Three-dimensional echocardiographic analysis of electromechanical synchrony: comparison with three-dimensional and two-dimensional ejection fraction for evaluation of left ventricular systolic performance

Sincronia eletromecânica ecocardiográfica tridimensional: comparação com a fração de ejeção tridimensional e bidimensional para a análise da performance sistólica ventricular esquerda

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ABSTRACT
Objective: To compare the three-dimensional echocardiographic analysis of left ventricular (LV) synchrony to LV ejection fraction (LVEF) as measured by two-dimensional (2D) and three-dimensional (3D) echocardiography (ECHO).

Methods: This is a prospective study of 71 patients (41 males, aged 49 ± 11 years), 40 of whom with normal cardiac anatomy (ECHO) and electrocardiography (ECG) (Group N), and 31 with dilated cardiomyopathy (Group DCM). LVEF, volumes and 16-segment dyssynchrony index % (DI) were measured using 3D-ECHO. LVEF (Simpson’s rule) and volumes were measured using 2D-ECHO. Data were compared using Pearson correlation coefficient (r), 95% CI, linear regression equation and Bland-Altman analysis, p < 0.05.

Results: DI% ranged from 0.32 to 21.7% (5.94 ± 6.46), 3D LVEF from 0.16 to 0.73 (0.51 ± 0.15); and 2D LVEF from 0.2 to 0.7 (0.47 ± 0.17). The correlation coefficient (r) for DI and 3D LVEF was (r): -0.8203, p < 0.0001, CI = -0.8844 to -0.7259, linear regression for DI% (x) and 3D LVEF (y) was: \( y = 63.4515 + (-2.0233) x \), p < 0.0001. The correlation coefficient (r) for DI% and 2D LVEF was (r): -0.7046, p < 0.0001, CI = -0.7675 to -0.5824, linear regression for DI% (x) and 2D LVEF (y) was: \( y = 59.345 + (-3.8721) x \), p < 0.0001.

Conclusions: Good negative correlation between LV synchrony (3D-ECHO) and echocardiographic LVEF (2D and 3D) was observed in this series.

Keywords: Echocardiography, three-dimensional; Ventricular function; Systole

RESUMO
Objetivo: Comparar a análise da sincronia do ventrículo esquerdo (VE) aferida com a ecocardiografia (ECO) tridimensional com as medidas de fração de ejeção do VE (FEVE) obtidas com ECO bidimensional (2D) e tridimensional (3D).

Métodos: Estudo prospectivo de 71 indivíduos (41 homens, 49 ± 11 anos), 40 apresentando anatomia cardíaca (ECO) e eletrocardiografia (ECG) normais (Grupo N), 31 pacientes portadores de cardiomiopatia dilatada (Grupo DCM). Foram medidos com a ECO 3D: FEVE, volumes e o índice de dissincronia (ID) % para 16 segmentos do VE; com o ECO 2D foram aferidos: FEVE.

Study carried out at Hospital Israelita Albert Einstein – HIAE, São Paulo (SP), Brazil.
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INTRODUCTION

Left ventricular contractility can be currently observed by analyzing longitudinal myocardial fiber thickening, longitudinal motion of fibers located between the atrioventricular ring and the ventricular apex, and also by measuring ventricular rotation accomplished by the motion of circumferential fibers evidenced in the different left ventricular (LV) planes (1-4). Another key aspect for the analysis of global LV performance is the evidence of its adequate electromechanical coupling (synchrony) during the cardiac cycle. Maintaining cardiac synchrony is fundamental for a satisfactory response to cardiac resynchronization therapy in patients with severe ventricular dysfunction.

Several echocardiographic methods allow the analysis of myocardial systolic performance. Myocardial contractility can be analyzed using older techniques such as the M-mode and two-dimensional methods with the strain, strain-rate and tissue tracking techniques, which analyze longitudinal ventricular deformation and three-dimensional echocardiography can also be used (1-9).

Three-dimensional echocardiography provides global LV visualization from multiple observation planes. It offers additional anatomical and functional information in relation to two-dimensional echocardiographic analysis, because it is not based on geometric assumptions for the calculation of cardiac chamber volumes and LV ejection fraction (9-10). Analysis of cardiac synchrony using three-dimensional echocardiography provides not only qualitative discrimination of LV synchrony (with determination of the site with the most severe cardiac dyssynchrony), but also allows the quantification of the cardiac dyssynchrony percentage (15,16). LV dyssynchrony is quantified by measuring the three-dimensional cardiac dyssynchrony index percentage (DI%) (15,16). DI% is calculated by the standard deviation of the mean end-systolic contraction time of each one of the cardiac segments in comparison with the global end-systolic contraction (lower indexes correspond to lower dyssynchrony). Little information is available in the literature correlating LV fraction with ventricular electromechanical coupling (synchrony) (15).

OBJECTIVE

The objective of this study was to compare the DI% with LV ejection fraction as measured by two and three-dimensional echocardiography in individuals with normal cardiac anatomy as well as in patients with LV dysfunction.

METHODS

Population

From January 2007 to January 2008, 71 individuals undergoing echocardiographic study in the echocardiography laboratory of Hospital Israelita Albert Einstein (HIAE), São Paulo, were prospectively studied. Demographic, clinical and electrocardiographic characteristics of the study population are shown in Table 1. A total of 40 individuals with normal cardiac structure (as analyzed by two- and three-dimensional echocardiographic studies, conventional Doppler and tissue Doppler) and 12-lead electrocardiography (ECG) within normal limits, and 31 patients with abnormal cardiac anatomy (ventricular dilatation) and intraventricular conduction disturbances (ECG) were included in the study.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>General population (n = 71)</th>
<th>Normal Group (n = 40)</th>
<th>DCM Group (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49 ± 11</td>
<td>44 ± 5</td>
<td>55 ± 8</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>41/30</td>
<td>23/17</td>
<td>18/13</td>
</tr>
<tr>
<td>Clinical condition (ICMD/COI/PRE TX/N)</td>
<td>(11/20/-/-)</td>
<td>(11/20/-/-)</td>
<td>(11/20/-/-)</td>
</tr>
<tr>
<td>ECG</td>
<td>40/26/5</td>
<td>40/-/-</td>
<td>-26/5</td>
</tr>
<tr>
<td>ECG Duration (minutes)</td>
<td>101 ± 32</td>
<td>75 ± 5</td>
<td>148 ± 14</td>
</tr>
<tr>
<td>3D-ECHO LVEF</td>
<td>0.51 ± 0.15 (0.16-0.73)</td>
<td>0.62 ± 0.1</td>
<td>0.33 ± 0.11</td>
</tr>
<tr>
<td>3D-ECHO (LVEDV) ml</td>
<td>59.5 ± 22.9</td>
<td>29.37 ± 11.85</td>
<td>121.2 ± 24.3</td>
</tr>
<tr>
<td>2D-ECHO LVEF</td>
<td>114.8 ± 31.7</td>
<td>88.7 ± 12.4</td>
<td>177.9 ± 20.2</td>
</tr>
<tr>
<td>2D-ECHO (LVEDV) ml</td>
<td>51.8 ± 24.8</td>
<td>25.9 ± 13.7</td>
<td>114.6 ± 23.6</td>
</tr>
</tbody>
</table>

M = male; F = female; DCM = dilated cardiomyopathy; ICMD = idiopathic dilated cardiomyopathy; COI = coronary insufficiency; PRETX (donor) = before renal or hepatic transplant; N = normal; LBBB = left bundle branch block; RBBB = right bundle branch block; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume. The values are expressed as mean ± standard deviation.
the study. Of the 40 individuals with normal cardiac anatomy, 25 were undergoing clinical evaluation as renal or liver transplant donors. The study was approved by the Research Ethics Committee of the Teaching and Research Institute of HIAE.

**Echocardiography**

The individuals underwent two-dimensional echocardiographic study, cardiac flow analysis using conventional Doppler and tissue Doppler, and morphological and functional analysis with three-dimensional echocardiography. The two-dimensional echocardiographic studies were performed according to recommendations of the American Society of Echocardiography in a commercially available equipment (Philips IE33, Andover, MA, USA), equipped with a 2 to 5 MHZ transducer and X3 matrix-array transducer for three-dimensional image acquisition. The following echocardiographic parameters were studied:

- two-dimensional echocardiography: left ventricular end-diastolic volume (LVEDV); left ventricular end-systolic volume (LVESV); left ventricular ejection fraction (LVEF) by Simpson’s rule;
- three-dimensional echocardiography: LVEDV; LVESV; LVEF; DI% of the LV. LV dyssynchrony indexes ≤ 8% are considered normal\(^{(15)}\). The 16-segment model was used for the analysis of left ventricular contractility. DI% and left ventricular volumes and ejection fraction measurements are shown in Figures 1 and 2.

Three-dimensional images were acquired after the two-dimensional echocardiographic study. The images were obtained with the same echocardiography equipment using a matrix-array transducer with the patient in expiratory breath-hold, and the image was gated to the electrocardiographic recording. The images were stored in the hard disk of the echocardiography equipment and analyzed off-line in equipment’s specific software (Q Lab, version 5.0, Philips, Andover, MA, USA). The analyses were carried out by two independent observers. Nine patients were excluded from the study, five due to images considered inadequate for left ventricular analysis, and four due to significantly irregular heart rhythm (atrial fibrillation).

**Statistical analysis**

Descriptive, correlation and comparison analyses between the methods were carried out. Continuous variables were described by the minimum and maximum values and by the calculation of means and standard deviation. The Pearson’s correlation method (r) and 95% confidence interval, was used for correlation analysis. Bland-Altman analysis was used for comparison between methods. Linear regression test between the parameters obtained with two and three-dimensional echocardiography was also performed. Measurements were taken by two independent observers. P values < 0.05 were considered significant. The MedCalc statistical analysis system, Mariakerke, Belgium, was used for data analysis.
RESULTS

Clinical and electrocardiographic characteristics as well as echocardiographic measurements (volumes and ejection fraction) of the study population are shown in Table 1. Descriptive statistical analysis of the 16-segment DI% is shown in Table 2. Good concordance (r) was observed for 3D LVEF and 2D LVEF, (r): 0.8543, p < 0.0001, CI: 0.8132 to 0.9167. Intra and interobserver agreement coefficients in relation to ejection fraction, as measured using three-dimensional echocardiography, and to the ventricular DI are shown in Table 3.

Correlation analysis (r: Pearson) and linear regression equation for DI% and LV ejection fraction as measured by 2D and 3D echocardiography are shown in Table 4. Distribution of measurements (histogram and cumulative relative frequency) of ejection fraction as determined using three-dimensional echocardiography and 16-segment DI% is shown in Graphics 1, 2, 3 and 4. Most of the individuals presented a DI of up to 4%, and LVEF (3D ECHO) above 50%. Linear regression analysis between three-dimensional ejection fraction and 16-segment DI% measurements is shown in Graphic 5.

The concordance (Bland-Altman analysis) between three-dimensional ejection fraction measurements and 16-segment DI% measurements is shown in Graphic 6. Good concordance was observed between ejection fraction measurements (3D ECHO) and cardiac dyssynchrony index measurements.

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**Table 2.** Description of left ventricular 16-segment dyssynchrony index (DI) measured by three-dimensional echocardiography of the population studied

<table>
<thead>
<tr>
<th>LV DI% 16 segments</th>
<th>Population (n = 71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>0.32</td>
</tr>
<tr>
<td>Maximum</td>
<td>21.7</td>
</tr>
<tr>
<td>Mean</td>
<td>5.94</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>6.46</td>
</tr>
<tr>
<td>Mean 95% CI</td>
<td>1.7132 to 3.8317</td>
</tr>
<tr>
<td>Median</td>
<td>2.65</td>
</tr>
</tbody>
</table>

**Table 3.** Intraobserver and interobserver agreement coefficients for ejection fraction and dyssynchrony index (DI%) of the left ventricle, measured by three-dimensional echocardiography

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Intraobserver agreement coefficient</th>
<th>Interobserver agreement coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D LVEF</td>
<td>0.8476</td>
<td>0.8145</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.7175-0.9135</td>
<td>0.5978-0.9154</td>
</tr>
<tr>
<td>Precision (Pearson):</td>
<td>0.8578</td>
<td>Precision (Pearson):</td>
</tr>
<tr>
<td>LV DI% 16 segments</td>
<td>0.8578</td>
<td>0.8156</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.7534-0.9321</td>
<td>0.6332-0.9081</td>
</tr>
<tr>
<td>Precision (Pearson):</td>
<td>0.9187</td>
<td>Precision (Pearson):</td>
</tr>
</tbody>
</table>

**Table 4.** Correlation analysis (r) and linear regression equation for left ventricular 16-segment dyssynchrony index (DI) measured by three-dimensional echocardiography in the population studied, in relation to ejection fraction measured by 2D and 3D echocardiography

<table>
<thead>
<tr>
<th>LV 16 DI% 16 segments (n = 71)</th>
<th>Pearson’s correlation (r)</th>
<th>Linear regression DI (x) e LVEF (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D EF</td>
<td>-0.8203</td>
<td>y = 63.4515 + (- 2.0233) x</td>
</tr>
<tr>
<td>p &lt; 0.0001</td>
<td></td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>CI = -0.8844 to -0.7259</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D EF</td>
<td>-0.7046</td>
<td>y = 59.3456 + (- 3.8721) x</td>
</tr>
<tr>
<td>p &lt; 0.0001</td>
<td></td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>CI = -0.7675 to -0.5824</td>
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</tbody>
</table>
DISCUSSION

From the possibility of the utilization of new computer programs and of matrix-array technology of ultrasound transducers, real-time three-dimensional transthoracic echocardiography became a noninvasive technique available for the analysis of cardiac anatomy and performance\(^5\)\(^{-16}\). Three-dimensional echocardiography allows the structural analysis of the heart from its orthogonal and diagonal planes, thus permitting global and segmental volumetric analysis, and providing information and quantification of the LV synchrony. It also adds information in relation to methods in which Doppler analysis is used (such as conventional Doppler and tissue Doppler).

The limitations of tissue Doppler are related to the angle of incidence of the ultrasound beam, the lack of information regarding LV apical segments, and the non-simultaneous analysis of the different ventricular segments. Three-dimensional echocardiography, in turn, allows global LV analysis at the same moment of the cardiac cycle, thus providing measurement of the D1\%, which gives information on the severity of cardiac dyssynchrony and determines the LV segment in which the most severe dyssynchrony occurs.

In the present study it was found a good negative correlation between ventricular dyssynchrony indexes and LV ejection fraction as measured both by two and three-dimensional echocardiography (\(r: -0.7046\) and \(r: -0.8203\), respectively, \(p < 0.0001\)). Thus, for higher D1, lower ejection fraction values were observed. That is, a negative correlation was found between LV electromechanical coupling (D1) and the relative variation between ventricular volumes (ejection fraction). This information is important for the discrimination of patients eligible for cardiac resynchronization therapy using biventricular pacemaker implantation. Cardiac resynchronization therapy is highly beneficial for patients with severe heart failure. It provides improvement of quality of life, of LVEF, of oxygen consumption (\(\text{VO}_2\)), of the six-minute-walk test performance, decreased serum catecholamines, and improved survival. However, cardiac resynchronization therapy is costly; it is related to a 5 to 8\% morbidity rate, and in up to 30\% of the patients in whom implantation is based only on electrical criteria (wide QRS complex) no satisfactory clinical response is observed. Thus, discrimination and quantification of LV electromechanical dyssynchrony are fundamental.

Reproducibility (intra and interobserver agreement) in obtaining three-dimensional ejection fraction, as well as for the derivation of the D1 was satisfactory, as shown in Table 3. The possibility of obtaining three-dimensional images was also considered adequate. In nine out of
80 cases (11.25%) three-dimensional images could not be analyzed due to inadequate echocardiographic image or to significantly irregular heart rhythm (atrial fibrillation). These limitations will certainly overcome in the near future with the use of new three-dimensional imaging interpretation programs.

Good correlation for 2D and 3D echocardiographic ejection fraction measurement, \( r = 0.8543, p < 0.0001 \), as well as good concordance (Bland-Altman analysis) for 3D-ECHO ejection fraction measurements and for LV of the DI were also observed (Graphic 6).

Thus, three-dimensional echocardiography should always be used for the analysis and diagnosis of cardiac synchrony, in conjunction with traditional echocardiographic modalities (M-mode, conventional Doppler, tissue Doppler) for the assessment of cardiac synchrony. This analysis should be regarded as a set of information resulting from the analysis of each technique and observed within the particular clinical context of each patient.

Study limitations
The study included a limited number of patients with cardiomyopathy (31), so that further investigation with greater case series is required. Further research should also include individuals with heart rhythm irregularities (such as atrial fibrillation) to bring the investigational setting closer to daily clinical practice.

CONCLUSIONS
In this study, a good negative correlation was observed between LV electromechanical coupling (3D-ECHO LV synchrony) and LVEF as measured by echocardiography (3D and 2D).

REFERENCES


