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Echocardiographic assessment of right ventricular volumes: a comparison of different techniques in children after surgical repair of tetralogy of Fallot

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Aims Different echocardiographic techniques are available for assessing right ventricular (RV) volumes but their clinical validity has not been well established. We compared the feasibility, reproducibility and accuracy of three different echocardiographic techniques for measuring RV volumes and ejection fraction (EF) in children after tetralogy of Fallot (TOF) repair.

Methods and results Seventy patients (age 14.2 ± 7.3 years) were studied using three-dimensional (3D) volume acquisition analysis (Tomtec, Germany), 2D echo with knowledge-based 3D reconstruction (3DR) (Ventripoint, USA) and the four-chamber area (4C area) methods. Parameters analysed were RV end-diastolic volume (EDV), end-systolic volume and EF. Magnetic resonance imaging (MRI) data were available in 41 patients. Intra- and inter-observer as well as inter-technique variability was assessed using Pearson's correlation analysis (*R*), coefficient of variance, and Bland–Altman analysis. Feasibility was good for all echo techniques (91% for the 3D, 98% for the 3DR, and 100% for the 4C area method). Intra- and inter-observer variability was low for both 3DR and the 3D echo, while more variability was observed for the 4C method. Compared with MRI volumes, 3DR and 3D underestimated EDV by 6.6 ± 10 and 18.2 ± 17.8 mL, respectively, ($P < 0.001$), while the 4C area method overestimated the EDV by 9.6 ± 33 mL, not significant due to a wide range.

Conclusion Current echocardiographic techniques to assess RV volumes are highly feasible and reproducible in paediatric post-operative TOF patients. When compared with MRI measurements, 3DR was the most accurate technique but requires extra equipment that is not readily available.

Keywords Echocardiography • Right ventricular volume • Tetralogy of Fallot • Magnetic resonance imaging

Introduction

In patients after tetralogy of Fallot (TOF) repair progressive right ventricular (RV) dilatation and dysfunction related to pulmonary regurgitation is an important clinical problem.[1,2] Timing for pulmonary valve replacement (PVR) is currently based on the occurrence of clinical symptoms and on RV volumetric measurements.[3,4] Cardiac magnetic resonance imaging (MRI) data have suggested that an RV end-diastolic volume (EDV) index above 150–170 mL/m^2 causes incomplete remodelling of RV volumes after PVR with persistent RV dilatation.[5–7] The complex three-dimensional (3D) RV geometry and the anterior position of the RV in the chest hamper the echocardiographic quantification of RV volumes but different echocardiographic techniques have been proposed for quantifying RV volumes.[8–12] Various geometrical formulas based on two-dimensional (2D) echocardiographic

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measurements have been developed but have not been widely applied in clinical practice due to their complexity and relative poor correlation with MRI-based volumetric measurements.[8] Recently, a simplified formula based on RV area measurements from the apical four-chamber (4C) view was introduced as an attractive simple alternative but has not been well validated prospectively.[9] Developments in 3D echocardiography allow real-time volumetric acquisition and dedicated software for RV volumetry has been developed and validated.[10,12–15] The feasibility of 3D echocardiography in post-operative patients has, however, been variable and reports on its accuracy showed the method underestimates RV volumes, especially when the RV is dilated.[12,13,16] Knowledge-based 3D reconstruction (3DR) is a 2D-based echocardiographic method for quantifying RV volumes that was recently validated.[17] It is based on 2D images localized in 3D space using a magnetic tracking technique. Different RV anatomical landmarks are localized in a magnetic 3D space and RV volumes are reconstructed using a database of RV shapes and sizes obtained in patients after TOF repair.[11,17]

Although the different methods have been validated individually, they have not been compared in a clinical environment. The aim of the current study was to compare the feasibility, reliability and accuracy of 2D, 3D, and 3DR methods to measure RV volumes in paediatric patients after TOF repair. The reliability and accuracy of the echocardiographic methods were compared with RV measurements obtained by cardiac MRI.

Methods

This is a single-centre prospective clinical study. The study was approved by the institutional research ethics board and informed consent was obtained in all participants and/or their legal guardians prior to enrolment. Patients after TOF repair, between 7 and 18 years of age, who were scheduled to undergo a routine follow-up clinical transthoracic echocardiogram and/or clinically indicated MRI were included. Exclusion criteria were: inability to cooperate, known or detected arrhythmia interfering with image acquisition and contraindications for performing a cardiac MRI. In total 41 consecutive patients scheduled to undergo a clinically indicated MRI were included. Just prior to or immediately after the MRI, a limited echocardiographic study, including image acquisition for 3DR and 3D full volume acquisition, was performed. Additionally, we included 29 patients scheduled for a routine clinical echocardiographic follow-up. These patients first underwent a complete echocardiographic study according to our routine clinical protocol, which includes 3D volumetric acquisition of the RV. At the end of the clinical study, additional 2D images for 3DR were obtained according to a standardized protocol, designed to visualize the entire RV from multiple acoustic windows. All echocardiographic studies were performed using a GE Vivid 7 machine (GE Ultrasound, USA). Data were digitally stored and analysed off-line. All patients were analysed, regardless of image quality.

Using 3DR and 3D volumetric methods, RV EDV, end-systolic volume (ESV), and ejection fraction (EF) were calculated. For the 2D method only EDV was calculated.

A subset of randomly selected patients were used for the assessment of intra- and inter-observer variability, with one observer repeating the analysis for all echocardiographic methods at least 2 weeks apart. For inter-observer variability, a second observer independently analysed the echocardiographic data sets using the different methods. Data analysis was performed after agreement on the methodology was reached between the two observers. Accuracy was assessed by comparing the echocardiographic measurements with the MRI measurements. Inter-observer variability of the MRI data was obtained by comparing the measurements of two different experienced observers who independently traced the same subset of patients.

Three-dimensional reconstruction method

The 3DR echocardiographic method for assessing RV volumes in TOF patients (Ventripoint Inc., Seattle, WA, USA) has recently been described and validated by our group.[17] Briefly, this method is based on 2D echocardiographic images of the RV obtained while using a magnetic tracking system (Ascension Technologies, Andover, MA, USA). On the 2D images, anatomical structure points are identified in the magnetic 3D space and full 3D surface reconstruction of the RV is performed using a database of RV shapes of patients with similar anatomy. Using this method, RV EDV, RV ESV, and RV EF can be calculated.

Three-dimensional method

Four or six full volumetric 3D volumetric data sets were acquired from apical 4C views using the 1.5–3.6 MHz 3D probe with GE Vivid 7 Ultrasound System (GE Healthcare, USA) at a frame rate of 20–30 frames/s. The analysis was performed off-line using the 'Beutel model' method (TomTec, Germany) with semi-automated border detection and manual correction.[10,12,13,16] The analysis was performed according to the standard protocol.

Four-chamber area method

This method is based on the measurement of the RV end-diastolic area from the apical 4C view. The end-diastolic area indexed to body surface area is used to estimate the RV EDV index using the formula RV EDV index = 11.5 + (7 * indexed 4C area).[9] This formula was derived from correlation analysis between the echocardiographic RV end-diastolic area and MRI RV EDV.

Cardiac magnetic resonance imaging

MRI scans were performed on a 1.5 Tesla scanner ('Avanto' Siemens Medical Systems, Erlangen, Germany). For ventricular volumetry, a short-axis cine stack was acquired during breath hold, to allow for 20 true reconstructed phases per cardiac cycle, 5–6 mm of slice thickness, 10–12 slices, gap adjusted to cover both ventricles including the RV outflow tract. The MRI data were analysed with commercially available software packages (Mass Analysis and CV Flow, Medis Medical Imaging Systems, Leiden, The Netherlands). RV end-diastolic (maximal) and end-systolic (minimal) volumes, stroke volumes, and EF were measured.

Statistics

Inter- and intra-observer as well as inter-method variability is described using Bland–Altman statistics, including the calculation of mean bias (average difference between measurements), with standard deviation, the statistical significance of the mean bias as tested using a paired, two-tailed *t*-test (the null hypothesis was zero bias), lower and upper limits of agreement (95% limits of agreement of the mean bias) and calculation of the coefficient of variation (calculated as the standard deviation of the difference of paired samples divided by the average of the paired samples). The percentage differences (the difference between paired measurements divided by the average of the two measurements times 100) were calculated for all Bland–Altman plots. Pearson's correlations were calculated as measures of raw associations between measurements.

Results

Feasibility

Overall, 70 children (mean age 14.2 ± 7.4 years) were studied with the 3DR, 3D, and 4C area methods; a subset of 41 children also had MRI. The feasibility of the 3DR method was 98.4% (65 of 66). One young patient was very uncooperative during the study, which resulted in motion artefacts and poor image quality, precluding off-line analysis. Four patients had their data sets acquired, but analysis was impossible to due to an operator error in the settings that was unrecognized at the time of acquisition. These data were excluded from the feasibility calculation. For the 3D method, the feasibility was 91.2% (62 of 68). In four patients the 3D volume data set did not include the entire RV in the volume while in two others the image quality did not allow calculation of ESV. Two data sets were lost and were excluded from calculations. The apical 4C view could be obtained in all patients, which translates to 100% feasibility for the 4C area method. *Figure 1* depicts an example of a patient in which all methods were used and the RV EDV calculated.

Reproducibility

A subgroup of 20 randomly selected patients with complete investigations was used to determine the reproducibility of the different echocardiographic methods. The results of the intra- and inter-observer variability analysis are shown in *Table 1*. The 3DR method had low intra- and inter-observer variability, with no important bias and low variance. This was observed for all measurements (EDV, ESV, and EF). The volumetric 3D method had a significant inter-observer bias and higher variability, especially for ESV. This influenced the variability in EF estimation. The 4C area method, available only for the EDV, had the highest variability and a significant inter-observer bias. The Bland–Altman analysis of the intra and inter-observer variability for EDV calculation by each method is represented in *Figure 2*. The differences between intra and inter-observer measurements were not significant for any of the parameters analysed using the 3DR method, while they were significant for the 3D and 4C methods ($P < 0.01$). The reproducibility of MRI measurements between observers is presented in *Table 1*, with good agreement, but a significant, albeit small bias.

Accuracy

MRI results were compared with the different echocardiographic measurements. The Bland–Altman analysis and Pearson correlations are presented in *Table 2* and *Figures 3–5*. All echocardiographic data correlated very well with MRI measurements ($P <$ 0.001). Both 3DR and the 3D method underestimated (negative bias) EDV compared with the MRI measurements, with a higher bias for the 3D method. The 3DR method resulted in a small but statistically significant underestimation of the EDV by 2.5% (6.6 mL). The 3D method underestimated EDV by 7% (18.2 mL) compared with MRI, with a slightly larger, but statistically significant variance ($P < 0.001$). The 4C area method overestimated RV volumes by 5.9% (9.6 mL) with a wide range of differences between values (SD = 33.1 mL), also expressed by the high

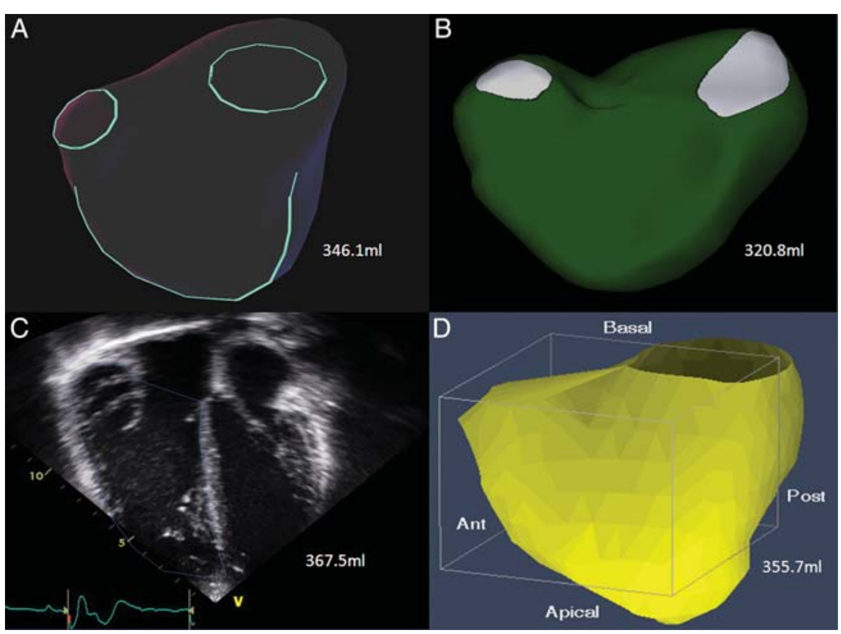

Figure 1 Example of right ventricular end-diastolic volume estimation using different echocardiography methods in the same patient. (*A*) three-dimensional reconstruction; (*B*) three-dimensional; (*C*) four chamber area method; (*D*) magnetic resonance imaging.

Table 1 Reproducibility of echocardiographic methods and magnetic resonance imaging for right ventricular volumes and ejection fraction

Intra-method variability	*n*	Correlation coefficient*	Coefficient of variance	Mean bias ± SD (mL)	*P*
3DR intra-observer	20				
EDV		0.997	3.4	1.1 ± 7.6	0.68
ESV		0.984	7.4	1.6 ± 9.5	0.75
EF		0.733	7.9	−0.7 ± 3.7	0.51
3DR inter-observer	20				
EDV		0.995	3.8	−2.2 ± 8.8	0.28
ESV		0.989	5.7	−0.5 ± 7.2	0.78
EF		0.611	8.4	−0.5 ± 3.8	0.56
3D intra-observer	20				
EDV		0.986	5.2	4.6 ± 12.2	0.11
ESV		0.966	8.9	−0.5 ± 11.9	0.99
EF		0.817	10	1.1 ± 4.2	0.3
3D inter-observer	20				
EDV		0.951	8	−13.4 ± 17.6	0.01
ESV		0.917	13.5	−11.6 ± 16.5	0.008
EF		0.534	15	1.7 ± 6.7	0.81
4C area intra-observer	20				
EDV		0.947	8.5	−1.2 ± 21.6	0.67
4C area inter-observer	20				
EDV		0.919	10.8	−33 ± 29.1	0.0001
MRI inter-observer	20				
EDV		0.993	3.5	−5.3 ± 8.7	0.01
ESV		0.986	5.3	−5.7 ± 7.2	0.002
EF		0.911	6.6	1 ± 2.9	0.11

*All correlations are significant at the 0.001 level.

coefficient of variance (COV). For ESV, the accuracy of the echocardiographic methods was slightly lower, with higher COV and wider limits of agreement. 3DR underestimated ESV by 4% (6 mL) and the 3D method by 5.1% (9.1 mL). ESV was not available by the 4C method. There was no significant bias in the estimation of RV EF by the 3DR or 3D method. For all echocardiographic methods the bias for volume calculations correlated significantly with RV wall thickness, with $R \sim -0.5$ for all measurements, $P < 0.01$.

Discussion

Accurate assessment of RV volumes and function is important in the follow-up of patients with congenital heart disease especially after TOF repair. Despite multiple limitations MRI is considered the clinical reference technique but different echocardiographic methods are available for assessing RV volumes. This study compares the feasibility and reliability of the different echocardiographic methods and compares their accuracy using cardiac MRI as the clinical gold standard. Our findings show that both 3DR and 3D methods are both reproducible and fairly accurate methods, with higher feasibility, better reproducibility, and slightly better accuracy for the 3DR method. Not surprisingly the 2D area method is more variable and less accurate.

Two-dimensional echocardiography is highly feasible and could be performed in all our patients as an apical 4C view can be easily obtained in most patients. 3DR is based on 2D imaging also, explaining the high feasibility of this method. As a stable position of the patient in the magnetic field is required throughout the entire acquisition of the different 2D images, this can limit the feasibility, especially in younger children. Compared with previous studies, the feasibility of the 3D method in our series was slightly higher. While reported feasibility varies between 50 and 80% of patients,[13,16] we successfully estimated RV volumes in over 90% of patients. This difference can be explained by different factors. First, our study group is younger compared with previous studies, possibly with better imaging windows. A second reason might be related to data set analysis, as we accepted reasonable assumptions about endocardial borders when parts of RV walls were not entirely and clearly visible. In previous studies, data sets were excluded for poor image quality and incomplete visualization of the different RV walls. We only excluded data sets where significant parts of the RV were not visualized precluding volumetric reconstruction. This might explain, at least in part, the lower accuracy as well.

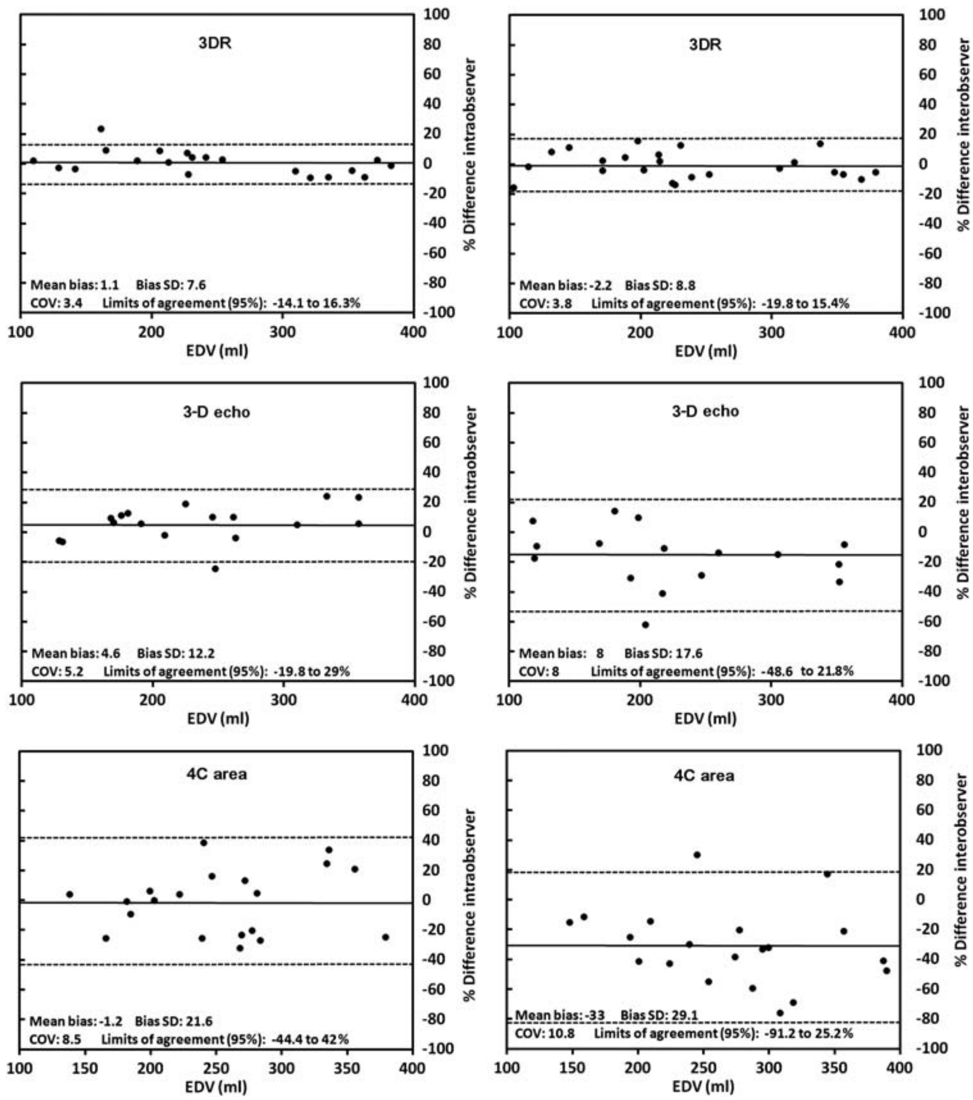

Figure 2 Bland–Altman curves depicting intra- and inter-observer reproducibility of right ventricular end-diastolic volume measurements with calculated bias and limits of agreement for three-dimensional reconstruction, three-dimensional, and four-chamber area methods.

Table 2 Accuracy of echocardiographic methods for right ventricular volumes and ejection fraction in comparison with magnetic resonance imaging

Inter-method variability	*n*	Correlation coefficient*	Coefficient of variance	Mean bias ± SD (mL)	*P*
3DR vs. MRI	40				
EDV		0.994	4.1	−6.6 ± 10.7	0.0009
ESV		0.992	6.5	−6 ± 9.3	0.007
EF		0.942	6.4	0.8 ± 2.9	0.66
3D vs. MRI	36[a]				
EDV		0.988	7.1	−18.2 ± 17.8	<0.0001
ESV		0.986	11.1	−9.1 ± 16.2	0.002
EF		0.855	11	−1.1 ± 4.8	0.2
4C area vs. MRI	41				
EDV		0.943	12.4	9.6 ± 33.1	0.132

*All correlations are significant at the 0.001 level.
[a]Two patients had only EDV data available (see text).

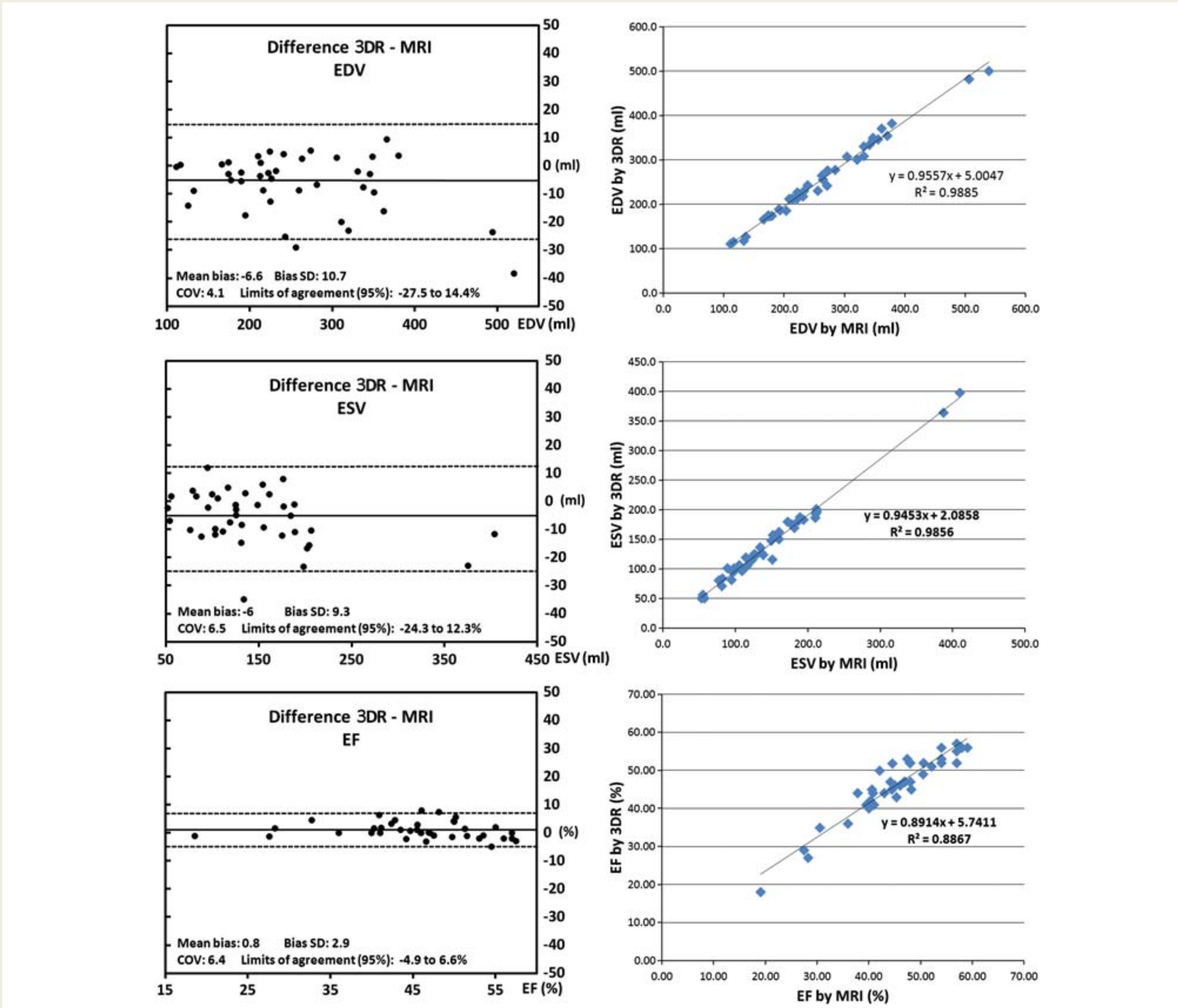

Figure 3 Bland–Altman and correlation curves depicting the accuracy of the three-dimensional reconstruction method in assessing the right ventricular end-diastolic volume, end-systolic volume, and ejection fraction compared with magnetic resonance imaging.

This study shows that the reproducibility of the 3D and 3DR methods is good for the EDV with slightly higher variability for the ESV and the EF. The 4C area method had a higher inter-observer variability while it is conceptually the easiest method. For all the methods we tried to reduce the variability by standardizing image acquisition and post-processing. RV trabeculations were included in the different RV volumetric techniques. This has been shown to improve the reliability of RV volumetry by cardiac MRI[18] and is also the methodology used in our institution. When differences in volumes are detected, often this is related to difficulties in identifying certain anatomical markers. Especially when the RV is dilated, it can be difficult or impossible to identify the real RV apex from the apical 4C views due to ventricular foreshortening (*Figure 6*). This is an important limitation for the 4C area method. For 3DR analysis we used modified RV views to identify the real RV apex (*Figure 6*). Correct identification of the real RV apex can also be challenging with the 3D method. Another anatomical landmark that can be difficult to identify after TOF repair is the level of the pulmonary valve. This can be challenging in patients with a large trans-annular patch with only remnants of the pulmonary valve and can be especially difficult during off-line analysis of 3D data sets and MRI images. Despite these limitations, both 3DR and 3D echocardiography are fairly reproducible techniques for assessing RV volumes in this patient population and our results using real-time 3D echocardiography are similar to previous studies.[14,19] In clinical practice, cardiac MRI is considered the reference technique and current clinical recommendations rely on MRI volumetric measurements.[3,4] Previous studies have shown that there can be significant variability in MRI measurements.[20] This is obviously important when using MRI as a reference. In our study,

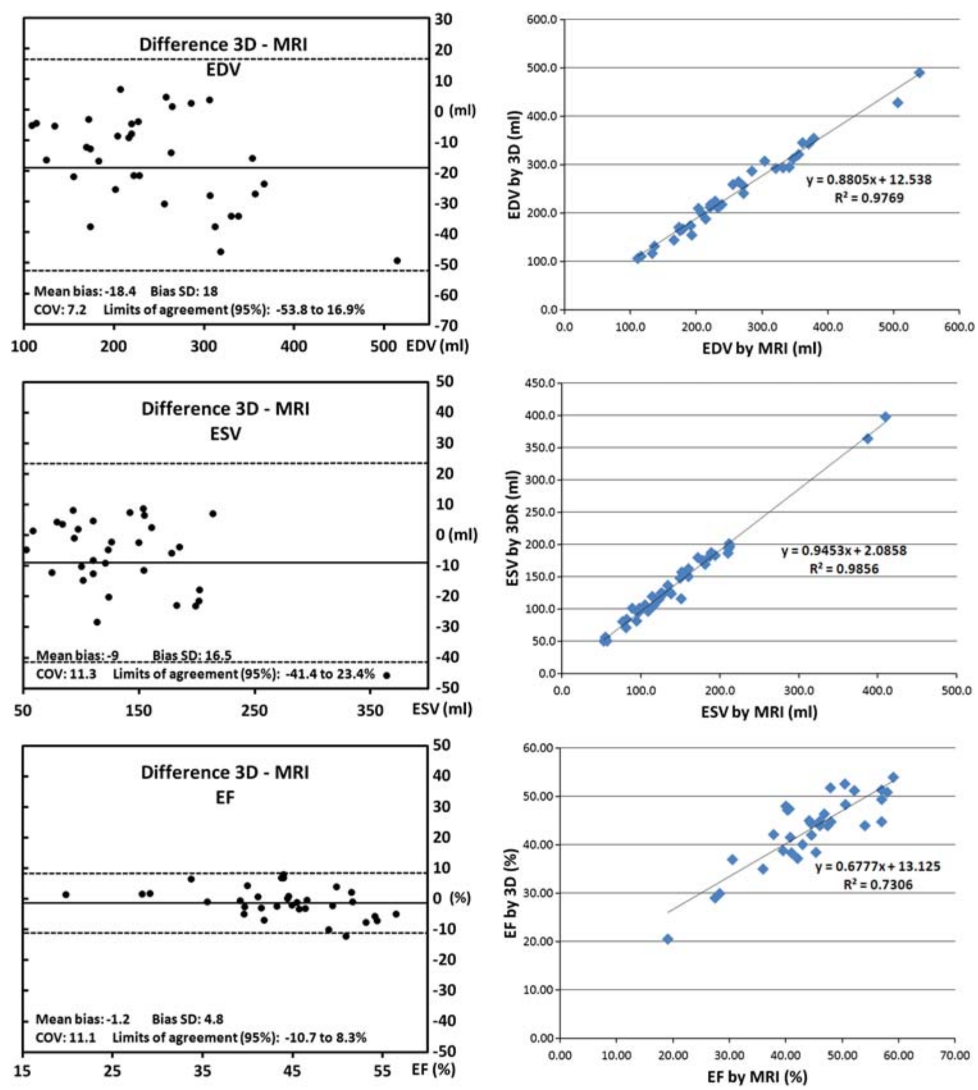

Figure 4 Bland–Altman and correlation curves depicting accuracy of three-dimensional method in assessing right ventricular end-diastolic volume, end-systolic volume, and ejection fraction compared with magnetic resonance imaging.

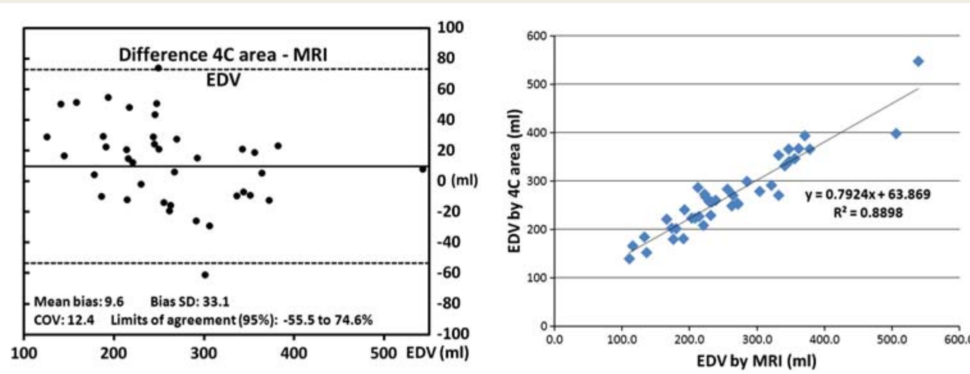

Figure 5 Bland–Altman and correlation curves depicting the accuracy of the four-chamber area method in assessing the right ventricular end-diastolic volume compared with magnetic resonance imaging.

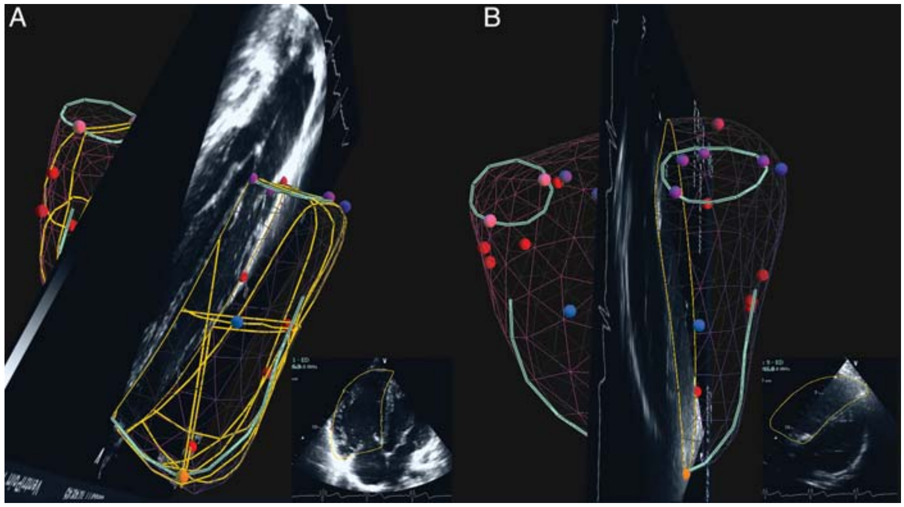

Figure 6 Patient with significantly dilated right ventricle (end-diastolic volume index: 198 mL/m2) demonstrating foreshortening of the apical four-chamber view when projected in the reconstructed ventricular volume (*A*). True apex obtained from a modified oblique apical view and its projection in the reconstructed volume (*B*).

inter-observer variability of MRI measurements was smaller compared with echocardiography, but overall similar to the 3DR method.

In this study, we compared the accuracy of the different echocardiographic techniques using MRI measurements as reference. The 4C area technique does n't take into account the RV outflow tract and could theoretically cause an underestimation of RV volumes. To our surprise, we found a significant overestimation of the RV EDV when compared with MRI (*Table 1*, *Figure 5*). We suspect this could be related to differences between paediatric and adult populations. The regression analysis used to derive the EDV is based on adult volumes and this might not be applicable to paediatric data. In the mid-1990s there was a change in surgical strategy in our centre to limit the size of the RV outflow tract patch, potentially resulting in smaller outflow tracts in a more recent cohort of post-operative patients.[21] This could explain why the regression formula leads to overestimation of RV volumes and cannot be applied to different patient groups.

The accuracy of both 3D and 3DR methods is good and they seem equivalent. For both techniques we found a small bias with underestimation of the RV volumes when compared with cardiac MRI. Overall, the underestimation is small, within the range of variability of the techniques. Our results for the 3D method are similar compared with previous publications.[10,14] Despite a relatively wide range of RV volumes (100–500 mL), we did n't find an increase in bias with larger RV volumes as previously suggested.[13] This could be related to careful manual correction after automatic border detection to delineate apical and outflow bulges. In our study, volume underestimation seems to be related to the degree of RV hypertrophy and could be explained by difficulties in endocardial definition.

Each technique has advantages and disadvantages. The 4C area method is the easiest method, as it is based on a simple measurement not requiring any extra equipment or software. Still, its application to different types of surgical corrections will require further validation. The 3D method requires a 3D volumetric probe and specific analysis software. The major limitation, especially in the adult population, seems to be the feasibility, as poor imaging windows in post-operative patients can limit RV wall definition. With significant RV dilatation, it can be difficult to obtain full coverage in a single volumetric acquisition. Wide angle acquisitions can result in low frame rates influencing time definition of end-systolic and end-diastolic frames, as well as low 2D resolution, which influences wall definition, adding variability and reducing accuracy. 3DR has the advantage of not being dependent on clear wall definition as the model-based reconstruction relies on identification of anatomic landmarks and not on border detection. It is possible to obtain reasonable 2D images of the important landmarks (tricuspid valve, apex, pulmonary valve, septum) and define some endocardial points in most patients. The database 'fills in the gaps' not based on user estimation, as when using the 3D method, but is based on data from hearts with a similar anatomy. The method was shown to be very reproducible and highly accurate.[17] The disadvantage of the 3DR techniques is the additional equipment and software required. The scan needs to be performed on a special non-ferromagnetic bed with a magnetic localizer attached to the probe. The 2D images need to be exported to a stand-alone computer system linked to the ultrasound machine. Post-processing requires specialized software and the reconstruction is dependent on a database. Reconstruction of an RV volume using this technique requires about 10–15 min with 5 min of image acquisition. In children, the feasibility is limited by the susceptibility to motion and respiration artefacts, more problematic with younger age. Additional databases for other heart conditions need to be established for a broader use of the system.

We consider the different complementary techniques. The 4C area method or 2D measurements can be used to identify those patients after TOF correction with RV dilatation in whom further volumetric analysis may be required. The choice of volumetric technique is dependent on the image quality and patient cooperation. In patients with good imaging windows the 3D technique can be used and 3D data sets can be obtained and analysed. In patients with poor imaging windows the 3DR technique can be used if the patient is able to cooperate for the image acquisition. It can be expected that knowledge-based reconstruction will become available for 3D reconstruction in the future allowing the operator to fill in gaps within the 3D data sets based on knowledge obtained on hearts with a similar anatomy instead of based on an operator-dependent estimation.

Overall, accurate echocardiographic methods for the assessment of RV volumes can become an important clinical tool in the follow-up of patients with RV disease. Cardiac MRI can still provide additional information, like quantification of pulmonary regurgitation, visualization of the branch pulmonary arteries, the size and shape of the RVOT, and the relation of coronary arteries to the RVOT, which may be important in management decisions. For serial volumetric follow-up of the RV echocardiography seems to be a good alternative.

Limitations

Our study group is relatively small, and we could only include children and adolescents undergoing MRI without sedation. Also, all MRI studies were clinically indicated, likely introducing bias towards higher ventricular volumes, which may have influenced results. Further data are required in a wider paediatric population as well as in the adult population, including a wider spectrum of cardiac anomalies.

Conclusion

Different echocardiographic techniques have become available that allow to reliably and accurately assess RV volumes and function. Our study indicates that both 3D an 3DR can be used in post-operative paediatric patients after TOF correction. Cardiac MRI currently still is the reference technique but it can be expected that further improvements in acquisition and analysis software will facilitate the use of echocardiography for RV volumetric assessment.

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