Original Article

Ventricular Dyssynchrony Index: Comparison with Two-Dimensional and Three-Dimensional Ejection Fraction

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Summary

Background: **Left ventricular (LV) electromechanical coupling (synchrony) is important in the analysis of the systolic performance, especially for the indication of cardiac resynchronization therapy in patients with advanced CHF.**

Objective: **To compare LV synchrony as analyzed by real-time three-dimensional (3D) echocardiography (ECHO) with LVEF measurements as obtained with 2D and 3D ECHO.**

Methods: **Prospective study of 92 individuals (56 men, 47 ± 10 years of age), of which 60 had normal heart structure (ECHO) and ECG (N group), and 32 had dilated cardiomyopathy (DCM group). Using 3D ECHO, LVEF, volumes and dyssynchrony index (%DI) for 16 LV segments were measured. Using 2D ECHO, LVEF (Simpson's method), and LV systolic and diastolic volumes were measured. Statistical analysis: Pearson's correlation coefficient, 95% CI, linear regression model, Bland & Altman analysis, $p<0.05$.**

Results: **%DI ranged from 0.2900 to 28.1000 (5.2014±6.3281), 3D LVEF ranged from 0.17 to 0.81 (0.52±0.17); and 2D LVEF ranged from 0.3 to 0.69 (0.49±0.11). The correlation between DI and 3D LVEF was (r): -0.7432, $p<0.0001$, CI: -0.8227 to -0.6350, the linear relation between DI (x) and 3D LVEF (y) was $y = 19.8124 + (-27.9578)\,x$, $p<0.0001$. The correlation between DI and 2D LVEF was (r): -0.7012, $p<0.0001$, CI: -0.7923 to -0.5797.**

Conclusion: **In this case series, a good negative correlation was observed between LV electromechanical three-dimensional systolic coupling and LVEF as measured by echocardiography (3D and 2D). (Arq Bras Cardiol 2008;91(3):142-147)**

Key words: **Ventricular function, left; systole; echocardiography; stroke volume.**

Introduction

The analysis of ventricular systolic performance represents an important aspect for the diagnostic and prognostic assessment, as well as for the understanding of the natural history of heart diseases[1-4]. The ventricular systolic performance may be studied using echocardiography based on the left ventricular radial, longitudinal and circumferential motion (vetoechocardiography)[1-4]. The temporal aspect of the moment of contraction – left ventricular (LV) electromechanical systolic coupling, is also important to determine ventricular performance, mainly in the evaluation of the indication of cardiac resynchronization therapy in patients with advanced congestive heart failure (CHF).

The left ventricular systolic function may be analyzed using the M-mode, the two-dimensional mode with techniques such as strain, strain-rate and tissue tracking which analyze ventricular longitudinal deformation, and also using the three-dimensional echocardiography[1-9]. Three-dimensional echocardiography is more improved in relation to two-dimensional echocardiography because it is not based on geometric inferences for the calculation of volumes of cardiac chambers, ventricular mass, and left ventricular ejection fraction, considering a limited number of observation planes[9-16]. An application of three-dimensional echocardiography that may have a great clinical impact is related to the indication and clinical follow-up of patients with NYHA functional class III and IV CHF undergoing cardiac resynchronization therapy with biventricular pacemaker.

Today, we recognize that electrical dyssynchrony as evidenced by ECG alone may be not enough to discriminate patients with advanced CHF who will respond satisfactorily to biventricular pacemaker implantation therapy[16-19]. The evaluation of electromechanical ventricular synchrony is necessary to improve the indication of cardiac resynchronization therapy[16-19]. In this context, the use of three-dimensional echocardiography enables the determination and quantification of the presence of ventricular electromechanical dyssynchrony[15,16]. Three-dimensional echocardiography provides details of the percentage cardiac dyssynchrony by measuring the cardiac dyssynchrony index (%DI)[15,16]. %DI represents the standard deviation of the mean end-systolic

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contraction time of each one of the cardiac segments as compared with global end-systolic contraction (a lower index indicates lower dyssynchrony).

The analysis of DI also allows the indication of the best site for biventricular electrode implantation (which is the segment of maximum dyssynchrony). Few studies in the literature aimed at comparing the left ventricular assessment using volumetric variation (ejection fraction) with ventricular electromechanical coupling[15].

Thus, the objective of this study was to compare the three-dimensional percentage cardiac dyssynchrony index (%DI) with left ventricular ejection fraction as measured by two-dimensional and three-dimensional echocardiography in individuals with normal cardiac structure as well as in patients with ventricular dysfunction.

Methods

Population

In the period from January 2006 to January 2007, 92 consecutive individuals undergoing echocardiographic investigation in the echocardiography laboratory of *Hospital Israelita Albert Einstein*, Sao Paulo, were prospectively studied. Demographic, clinical and electrocardiographic characteristics of the study population are shown in Table 1. This study included 60 individuals who presented a structural cardiac analysis considered normal (two-dimensional and three-dimensional echocardiographic analysis, conventional Doppler and tissue Doppler), and a 12-lead ECG with normal limits. It also included 32 patients with abnormal cardiac structure (ventricular dilation) and intraventricular conduction abnormalities (ECG). Of the 60 individuals who presented a normal cardiac structure, 25 were being clinically assessed to be donors for kidney or liver transplantation.

Table 1 - **Demographic, clinical, electrocardiographic and echocardiographic characteristics of the study population**

	General population (n- 92)	Normal group (n-60)	DCM (n-32)
Age (years)	47±10	46±8	56±7
Gender (M/F)	56/36	36/24	18/14
Clinical condition (IDMC/ COI/ PRET X/ N)	11/21/25/ 35	(-/-/25/35)	(11/21/-/-)
ECG Morphology (N/ LBBB/ RBBB)	60/27/5	60/-/-	-/27/5
ECG Duration (ms)	103±32	80±8	147±16
3D ECHO LVEF	0.52±0.17 (0.18-0.80)	0.61±0.11 (0.55-0.80)	0.34±0.12 (0.18-0.32)
3D ECHO (ESV) mL	59.57±21.63 (25.2-76.4)	30.32±13.45 (25.2 - 34.2)	119.87±25.1 (46.2-76.4)
3D ECO (EDV) mL	119.31±36.58 (78.3-234.1)	89.42±13.74 (78.3-87.1)	179.98±19.75 (134.7-234.1)
2D ECHO LVEF	0.49±0.10 (0.20-0.69)	0.59±0.17 (0.56-0.69)	0.32±0.18 (0.20-0.34)
2D ECHO (ESV) mL	55.32±28.72 (26.7-81.3)	29.45±14.7 (26.7-41.2)	113.58±22.98 (51.2-81.3)
2D ECHO (EDV) mL	115.58±31.23 (82.3-251.2)	84.12±16.27 (82.3-89.1)	172.37±17.36 (142.1-251.2)

M - male; F - female; DCM - dilated cardiomyopathy; IDCM - idiopathic dilated cardiomyopathy; COI - coronary insufficiency; Pre TX (donor) - kidney or liver pre-transplantation; N - normal; LBBB - left bundle branch block; RBBB - right bundle branch block; LVEF - left ventricular ejection fraction; ESV - left ventricular end-systolic volume; EDV - left ventricular end-diastolic volume. Values are expressed as mean ± standard deviation. LVEF and LV volume measurements are expressed as mean ± standard deviation, minimum and maximum values for the different groups.

Echocardiography

The individuals underwent two-dimensional echocardiography, conventional Doppler, tissue Doppler and three-dimensional echocardiography. The two-dimensional echocardiographic tests were performed according to recommendations of the American Society of Echocardiography, using a commercially available instrument (Philips IE33, Andover, MA, USA) equipped with a 2.5 MHZ transducer, and an X3 matrix transducer for the acquisition of three-dimensional images. The following echocardiographic parameters were studied:

I- Two-dimensional echocardiography

1. Left ventricular end-diastolic volume (LVEDV); 2. Left ventricular end-systolic volume (LVESV); 3. Left ventricular ejection fraction (LVEF) (Simpson's rule);

II- Three-dimensional echocardiography

1- Left ventricular end-diastolic volume (LVEDV); 2- Left ventricular end-systolic volume (LVESV); 3- Left ventricular ejection fraction (LVEF) (Figures 1, 2); 4- Percentage left ventricular dyssynchrony index (DI) (Figure 3). The 16-ventricular segment model was used for the analysis of left ventricular contractility.

Three-dimensional images were acquired in the sequence of the two-dimensional echocardiographic test. The images were obtained with the same echocardiographic equipment, using a matrix transducer with the patient in expiratory breath-hold; the image was coupled to the electrocardiographic recording. The images were stored in the hard disk of the echocardiographic equipment and analyzed off-line in a specific software of the equipment. The analyses were performed by two independent observers. The patients who did not have two-dimensional or three-dimensional images whose quality was considered technically adequate for the analysis of the parameters studied or those who presented a significant irregularity of the heart rhythm were not included in this study. Thus, ten patients were not included in the study: seven who had images considered inadequate for the left ventricular analysis, and three due to a significant irregularity of the heart rhythm.

The left ventricular dyssyncrhony index (DI) represents the variation of left ventricular volumes in relation to their temporal occurrence within the cardiac cycle, that is, it represents the chance of the global systolic volume into global diastolic volume from the temporal point of view. As

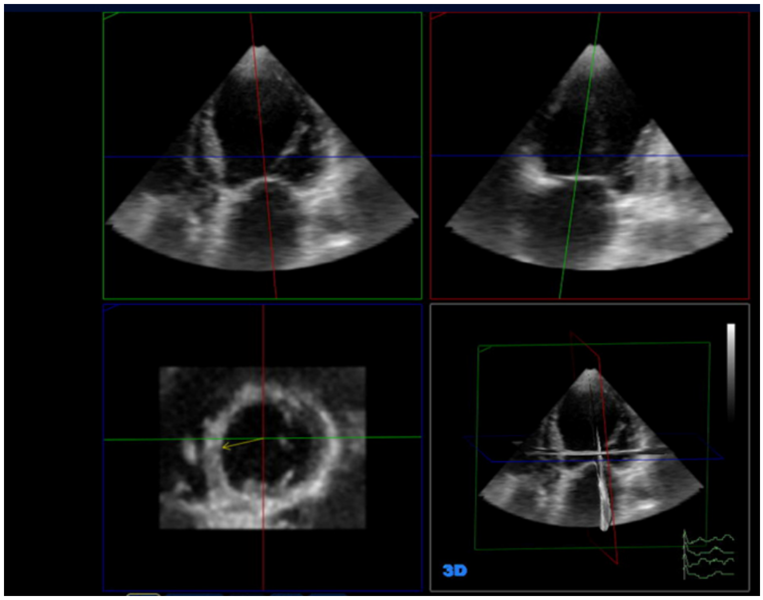


Figure 1 - Two-dimensional transthoracic echocardiographic image with the three basic planes (inferosuperior in the blue line, midlateral in the green line, elevation or depth in the red line) for composition of the three-dimensional images.

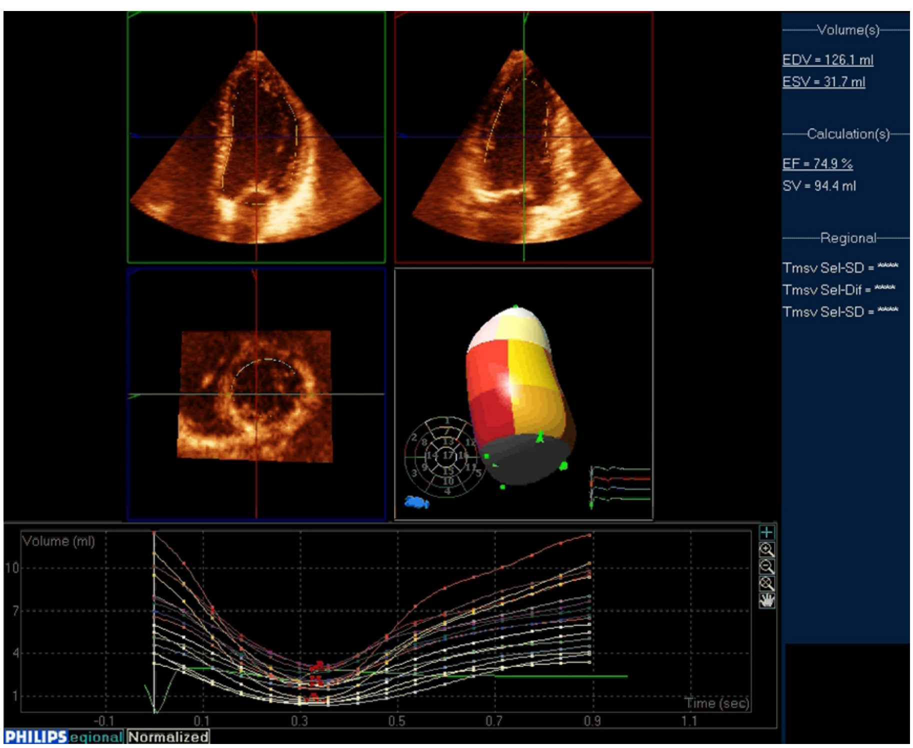


Figure 2 - Real-time three-dimensional transthoracic image demonstrating the left ventricular end-diastolic volume (EDV), left ventricular end-systolic volume (ESV), and the curves for derivation of left ventricular regional dyssynchrony indexes in a normal individual.

a greater left ventricular synchrony occurs, the change of the global systolic volume into global diastolic volume will be more homogeneous and synchronic. Conversely, as ventricular dyssynchrony occurs, the change between the systolic and diastolic volumes will be heterogeneous and dyssynchronic, thus leading to a loss in ventricular systolic performance. The DI may be represented in a global or regional form, demonstrating regional synchrony or dyssynchrony for the

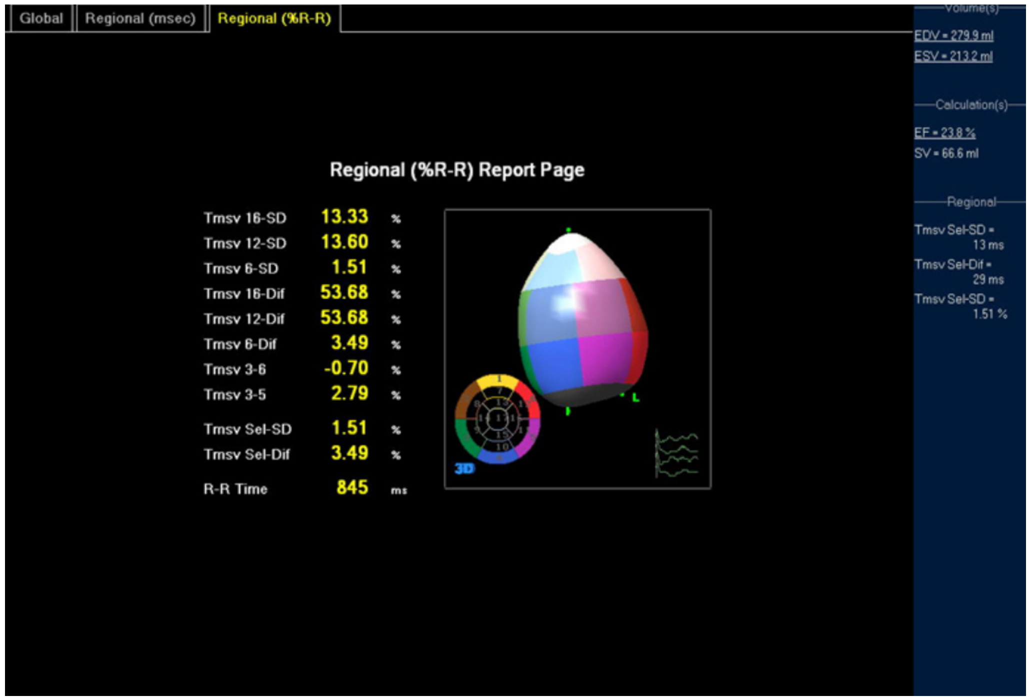


Figure 3 - Real-time three-dimensional transthoracic image demonstrating the 16-ventricular segment dyssynchrony index (Tmsv 16 SD: 13.33%) in a patient with ventricular dysfunction and left ventricular dyssynchrony. EDV - left ventricular end-diastolic volume; EF - left ventricular ejection fraction.

left ventricular contraction model (16 or 17 segments). The regional DI is represented by the standard deviation of the mean end-systolic contraction time of each one of the cardiac segments. The DI may be expressed as: 1- percentage of the cardiac cycle (%DI) or Tmsv (time in milliseconds relative to the total cardiac cycle); 2- absolute time (in milliseconds).

Statistical analysis

Descriptive, correlation and comparative analyses between the methods were performed. The descriptive analysis of continuous variables was performed by the observation of the minimum and maximum values, and of the calculation of means and standard deviations. The correlation analysis was performed using Pearson's correlation (r), 95% confidence interval. The comparison between methods was performed using the Bland & Altman analysis. Linear regression model was also performed between the parameters measured with two-dimensional and three-dimensional echocardiography. The measurements were taken by two independent observers. P values < 0.05 were considered significant. Data were processed with the SAS Institute statistical analysis system, Cary, North Carolina, USA.

Results

Two-dimensional and three-dimensional echocardiographic measurements of volumes and ejection fraction of the study population are shown in Table 1. The descriptive analysis of the dyssynchrony index measurements (%DI) for 16 LV segments is shown in Table 2. Good agreement (r) was observed between 3D LVEF and 2D LVEF measurements, (r): 0.8976, $p<0.0001$, CI: 0.8488 to 0.9312. The intra and interobserver agreement coefficients for ejection fraction measurements by three-dimensional echocardiography and for the ventricular dyssynchrony index are shown in Table 3.

The results regarding the correlation analysis (r: Pearson) and linear regression for percentage dyssynchrony index measurements (%DI) and for LV ejection fraction measurements by 2D and 3D echocardiography are shown in Table 4. The

Table 2 - Descriptive analysis of % left ventricular dyssynchrony index (DI) measurements (16 segments) by three-dimensional echocardiography in the study population

% LV DI 16 segments	Population (n- 92)
Minimum	0.2900
Maximum	27.1000
Mean	5.2014
Standard deviation	6.3281
Mean 95% CI	3.8909 to 6.5119
Median	1.9200
Median 95% CI	1.4000 to 3.1176
Relative standard deviation	1.2166 (121.66%)
Standard error of the mean	0.6598

% DI - % left ventricular dyssynchrony index (DI); CI - confidence interval; LV - left ventricle.

Table 3 - Intra and interobserver agreement coefficients for ejection fraction as measured by three-dimensional echocardiography and for ventricular dyssynchrony index

	Intraobserver agreement coefficient	Interobserver agreement coefficient
3D LVEF	0.8698 95% CI (0.7194 to 0.9423) Accuracy (Pearson): 0.8758	0.8061 95% CI (0.5995 to 0.9120) Accuracy (Pearson): 0.8167
% LV DI 16 segments	0.8749 95% CI (0.7441 to 0.9411) Accuracy (Pearson): 0.9394	0.8109 95 % CI (0.6504 to 0.9020) Accuracy (Pearson): 0.9383

comparison between ejection fraction measurements by three-dimensional echocardiography and 16-segment left ventricular dyssynchrony index (Bland & Altman analysis) is shown in Graph 1.

DISCUSSION

Real-time three-dimensional transthoracic echocardiography is a novel method of structural and functional analysis of the heart that permits real-time three dimensional investigation of the heart without using ionizing radiation, and is highly reproducible and easy to obtain[5-16]. It has a good cost-benefit ratio when compared with methods such as magnetic resonance imaging and also increases the possibility of identifying patients with advanced heart failure who can benefit from cardiac resynchronization therapy using biventricular pacemaker implantation. In these patients eligible to biventricular pacemaker implantation, the determination of ventricular diameters, left ventricular ejection fraction, and of the existence of electromechanical dyssynchrony is fundamental[17-19]. The determination of the global left ventricular volume variation ratio (ejection fraction) alone may not be enough to provide overall and customized information on the temporal profile of contraction of all the left ventricular segments. In this sense, real-time three-dimensional echocardiography allows the measurement of temporal contraction of the left ventricular segments both in a global and segmental fashion[15,16] (Figure 3, curves in different colors). It can also provide the identification of cardiac dyssynchrony in segments that are not studied in standard analysis protocols of cardiac synchrony (protocols using conventional Doppler and tissue Doppler with the analysis of the left ventricular basal segments). An example of this situation may be observed in Figure 3, which shows the evidence of electromechanical dyssynchrony in the mid-cavity segments (% dyssynchrony index: Tmsv 12-SD of 13.60%, normal value < 8%); this dyssynchrony would not be identified by the usual analysis protocols of cardiac synchrony.

In the present study, two thirds of the population was comprised of individuals with a normal cardiac structure, who were asymptomatic and had a normal 12-lead ECG. With this part of the population we could determine reference values for the three-dimensional echocardiographic findings. These data are shown in Table 1. We observed that systolic and diastolic volumes, as well as left ventricular ejection fraction as measured by 3D ECHO were slightly higher than those measured using 2D ECHO, although without statistical significance (p=0.52). A similar result was found in the group of patients with cardiomyopathy.

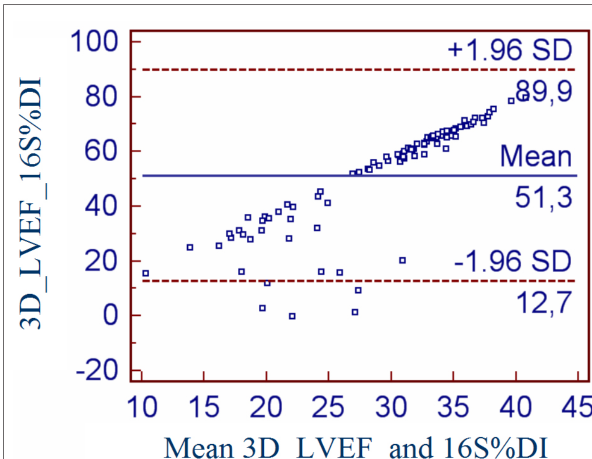
Intra and interobserver agreement for the measurement of three-dimensional ejection fraction and for DI was adequate, thus demonstrating a good reproducibility in the determination of three-dimensional measurements (Table 3). We also observed a good correlation for the measurement of ejection fraction using 2D and 3D ECHO (r): 0.8976, p<0.0001, and good agreement (Bland & Altman analysis) for the measurements of ejection fraction by 3D ECHO as well as for the left ventricular dyssynchrony index (Graph 1).

There was great variability in the descriptive analysis and distribution frequency of % left ventricular dyssynchrony index (DI) (16 segments) (Table 2) due to the study sample (two thirds of the population comprised of normal individuals and one third comprised of patients with ventricular dysfunction). However, the correlation between three-dimensional ejection fraction and dyssynchrony index (DI) was adequate both for the total group (r= -0.7432, p<0.0001, Table 4), and for the group of

Table 4 - Correlation (r) and linear regression analyses for left ventricular % dyssynchrony index (DI) (16 segments) as measured using three-dimensional echocardiography in the study population in relation to ejection fraction values as measured by 2D and 3D echocardiography

LV % DI 16 segments (n-92)	Pearson's correlation (r)	Linear regression DI (y) and LVEF (x)
3D EF	-0.7432 p < 0.0001 CI: 0.8227 to -0.6350	y = 19.8124 + (-27.9578) x p<0.0001
2D EF	-0.7012 p<0.0001 CI: -0.7923 to -0.5797	y = 25.2756 + (-40.5005) x p<0.0001

CI - confidence interval; LV - left ventricle.



Graphic 1 - Comparison (Bland & Altman analysis) between left ventricular ejection fraction values as measured using three-dimensional echocardiography (3D LVEF) and 16-segment left ventricular dyssynchrony index (16S% DI). Mean 3D LVEF and 16S % DI – mean left ventricular ejection fraction and ventricular dyssynchrony index for a 16-segment left ventricular model.

normal individuals (r= -0.67, p<0.0001), as well as for the group of patients with cardiomyopathy (r= -0.79, p<0.0001). The correlation with two-dimensional ejection fraction was also adequate for the total group (r= -0.7012, p<0.0001), but was lower for the group of patients with cardiomyopathy (r= -0.56, p<0.0001). Certainly the dyssynchrony index will be useful in the observation of patients with cardiac dyssynchrony not detected in protocols in which more usual procedures such as conventional Doppler or tissue Doppler were used.

We can imagine a hierarchical use of echocardiographic techniques of investigation of cardiac dyssynchrony considering the M-mode analysis, conventional Doppler, tissue Doppler, and three-dimensional echocardiography. DI has a higher representativeness and will possibly be performed in the daily clinical practice for the identification of cardiac dyssynchrony in patients with advanced CHF who are eligible for cardiac resynchronization therapy. This is probably the situation in which this new echocardiographic concept for the analysis of left ventricular performance will be useful.

It is reasonable to consider that the use of novel techniques such as three-dimensional echocardiography will add costs to the methods of diagnostic investigation. However, we should consider that the cost of the cardiac resynchronization therapy with biventricular pacing is already established, and that this method should have a precise and well-grounded indication in order to prevent the failure of clinical response to its performance.

Study limitations

The study should be broadened to include a greater number of patients with ventricular dysfunction in different clinical situations, such as individuals with atrial fibrillation and patients with narrow QRS with evidence of electromechanical dyssynchrony, as well as a greater number of patients with right bundle branch block (important for patients with Chagas disease).

Conclusion

In this case series, a good correlation was observed between left ventricular electromechanical coupling and ejection fraction as measured by three-dimensional and two-dimensional echocardiography.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any graduation program.

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