of interest

None.

Funding

None.

References

1. Daubert JC, Saxon L, Adamson PB, et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management. *Heart Rhythm*. 2012;9:1524–1576.
2. Risum N, Tayal B, Hansen TF, et al. Identification of typical left bundle branch block contraction by strain echocardiography is additive to electrocardiography in prediction of long-term outcome after cardiac resynchronization therapy. *J Am Coll Cardiol*. 2015;66(6):631–641.
3. Kapetanakis S, Kearney MT, Siva A, et al. Real-time three-dimensional echocardiography: a novel technique to quantify global left ventricular mechanical dyssynchrony. *Circulation*. 2005;112(7):992–1000.
4. Penicka M, Bartunek J, De Bruyne B, et al. Improvement of left ventricular function after cardiac resynchronization therapy is predicted by tissue Doppler imaging echocardiography. *Circulation*. 2004;109(8):978–983.
5. Miyazaki Chinami, Powell Brian D, Bruce Charles J, et al. Comparison of echocardiographic dyssynchrony assessment by tissue velocity and strain imaging in subjects with or without systolic dysfunction and with or without left bundle-branch block. *Circulation*. 2008;117(20):2617–2625.

6. Zweerink A, van Everdingen WM, Nijveldt R, et al. Strain imaging to predict response to cardiac resynchronization therapy: a systematic comparison of strain parameters using multiple imaging techniques. *ESC Heart Fail*. 2018;5(6):1130–1140.
7. Surawicz B, Childers R, Deal BJ, et al, American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; American College of Cardiology Foundation; Heart Rhythm Society. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol*. 2009;53(11):976–981.
8. Mele D, Pasanisi G, Capasso F, et al. Left intraventricular myocardial deformation dyssynchrony identifies responders to cardiac resynchronization therapy in patients with heart failure. *Eur Heart J*. 2006;27:1070–1078.
9. van Everdingen WM, Zweerink A, Nijveldt R, et al. Comparison of strain imaging techniques in CRT candidates: CMR tagging, CMR feature tracking and speckle tracking echocardiography. *Int J Cardiovasc Imaging*. 2018;34(3):443–456.
10. Bhambhani A, John N, Kumar B, et al. Three-dimensional echocardiographic evaluation of mechanical dyssynchrony in systolic heart failure with narrow QRS complex. *Indian Heart J*. 2018;70(3):387–393.
11. Mullens W, Grimm RA, Verga T, et al. Insights from a cardiac resynchronization optimization clinic as part of a heart failure disease management program. *J Am Coll Cardiol*. 2009;53(9):765–773.
12. Soliman OI, Theuns DA, Geleijnse ML, et al. Spectral pulsed-wave tissue Doppler imaging lateral-to-septal delay fails to predict clinical or echocardiographic outcome after cardiac resynchronization therapy. *Europace*. 2007;9:113–118.
13. Duncan AM, Lim E, Clague J, et al. Comparison of segmental and global markers of dyssynchrony in predicting clinical response to cardiac resynchronization. *Eur Heart J*. 2006;27:2426–2432.
14. D'Hooge J, Barbosa D, Gao H, et al. Two-dimensional speckle tracking echocardiography: standardization efforts based on synthetic ultrasound data. *Eur Heart J Cardiovasc Imaging*. 2016;17(6):693–701.
15. van Everdingen WM, Maass AH, Vernooy K, et al. Comparison of strain parameters in dyssynchronous heart failure between speckle tracking echocardiography vendor systems. *Cardiovasc Ultrasound*. 2017;15(1):25.
16. Urheim S, Edvardsen T, Torp H, et al. Myocardial strain by Doppler echocardiography: validation of a new method to quantify regional myocardial function. *Circulation*. 2000;102:1158–1164.
17. Mafi Rad M, Blaauw Y, Dinh T, et al. Different regions of latest electrical activation during left bundle-branch block and right ventricular pacing in cardiac resynchronization therapy patients determined by coronary venous electroanatomic mapping. *Eur J Heart Fail*. 2014;16(11):1214–1222.
18. Ludwig DR, Tanaka H, Friehling M, et al. Further deterioration of LV ejection fraction and mechanical synchrony during RV apical pacing in patients with heart failure and LBBB. *J Cardiovasc Transl Res*. 2013;6:425–429.
19. Ypenburg C, van Bommel RJ, Delgado V, et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. *J Am Coll Cardiol*. 2008;52:1402–1409.
20. Becker M, Kramann R, Franke A, et al. Impact of left ventricular lead position in cardiac resynchronization therapy on left ventricular remodelling. A circumferential strain analysis based on 2D echocardiography. *Eur Heart J*. 2007;28:1211–1220.
21. Khan FZ, Virdee MS, Palmer CR, et al. Targeted left ventricular lead placement to guide cardiac resynchronization therapy: the TARGET study: a randomized, controlled trial. *J Am Coll Cardiol*. 2012;59:1509–1518.
22. Saba S, Marek J, Schwartzman D, et al. Echocardiography-guided left ventricular lead placement for cardiac resynchronization therapy: results of the Speckle Tracking Assisted Resynchronization Therapy for Electrode Region trial. *Circ Heart Fail*. 2013;6:427–434.
23. Kydd AC, Khan FZ, Watson WD, et al. Prognostic benefit of optimum left ventricular lead position in cardiac resynchronization therapy: follow-up of the TARGET Study Cohort (Targeted Left Ventricular Lead Placement to guide Cardiac Resynchronization Therapy). *JACC Heart Fail*. 2014;2(3):205–212.
24. Engels EB, Mafi-Rad M, van Stipdonk AM, et al. Why QRS duration should be replaced by better measures of electrical activation to improve patient selection for cardiac resynchronization therapy. *J Cardiovasc Transl Res*. 2016;9(4):257–265.
25. Auricchio A, Fantoni C, Regoli F, et al. Characterization of left ventricular activation in patients with heart failure and left bundle-branch block. *Circulation*. 2004;109:1133–1139.
26. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. *Circulation*. 2008;117:2608–2616.