Right ventricle three-dimensional echography in corrected tetralogy of fallot: accuracy and variability

Xavier Iriart1, Michel Montaudon2*, Stéphane Lafitte3, Julie Chabaneix1, Patricia Réant3, Thomas Balbach4, Helene Houle5, François Laurent2, and Jean-Benoît Thambo1

1Service des Cardiopathies Congénitales de l'Enfant et de l'Adulte, CHU de Bordeaux, Pessac, France; 2Unité d’Imagerie Thoracique et Cardiovasculaire, CHU de Bordeaux, Hôpital du Haut-Lévêque, 5 Avenue de Magellan, 33600 Pessac, France; 3Service de Cardiologie et d’Échocardiographie, CHU de Bordeaux, Pessac, France; 4Tomtec Imaging Systems, Unterschleissheim, Germany; and 5Siemens Medical Solutions, Mountain View, CA, USA

Received 3 March 2009; accepted after revision 9 May 2009; online publish-ahead-of-print 6 June 2009

Aims To evaluate right ventricular (RV) volume and ejection fraction (EF) in adult normal subjects and repaired tetralogy of Fallot (ToF) with 3D trans-thoracic echocardiography (3DE) and a semi-automatic border detection algorithm.

Methods and results Fourteen healthy volunteers and 20 patients with repaired ToF (mean age 31 ± 14) underwent 3DE and MRI within the same day. Right ventricular end-systolic volume (ESV) and end-diastolic volume (EDV) and EF were measured by two observers using 3DE and compared with MRI measurements. Intra- and interobserver variability of 3DE and agreement between both methods were evaluated using Bland–Altman analysis. Over or underestimation of 3DE in comparison to MRI was assessed using paired t-test. Intra- and interobserver variability of 3DE was excellent with intraclass coefficient of correlation (ICC) ranging from 0.85 to 0.99 and from 0.85 to 0.98, respectively. Three-dimensional echocardiography underestimated ESV and EDV (P < 0.001) but agreement between 3DE and MRI was excellent (ICC = 0.88 and 0.87, respectively). Ejection fraction was 47.7 ± 7.8 with 3DE and 47.9 ± 6.7 with MRI, agreement between both methods was good (ICC = 0.72).

Conclusion Three-dimensional echocardiography combined to semi-automated quantification software shows fair agreement with MRI for RV volumes and EF measurement in patients with repaired ToF and adequate intra- and interobserver variability. These results suggest applicability for serial follow-up of patients with right heart congenital disease. However, the accuracy of 3DE echo diminishes with larger RV volumes, in part due to current difficulty to include the entire RV in the imaged sector. Technical progress in transducers beam geometry is likely to address this issue.

Keywords Right ventricle; Congenital; Fallot; Function; 3D echocardiography

Introduction Tetralogy of Fallot (ToF) is the most common type of malformation in patients with cyanotic congenital heart disease. Its incidence is estimated at 5–6% of all patients with congenital heart disease.1 Surgical repair of ToF has been available for 40–50 years, with a favourable outcome in most patients.2 However, despite a good long-term prognosis, life expectancy in those patients is still less than that of the normal population,3 and today we are faced with an increasing number of adult patients who require regular follow-up after initial correction of ToF. Amongst complications after surgical repair, pulmonary regurgitation is a common finding. It may be tolerated for many years without the occurrence of symptoms of right ventricular (RV) failure. However, chronic pulmonary regurgitation may eventually lead to severe RV dilatation, impaired RV function, and increased risk for ventricular arrhythmias.4–6

In such cases, pulmonary valve replacement (PVR) is considered to resolve pulmonary regurgitation and improve cardiac haemodynamics, if not planned too late.7,8 In a recent study, Therrien et al.9 reported that RV volumes could even recover when PVR was performed before RV end-diastolic volume (EDV) and end-systolic volume (ESV) reached 170 and 85 mL/m², respectively. Amongst methods for assessing RV volumes, cardiovascular MRI is considered the reference technique because it requires no geometrical assumptions.10 However, MRI is expensive and is not as widespread. As an alternative to MRI, real-time three-dimensional echocardiography (3DE) has recently been...
developed, and successfully applied for the assessment of in vitro and in vivo ventricular volumes using summation of disc method. In systems using second-generation matrix-array transducers, RV image quality and acquisition time have been improved over first-generation systems allowing assessment in clinical practice. Additionally, recent advances in offline analysis allow for semi-automatic border detection (SBD) and regional wall function assessment of the left ventricle (LV). This has the potential to further reduce the time for volume calculation, and allows for regional and dynamic left ventricular function analysis. However, SBD has not been applied to RV analysis.

The purpose of this study was to prospectively examine the variability and the accuracy of 3DE with new SBD algorithm in the assessment of RV volumes and ejection fraction (EF), in comparison to MRI.

**Methods**

**Subjects**

All subjects gave their written informed consent to participate to this study, which received the approval from the Ethics Committee of our institution. Thirty-seven subjects (17 men, 20 women, mean age 31 ± 14 years; range 17–54) were prospectively included from May 2007 to December 2007. The studied population comprised 22 consecutive patients with surgically repaired ToF (11 men, 11 women, mean age 26 years; range 17–54) and 15 healthy volunteers (seven men, eight women, mean age 32 years; range 22–44). All ToF patients had a total surgical correction, with a transannular patch in 16 of 22, and were followed up in our institution where annual echocardiography and consultation are part of the routine follow-up after correction. None of the healthy volunteers had a past history of respiratory or chronic cardiac disease. Exclusion criteria were contraindications to MRI (pacemaker, claustrophobia or intra-ocular metallic particles, and severe cardiac arrhythmia) and a poor apical window assessed on standard bi-dimensional echocardiography.

**Three-dimensional echocardiography**

**Data acquisition**

Three-dimensional echocardiography was performed using the 421c matrix-array transducer (1–4 MHz) and a Sequoia prototype ultrasound system (Siemens, Mountain View, USA). The entire echocardiography dataset was acquired from a single apical transducer location that was slightly modified from the traditional apical four-chamber view such that the right-sided structures were maximized, clearly visualized, and appeared in the centre of the field of view. A wide-angled full-volume scan was then acquired during an apnoea at low density to maximize sector width. The data acquisition required ECG gating, and therefore the output was not truly real time, but actually reconstructed from four sub-volumes. The entire reconstructed 3D dataset was first inspected for whole body motion artefacts that may have occurred during data acquisition. The reconstructed data were then reviewed as a loop with a temporal resolution of 55–65 ms (15–18 volumes/s).

**Automated border detection and volume computation algorithm**

Analysis of original raw was performed using a dedicated RV analysis software (TomTec, GmbH, Munich, Germany). The 3D dataset could be manipulated offline by a series of translational, rotational, and pivoting manoeuvres to best visualize the RV inflow and outflow tracts and displayed in reference planes. End-diastolic and end-systolic phases were first defined. Then, contours were manually drawn in end-diastolic and end-systolic images for three selected images (four-chamber, coronal, and sagittal views) and adjusted as close as possible to the endocardial border. Heavy parietal trabeculations were included in the RV chamber, as performed using MRI. These contours served for initiation of the semi-automatic algorithm. Briefly, this algorithm processed as follows:

1. from the manually defined contours, a spatio-temporal spline model based on Thin-Plate-Splines was initialized, ensuring both smooth contours in the spatial domain and continuous motion in the temporal domain.
2. Normal to the model’s surface, the algorithm found the image points which most likely defined the endocardium using finite impulse response and morphological filtering of grey value profiles perpendicular to the current surface estimate. Filter response and distance to the current surface were used to yield a likelihood estimate for each detected image point.
3. All detected image points were then approximated by the same spline model as used in Step 1. The approximation considered the derived likelihood measures.
4. If the approximation (Step 3) yielded a significant change, a new iteration was started with Step 2.

After contour detection, surface models for all temporal phases were available. For each phase, contours of arbitrary cross-sections could be reconstructed as intersection with the model in 3D space. The entire surface model was discretized as polyhedron and the enclosed volume was computed using Gaussian quadrature formulas.

Right ventricular volumes and EF were thus measured independently by two observers with 2 and 7 years experience and blinded to MRI results. To evaluate intra-observer agreement, measurements were performed twice at a 1 month interval by one of the observers.

**Magnetic resonance imaging acquisition and data post-processing**

MRI was performed on a 1.5 T system (Sonata, Siemens, Erlangen, Germany) with a phased-array radiofrequency receiver coil placed on the chest. All images were gated to the electrocardiogram. Double oblique long-axis and four-chamber scouts were acquired to obtain true short-axis reference. Steady state free precession prospectively ECG-gated breath hold images encompassing the whole RV were then acquired in short-axis orientation with no gap between slices (TrueFISP sequence: slice thickness: 7 mm, TE: 1.53 ms, TR: 33.6 ms depending on the R–R interval, matrix: 256 × 256 mm, field of view 38 cm). Right ventricular ESV, EDV, and EF were measured on post-processing workstation (Leonardo, Siemens) using commercially available software (Syngo Argus, Siemens) by a radiologist with 15 years experience in cardiac MRI and blinded to 3DE results.

**Statistical analysis**

Intra- and interobserver variability of 3DE ESV, EDV, and EF measurements as well as agreement between 3DE and MRI were evaluated using Bland–Altman analysis. Agreement between observers and between methods was evaluated using (i) Pearson correlation coefficient; (ii) the lack of agreement [i.e. bias estimated by the mean difference (d) and the standard deviation of the difference (SD)]; (iii) the intraclass correlation coefficient (ICC); and (iv) means between 3DE and MRI plotted against their differences. We also analysed the measurement error graphically, with the plotting of the individual subject’s SD against his mean and analytically by Spearman’s correlation coefficient of data and the within-subject SD. Lastly, the overestimation or underestimation significance of 3DE was tested using paired t-test. A P-value less than 0.05 was considered statistically significant.
Results
Display of RV 3D shape and its dynamic motion was possible in all but three patients (two corrected ToF and one normal subject) because of an insufficient US window. The final analysis included 34 subjects. Right ventricular EDV, ESV, and EF ranges measured by MRI were 67–290, 28–174 mL, and 31–63%, respectively.

Variability of three-dimensional echocardiography measurements
Table 1 shows absolute values and differences between 3DE measurements obtained by each observer. No statistical over or underestimation was found in all the studied parameters.

Measurement of intra- and interobserver agreement
Pearson’s correlation coefficient ranged from 0.86 to 0.99 and from 0.87 to 0.98 for intra- and interobserver agreement, respectively. Intraclass correlation coefficients were excellent from 0.85 to 0.99 and from 0.85 to 0.98 for intra- and interobserver agreement, respectively (Figures 1–3).

Measurement error between observers
The measurement error was correlated to the size of the measured parameter only for ESV and EDV assessed by the same observer (Figures 1–3).

Agreement between three-dimensional echocardiography and magnetic resonance imaging
Table 2 shows absolute values and differences between 3DE and MRI measurements. End-diastolic volume and ESV measured by 3DE were, respectively, 12.2 and 11.1% smaller than those obtained by MRI (P < 0.001). No statistical over or underestimation was found when measuring EF.

Measurement of agreement between three-dimensional echocardiography and magnetic resonance imaging
Plots of values obtained from both methods for calculating EDV, ESV, and EF are shown in Figures 4 and 5. Pearson’s correlation coefficient ranged from 0.73 to 0.93. Excellent ICCs between 3DE and MRI were found for EDV (ICC = 0.87) and ESV measurements (ICC = 0.88). Good agreement between both methods was found for RV EF (ICC = 0.72). When considering each subgroup of subjects, Pearson’s correlation coefficients and ICC were slightly higher in healthy subjects than those in ToF patients for ESV and EF and slightly lower for EDV (data not shown).

Measurement error between three-dimensional echocardiography and magnetic resonance imaging
Means of MRI and 3DE measurements were plotted against their standard deviation (Figure 6). Measurement error was 12.5, 19.5 mL, and 3.8% for ESV, EDV, and EF, respectively. The measurement error was correlated to the size of the measured parameter for ESV only.

Discussion
In this study, we evaluated the variability and accuracy of last generation 3DE system for RV volumes and function analysis. To our knowledge, this is the first study on the topic including adults with corrected ToF. We showed that RV 3D reconstruction and dynamic display using semi-automatic border detection in combination with matrix-array 3DE allow for the calculation of RV EDV, ESV, and EF with very low intra- and interobserver variability, and good to excellent agreement compared with MRI.

Accuracy of three-dimensional echocardiography measurements
In ToF patients, recent studies have shown the mortality increase over the third decade related to RV failure and arrhythmias in relation with pulmonary regurgitation and RV dilatation,2–6 which underlines the need for a regular follow-up of RV volumes and EF in this particular population. Several methods have been proposed using nuclear medicine,28,29 MRI,30,31 or multidetector computed tomography,32,33 All of these methods have proven their accuracy in RV assessment. However, they are expensive, sometimes not easily accessible, or provide high radiation doses, a condition unacceptable in annual follow-up. So, there is clearly the need for a safe, bedside, repeatable, and accurate method for RV assessment. The technique we propose has very low intra- and interobserver variability, which is a paramount condition in longitudinal follow-up.

However, despite 3DE and MRI were in excellent agreement when measuring RV EDV, and ESV, we found a significant underestimation using 3DE compared with MRI. Particularly, the measurement error was correlated with the RV volume only for ESV (r = 0.42, P = 0.01). Assessment of the RV using 2D echography has long been used but remains challenging because of the complex anatomy of the RV chamber. Although it is a relatively easy measurement to perform, its accuracy is poor because of the geometric assumptions that must be made with the RV.34 MRI is now considered the ‘gold standard’ for non-invasive assessment of RV function and volumes.31 However, the recent development of 3D probes allows a better analysis of RV using echography with no need for geometrical assumption. Difference in measurements between 3DE and MRI could also be explained by the difference in temporal and spatial resolution between both techniques. The use of 3DE for assessment of RV volumes and EF has previously been reported in children with congenital heart disease16

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Three-dimensional echocardiography measurements of right ventricular volumes and ejection fraction over time and observers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EDV (mL)</td>
</tr>
<tr>
<td>Obs 1–1</td>
<td>144.9 ± 51.7</td>
</tr>
<tr>
<td>Obs 1–2</td>
<td>143.6 ± 52.4</td>
</tr>
<tr>
<td>AD (%)</td>
<td>1.3 (0.9)</td>
</tr>
<tr>
<td>Obs 1</td>
<td>144.2 ± 51.9</td>
</tr>
<tr>
<td>Obs 2</td>
<td>144.6 ± 52.4</td>
</tr>
<tr>
<td>AD (%)</td>
<td>0.4 (0.3)</td>
</tr>
</tbody>
</table>

Data are means and standard deviations of RV volumes and ejection fraction measured using 3DE over time (upper part) and over observers (lower part). Obs, observer; AD, absolute difference between observers; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction.
and patients with pulmonary hypertension. Both studies have used a first-generation rotational 3DE system and showed that 3DE underestimated RV volumes compared with MRI, mainly for greatest volumes. This underestimation is thought to be related to boundary tracing error that remains the largest source of error when using 3DE methods. In our patients, when studying very dilated RV, a large portion of the infundibulum felt outside the field afforded by the 90 × 90° pyramidal sector size, so the accurate boundary tracing of this specific part of RV was

Figure 1 Three-dimensional echocardiography intra- (A–C) and interobserver (A′–C′) agreement when measuring RV end-diastolic volume (EDV). Plots of RV EDV assessed by one observer against those measured by the other observer (A and A′), average values of measurements between observers plotted against their differences (B and B′), and means of measurements between observers plotted against their standard deviation according (C and C′) to Bland–Altman analysis. r1: Pearson’s correlation coefficient, d ± SD: mean difference ± standard deviation, ICC: intraclass coefficient, Sw within-subject standard deviation, r2: Spearman’s correlation coefficient between within-subject standard deviation and mean of measurements, P: P-value of r2.
uncertain, which resulted in measurement error. This is in agreement with previous studies using first-generation 3DE system that underline the need and the difficulty of a complete visualization of the RV from a single probe position.\textsuperscript{16,21} The use of semi-automatic endocardial border detection for volume and function assessment has previously been investigated in the LV\textsuperscript{24} and in normal RV.\textsuperscript{22} Despite a good correlation, a consistent underestimation of LV EDV and ESV was found and partly explained by an incomplete incorporation of the apex into the conical imaging.
sector. Nesser et al. have also suggested that, in smallest RV, the effect of trabeculations and papillary muscles on endocardial border detection at end-systole leads to approximation in ESV measurement. In our study, RV ESV measurement error correlated positively with RV chamber size, with errors increasing with size (Figure 3B). Gopal et al. studied normal RV with 3DE and endocardial border detection and found a very high agreement between 3DE and MRI. However, they underlined the potential limitations of the method due to shape and size of very large RV, in which the convex pattern of the chamber could yield errors in contour detection by semi-automated border.

Figure 3 Three-dimensional echocardiography intra (A–C) and interobserver (A’–C’) agreement when measuring RV ejection fraction (EF). Plots of RV EF assessed by one observer against those measured by the other observer (A and A’), average values of measurements between observers plotted against their differences (B and B’), and means of measurements between observers plotted against their standard deviation according (C and C’) to Bland–Altman analysis. $r_1$: Pearson’s correlation coefficient, $d ± SD$: mean difference ± standard deviation, ICC: intraclass coefficient, $Sw$ within-subject standard deviation, $r_2$: Spearman’s correlation coefficient between within-subject standard deviation and mean of measurements, $P$: P-value of $r_2$. 

$\begin{align*}
A \quad r_1 &= 0.86 \\
&\quad \text{ICC} = 0.85 \\
A' \quad r_1 &= 0.87 \\
&\quad \text{ICC} = 0.85 \\
B \quad d ± SD &= 0.08 ± 4.13 \\
B' \quad d ± SD &= 0.24 ± 4.44 \\
C \quad r_2 &= 0.14 \\
&\quad P = 0.44 \\
&\quad Sw = 2.9 \\
C' \quad r_2 &= 0.01 \\
&\quad P = 0.96 \\
&\quad Sw = 3.1
\end{align*}$
detection algorithm. They also showed that limited temporal resolution of 3DE acquisitions could result in motion artefacts and difficulty in defining ESVs. In our experience, because both ESV and EDV were underestimated compared with MRI but highly repeatable over time and observers, we believe the limits of the method result from technical limitation in imaging sectors size. More accurate measurement of ventricular volumes may be possible with development of larger imaging sectors.

Intra- and interobserver variability

The agreement between both methods when measuring RV EF in our patients deserves further comments. Intraclass correlation coefficient was slightly lower for EF than for ESV and EDV. In our opinion, it should not be misinterpreted in terms of usefulness of 3DE for the assessment of RV EF. Indeed, ICC between both methods was, however, good, the lack of agreement and the measurement error were low, 0.2 ± 5.5 and 3.8%, respectively. Furthermore, EF was the only parameter for which 3DE did not over or underestimate the actual value when compared with MRI.

The proposed method is still limited by the difficulty to encompass the whole RV, particularly its infundibulum, within the imaging field of view but technical progress is very likely and should bring increased pyramidal sector size. We propose that the technique will then still be highly repeatable but should compare better with MRI. Integrating this technique into the follow-up of adults with repaired ToF will provide non-invasive, accurate, and repeatable assessment of RV in order to determine the best timing for PVR.

Study limitations

The major limitation of our study is the relative small range of EF in the studied population. Particularly, despite a wide range of RV ESV and EDV, no patient had a major impairment of RV EF. We were therefore unable to evaluate variability of 3DE and its agreement with MRI for small EF. A limitation of the technique we used is the echographic window, which remains a main issue in echocardiography. In this study, we have included patients based upon their good apical window assessed on standard 2D echocardiography, so the 3DE success rate we obtained does not reflect the actual success rate of RV 3DE in an adult population.

Table 2 Comparison of three-dimensional echocardiography and magnetic resonance imaging for right ventricular assessment

<table>
<thead>
<tr>
<th></th>
<th>EDV (mL)</th>
<th>ESV (mL)</th>
<th>EF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>163.1 ± 55.0</td>
<td>86.2 ± 38.0</td>
<td>47.9 ± 6.7</td>
</tr>
<tr>
<td>3DE</td>
<td>144.4 ± 51.7</td>
<td>77.1 ± 35.7</td>
<td>47.7 ± 7.8</td>
</tr>
<tr>
<td>AD (%)</td>
<td>18.7 (12.2)</td>
<td>9.1 (11.1)</td>
<td>0.2 (0.4)</td>
</tr>
</tbody>
</table>

Data are means, standard deviations, and absolute difference (AD) of right ventricular volumes and ejection fraction measured by MRI and 3DE. EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction.

Figure 4 Right ventricular volumes and ejection fraction assessed by three-dimensional echocardiography plotted against those measured by MRI. (A) End-diastolic volume (EDV), (B) end-systolic volume (ESV), (C) ejection fraction (EF). Solid lines: line of equality, dash lines: regression line, black circles: healthy subjects, white circles: ToF patients, r₁: Pearson’s correlation coefficients, ICC: intraclass coefficients.

Conclusion

Matrix-array 3DE with semi-automatic endocardial borders detection allows, in daily practice, assessment of RV
volumes and EF in agreement with MRI. However, the accuracy of 3DE echo diminishes with larger RV volumes, in part as a difficulty to include dilated RV outflow tracts, particularly if a transannular patch has been used for ToF correction. Although analysis of the RV infundibulum remains a limit in grown-up congenital heart disease patients, technical progress in transducers beam geometry is likely to address current technical issues.

Figure 5  Average values between three-dimensional echocardiography and MRI plotted against their differences according to Bland–Altman analysis. (A) End-diastolic volume (EDV), (B) end-systolic volume (ESV), (C) ejection fraction (EF). Solid lines: mean difference, dash lines: mean difference ± 2SD, black circles: healthy subjects, white circles: ToF patients, $\bar{d}$ ± SD: mean difference ± standard deviation.

Figure 6  Means of measurements between three-dimensional echocardiography and MRI plotted against their standard deviation according to Bland–Altman analysis. (A) End-diastolic volume (EDV), (B) end-systolic volume (ESV), (C) ejection fraction (EF). Black circles: healthy subjects, white circles: ToF patients, $r_2$: Spearman’s correlation coefficient, $P$: P-value of $r_2$, Sw within-subject standard deviation.
Conflict of interest: H.H. and T.B. are employed by Siemens Medical Solutions and Tomtec Imaging Systems, respectively (data acquisition was partly realized using a Siemens prototype ultrasound system and post-processed using a Tomtec software tool). The study benefited only from their technical and intellectual support and by no means from any financial help. M.M. also affirms that they did not try to influence either the results or the interpretation of the results, so no scientific misconduct results from this collaboration.

References