JACC: CARDIOVASCULAR IMAGING VOL. 3, NO. 1, 2010
© 2010 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
ISSN 1936-878X/10/$36.00
PUBLISHED BY ELSEVIER INC. DOI:10.1016/j.jcmg.2009.09.017

Multimodality Comparison of Quantitative Volumetric Analysis of the Right Ventricle

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OBJECTIVES We undertook volumetric analysis of the right ventricle (RV) by real-time 3-dimensional echocardiography (RT3DE), cardiac magnetic resonance (CMR), and cardiac computed tomography (CCT) on images obtained in RV-shaped phantoms and in patients with a wide range of RV geometry.

BACKGROUND Assessment of the RV by 2-dimensional (2D) echocardiography remains challenging due to its unique geometry and limitations of the current analysis techniques. RT3DE, CMR, and CCT, which can quantify RV volumes, promise to overcome the limitations of 2D echocardiography.

METHODS Images were analyzed using RV Analysis software. Volumes measured in vitro were compared with the true volumes. The human protocol included 28 patients who underwent RT3DE, CMR, and CT on the same day. Volumetric analysis of CMR images was used as a reference, against which RT3DE and CCT measurements were compared using linear regression and Bland-Altman analyses. To determine the reproducibility of the volumetric analysis, repeated measurements were performed for all 3 imaging modalities in 11 patients.

RESULTS The in vitro measurements showed that: 1) volumetric analysis of CMR images yielded the most accurate measurements; 2) CCT measurements showed slight (4%) but consistent overestimation; and 3) RT3DE measurements showed small underestimation, but considerably wider margins of error. In humans, both RT3DE and CCT measurements correlated highly with the CMR reference ($r = 0.79$ to 0.89) and showed the same trends of underestimation and overestimation noted in vitro. All interobserver and intraobserver variability values were $<14\%$, with those of CMR being the highest.

CONCLUSIONS Volumetric quantification of RV volume was performed on CMR, CCT, and RT3DE images. Eliminating analysis-related intermodality differences allowed fair comparisons and highlighted the unique limitations of each modality. Understanding these differences promises to aid in the functional assessment of the RV. (J Am Coll Cardiol Img 2010;3:10–8) © 2010 by the American College of Cardiology Foundation

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Manuscript received March 9, 2009; revised manuscript received September 3, 2009, accepted September 16, 2009.

Functional assessment of the right ventricle (RV) by 2-dimensional (2D) echocardiography remains a conundrum due to the unique geometry of this chamber and limitations of the current methods of quantification. Since the evaluation of the RV using 3-dimensional echocardiography (3DE) does not require geometric modeling, it has the potential of improved accuracy. In addition, this technique is advantageous over cardiac computed tomography (CCT) and cardiac magnetic resonance (CMR) imaging because of its portability, no need for ionizing radiation, and the ability to image patients with pacemakers and defibrillators. Most previous studies used the disc summation (DS) method with CMR, CCT, and 3DE to calculate RV volumes (1–5). It has been recognized that this methodology is imperfect due to its inability to accurately determine RV boundaries in the basal slices, since the tricuspid valve and the RV outflow tract are not in one plane.

Consequently, alternative approaches have been sought (6). Most recently, several studies tested and validated new software specifically designed for volumetric analysis of the RV from real-time 3-dimensional echocardiography (RT3DE) datasets. This software uses a combination of views that allows the visualization of the tricuspid valve, right ventricular outflow tract (RVOT), and apex in order to reconstruct RV endocardial surface and directly calculate RV volumes without using geometrical modeling (7,8). Most prior studies compared RV volumes calculated from 3DE and CCT datasets to CMR as a reference standard, with all measurements obtained using the DS technique. However, no studies have compared all 3 modalities using the new volumetric approach.

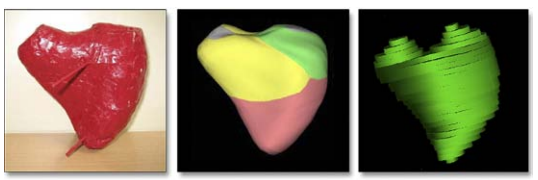
This study was designed to allow such side-by-side multimodality comparisons of RV volume calculations in separate in vitro and in vivo protocols by using the same volumetric analysis software with all 3 modalities to eliminate analysis-related differences as a potential source of error. The specific aims of the in vitro study were: 1) to determine the accuracy of the volumetric approach, when applied to all 3 imaging modalities using RV-shaped phantoms of known volumes; and 2) to determine whether the use of the volumetric and DS techniques within a single modality provide the same results. The in vivo protocol was designed to determine in a group of patients with a wide range of RV geometry to what extent RV volume measurements obtained with the 3 modalities are interchangeable, and to establish their respective reproducibility.

ABBREVIATIONS AND ACRONYMS

CCT = cardiac computed tomography
CMR = cardiac magnetic resonance
DS = disc summation
EDV = end-diastolic volume
EF = ejection fraction
ESV = end-systolic volume
RT3DE = real-time 3-dimensional echocardiography
RV = right ventricle/ventricular
RVOT = right ventricular outflow tract
2D = 2-dimensional
3DE = 3-dimensional echocardiography

METHODS

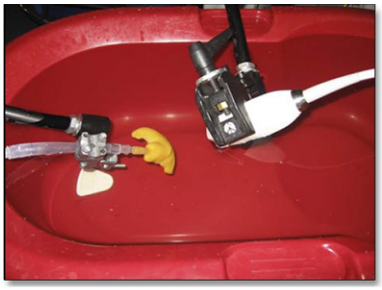
In vitro studies. The in vitro protocol was performed in RV-shaped phantoms made from different materials suitable for imaging with different imaging modalities. We first compared side-by-side the accuracy of DS technique and volumetric analysis using RV Analysis software (TomTec, Unterschleissheim, Germany) applied to CMR images of 3 static RV-shaped plastic phantoms (Fig. 1, top left) of different sizes. These measurements were compared against the true volumes of the phantoms, which were determined by measuring the displaced volume of water when submerging each phantom in a water bath. Subsequently, to allow intermodality comparisons of in vitro accuracy between CMR and CCT, another set of 3 RV-shaped cement models were imaged using both magnetic resonance imaging and computed tomography scanners, and volumes calculated using the volumetric analysis were then compared to the true volumes. Finally, RT3DE images of an ejecting RV-shaped latex phantom (Fig. 2, left) were acquired and analyzed using the same software to obtain end-systolic volume (ESV) and end-diastolic volume (EDV), which were compared against the true volumes of the model chamber.



Model	True Volume	CMR	
		Volumetric Analysis	Disk Summation
1	155	166	212
2	254	255	277
3	356	337	403
Error (%)	–	0.7±6.2	19.7±15.1

Figure 1. In Vitro Comparisons Between RV Volumetric Analysis and Disk Summation

In vitro accuracy of volumetric analysis **(top middle)** and disk summation method **(top right)** applied to cardiac magnetic resonance (CMR) images of a static right ventricle (RV) shaped phantom **(top left)**. See the Methods and Results sections for details.



Experiment	End-systole		End-diastole	
	True Volume	Volumetric Analysis	True Volume	Volumetric Analysis
1	13	19	23	28
2	17	15	28	23
3	25	28	35	38
4	27	23	37	30
5	37	37	48	47
Error (%)	–	-6.3±24.7	–	-1.7±17.4

Figure 2. In Vitro Accuracy of RV Volumetric Analysis of RT3DE Images

The accuracy of volumetric analysis applied to real-time 3-dimensional echocardiography (RT3DE) images of an ejecting right ventricle (RV) shaped latex phantom (**left**). See the Methods and Results sections for details.

Human protocol. **POPULATION.** Of 31 patients enrolled in the study, 1 was unable to undergo CMR due to claustrophobia, and 2 were not included in the analysis because of poor quality of RT3DE images. The remaining 28 patients (age 53 ± 18 years, 9 women) were referred for clinically indicated CCT studies (9 with congestive heart failure, 7 secondary pulmonary hypertension, 5 primary arterial hypertension, 4 congenital heart disease, and 3 coronary artery disease). Each patient was scanned for transthoracic 2D acoustic windows that allowed adequate RV endocardial visualization before enrollment. Patients with cardiac arrhythmias or dyspnea precluding a 10 to 15 s breath-hold and patients with implanted pacemakers or defibrillators were excluded. Also, patients with renal dysfunction (creatinine >1.3 mg/dl) or known allergy to iodine were excluded. In each patient, CMR, CCT, and RT3DE were performed on the same day. All patients agreed to participate and signed an informed consent.

CMR IMAGING. CMR images were obtained using a 1.5-T scanner (Siemens, Erlangen, Germany) with a phased-array cardiac coil. Spin-echo sequences were used to identify the long axis of the RV and allow imaging of anatomically correct RV short-axis views. Then electrocardiogram (ECG)-gated steady-state free precession sequence was used to obtain a stack of short-axis slices from the tricuspid annulus to the RV apex (10-mm slice thickness, no gaps). In addition, a 4-chamber view and an orthogonal view of the RVOT (coronal view) were obtained.

CCT IMAGING. CCT images were obtained using a 16-slice multidetector scanner (Toshiba, Otawara, Japan). Nonionic iodinated contrast agent (Ultravist-370, Schering, Berlin, Germany) was injected into the antecubital vein (140 ml, 3.5 ml/s) and followed by a 50-ml saline bolus. Image acquisition was triggered by the appearance of contrast in the aortic root. Imaging parameters included 250 ms gantry rotation time with 5 mm per rotation, and tube voltage of 120 kV with currents of 300 mA. Scan data were then reconstructed at 0.5-mm slice thickness and 0.5-mm in-slice resolution using retrospective ECG-gating from early systole (0% of the RR interval) to late diastole (90% of the RR interval) at 10% steps. Beta-blockers were not given during the CCT acquisition protocol.

RT3DE IMAGING. Transthoracic RT3DE images were acquired from an apical window using the iE33 imaging system (Philips, Andover, Massachusetts) with a matrix array transducer (X3-1). Care was taken to ensure that the RV was placed in the middle of the sector. Full-volume acquisition was performed using ECG gating over 4 consecutive cardiac cycles. Images were reviewed immediately to determine whether the RVOT and the free wall were visualized. Further determination of data quality was done in multiplanar reconstruction views. Image quality was judged as poor if ultrasound drop-out was present in more than one-half of the RV free wall in the coronal view.

RV DATA ANALYSIS. The RV analysis software was adapted to handle all imaging modalities (CMR, CCT, and RT3DE). CMR volumes were initialized on originally acquired slices. In contrast, CCT and RT3DE datasets were first converted into Cartesian coordinates to allow standardized positioning of the cut-planes. Manual initialization of contours was performed, while making an effort to include the endocardial trabeculae in the RV cavity, in predetermined end-systolic and -diastolic frames in the 4-chamber and coronal views as well as 1 mid-RV short-axis slice. Following automated identification of RV boundaries throughout the cardiac cycle, manual corrections were performed when necessary. Then the end-systolic RV cavity was displayed as a solid cast with a wire-frame representation of the end-diastolic cavity superim-

posed. ESV, EDV, and ejection fraction (EF) were automatically calculated. Endocardial tracing and volume measurements for each imaging modality were performed by experienced independent investigators blinded to the results of all prior measurements.

REPRODUCIBILITY. In 11 randomly selected patients, image analysis was repeated at least 1 month later by the same primary reader and by an additional investigator to determine the reproducibility of measurements for each imaging modality.

STATISTICAL ANALYSIS. All results are reported as a mean ± SD. In each in vitro experiment, measured volumes were compared against the actual volume by calculating the difference in percent of the actual volume. These values were averaged to estimate percent error for each imaging modality. In humans, comparisons with CMR included linear regression and Bland-Altman analysis, resulting in correlation coefficient, bias, and 95% limits of agreement. The reproducibility of the CMR-, CCT-, and RT3DE-derived measurements was evaluated by calculating intraobserver and interobserver variability, defined as the absolute difference between the corresponding repeated measurements and expressed in percent of their mean.

RESULTS

In vitro protocol. Figure 1 shows a phantom (top left) used to compare the volumetric analysis (top middle) and the DS method (top right) when applied to CMR images. In these experiments, the DS method resulted in volumes that were consistently overestimated by ~20% compared with true volumes. In contrast, volumetric analysis of the same images resulted in more accurate measurements, as reflected by percent error <1%. Volumetric analysis with CMR and CCT images obtained in another set of phantoms confirmed the accuracy of this analysis technique when applied to CMR images, and also demonstrated that when applied to CCT images, volumes were consistently overestimated by 4% compared with true volumes (Table 1). Volumetric analysis of RT3DE images of the ejecting RV phantom resulted in EDV and ESV that slightly underestimated the true volumes (Fig. 2), as reflected by errors of −6.3% and −1.7%. Of note, the standard deviations of the differences were quite considerable (order of magnitude 20%). Based on the results of these experiments, which demonstrated that volumetric analysis of CMR images provided the most accurate in vitro volume measurements, this analysis was used in the human protocol as the reference for CCT and RT3DE measurements.

Table 1. In Vitro Accuracy of 3-Dimensional RV Analysis Applied to CMR and CCT Images of 3 Different Static RV Shaped Phantoms*

Model	True Volume	Volumetric Analysis	
		CMR	CCT
4	102	101.8	105.4
5	96	97.7	100.4
6	99	98.3	103.1
Error (%)	—	0.3 ± 1.3	4.0 ± 0.6

*Volume data are presented in ml, and errors in % of the true volume.
CCT = cardiac computed tomography; CMR = cardiac magnetic resonance; RV = right ventricular.

Human protocol. No significant changes were noted in heart rate between imaging modalities. While volumetric analysis of the RV from CCT and CMR data was feasible in all patients, its feasibility with RT3DE images was 92% due to poor image quality in 2 of 30 patients. Time required for analysis of each image set was <5 min. Manual corrections were necessary to optimize the position of the endocardial boundaries in all patients for all 3 imaging modalities, but the required corrections were more extensive for RT3DE. Figure 3 shows an example of end-diastolic images obtained using all 3 imaging modalities in 1 patient, with the initialized RV boundaries superimposed, along with the resultant RV endocardial surfaces.

CMR measurements of ESV, EDV, and EF in the remaining 28 patients were 131 ± 54 ml, 205 ± 73 ml, and 40 ± 11%, respectively. Figures 4 and 5 show side by side the levels of agreement between CCT and RT3DE measurements of RV volumes with the CMR reference values. Correlation coefficients were similar for both modalities: 0.87, 0.85, and 0.79 for ESV, EDV, and EF, respectively, for CCT (Fig. 4, top), and 0.89, 0.87, and 0.87 for RT3DE (Fig. 4, bottom). CCT overestimated ESV by 17 ml (14% of the mean measured ESV) and EDV by 23 ml (12% of the mean measured EDV). In contrast, RT3DE underestimated ESV by 9 ml (7%) and EDV by 14 ml (7%). Both CCT and RT3DE underestimated EF by 2%. The limits of agreement with CMR reference were similar for both CCT and RT3DE.

Table 2 shows the results of the reproducibility analysis of RV volumes and EF for CMR, CCT, and RT3DE images. For both EDV and ESV, both interobserver and intraobserver variability were lowest for CCT-derived measurements. Interestingly,

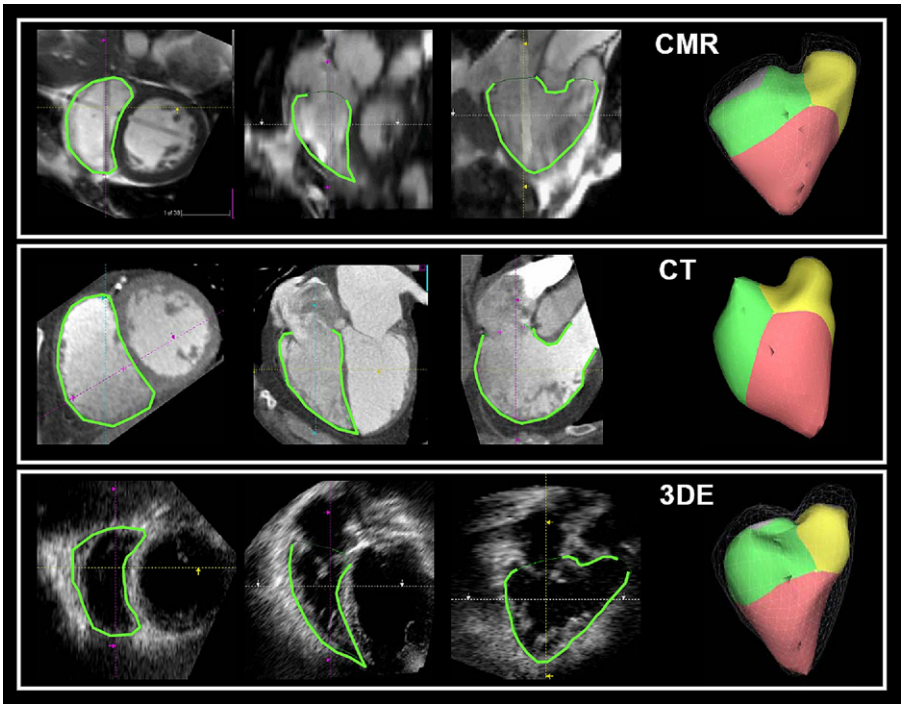


Figure 3. Example of RV Volumetric Analysis Across the 3 Imaging Modalities

Volumetric analysis of CMR **(top)**, cardiac computed tomography (CT) **(middle)**, and real-time 3-dimensional echocardiography (3DE) **(bottom)** images obtained in 1 patient. **(From left to right)** RV boundaries initialized in a midventricular short-axis view, apical 4-chamber view, and coronal view, shown along with the resultant calculated RV endocardial 3-dimensional surfaces **(right)**, with the solid cast representing end-systole and the wire frame representing end-diastole. Abbreviations as in Figure 1.

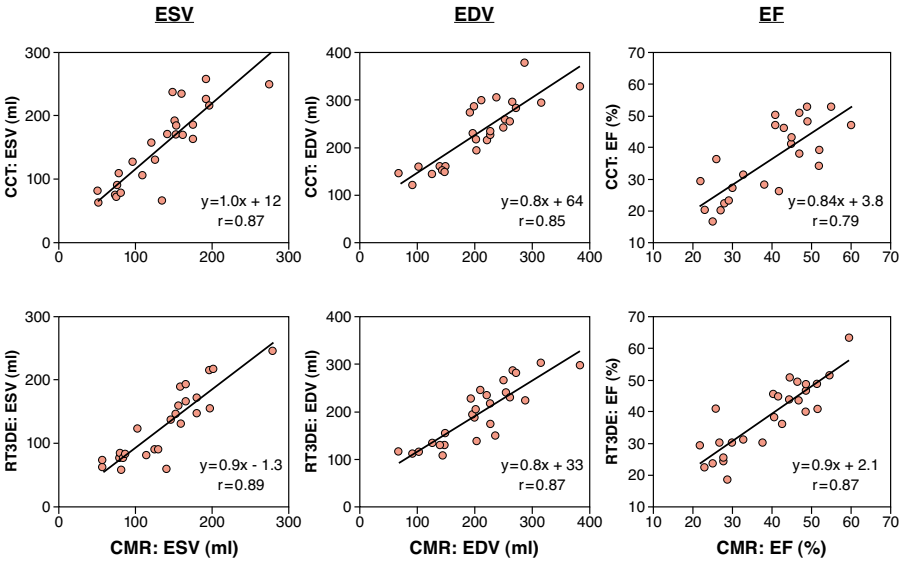


Figure 4. Regression Analyses of Right Ventricular Volumes Between Imaging Modalities

Results of linear regression analysis of right ventricular end-systolic volume (ESV), end-diastolic volume (EDV), and ejection fraction (EF), calculated using volumetric analysis of cardiac computed tomography (CCT) **(top)**, and real-time 3-dimensional echocardiography (RT3DE) **(bottom)** images against cardiac magnetic resonance (CMR) reference values obtained in 28 patients.

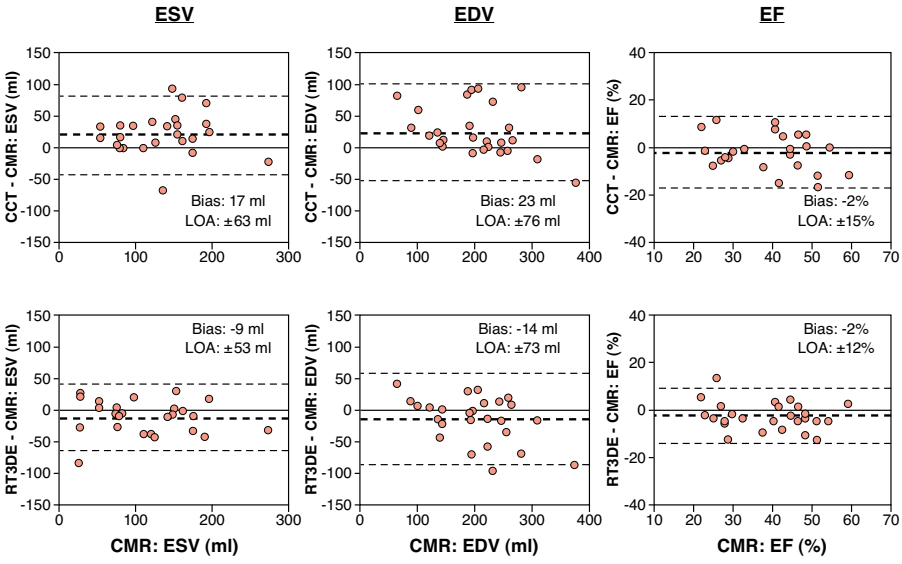


Figure 5. Bland-Altman Analyses of Right Ventricular Volumes Between Imaging Modalities

Results of Bland-Altman analysis of right ventricular ESV, EDV, and EF, calculated using volumetric analysis of CCT **(top)** and RT3DE **(bottom)** images against CMR reference values obtained in 28 patients. **Thick dashed lines** show the bias, while the **thin dashed lines** show the 95% limits of agreement (LOA). Abbreviations as in Figure 4.

the variability of RT3DE measurements was lower than that of CMR. Not surprisingly, for both EDV and ESV measured from all 3 imaging modalities, the interobserver variability was higher than the intraobserver variability. Importantly, all variability values were below 15%. However, in individual patients, variability levels of all 3 modalities exceeded the acceptable 10% to 15% levels.

DISCUSSION

The ability to accurately measure RV volumes and function plays a critical role in congenital heart disease, where the development of RV dysfunction leads to increased morbidity and mortality. The degree of RV involvement is also an important prognostic determinant after myocardial infarction (9), and in patients with primary pulmonary hypertension as a tool to determine the prognosis and response to treatment (10). RV size and function have been identified as powerful predictors of survival in patients with heart failure and outcomes in heart transplantation (11).

Despite the recent advances in cardiac imaging technology and multiple research studies aimed at the evaluation of the RV, accurate quantification of RV volumes and function from 2D images remains a challenge. This is due to the complex shape of this chamber, combined with prominent endocardial trabeculae, which make the identification of the RV endocardial boundaries in single cut-planes challenging. The single-plane 2D approach to the calculation of RV volumes frequently results in volume underestimation. It has been shown that even biplane approaches result at best in fair correlations with other independent reference techniques due to: 1) limitations of simplified geometric models used to approximate the RV cavity that usually exclude the RV infundibulum (6); and 2) difficulty in obtaining orthogonal long-axis views of the ventricle rotated around a common axis, which are necessary for the use of the biplane Simpson's and area-length techniques.

Table 2. Interobserver and Intraobserver Variability of Volumetric Analysis Applied to CMR, CCT, and RT3DE Images Obtained in a Subset of 11 Randomly Selected Patients*

	ESV	EDV	EF
Interobserver			
CMR	12 ± 7	13 ± 9	13 ± 13
CCT	8 ± 4	4 ± 3	13 ± 9
RT3DE	10 ± 9	7 ± 5	11 ± 11
Intraobserver			
CMR	13 ± 8	12 ± 9	10 ± 8
CCT	4 ± 4	4 ± 4	8 ± 6
RT3DE	9 ± 10	5 ± 7	13 ± 8

*Data shown are % of the mean of corresponding repeated measurements. EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; RT3DE = real-time three-dimensional echocardiography; other abbreviations as in Table 1.

The ability of 3DE imaging to directly measure RV volumes without the need for geometric modeling has resulted in improved accuracy (12). Initially, the potential advantages of RT3DE imaging were tested in vitro, using irregular RV models (6,13). Surprisingly, however, one of the first studies to compare 2D and 3D echocardiographic measurements in humans side by side against CMR reference found that 3D measurements offered no significant advantage (14). Another RT3DE study (15) reported only slightly better agreement with CMR in patients with RV dysplasia, compared with 2D-derived values, with a small negative bias, which was confirmed in another study in children (16). These findings have been postulated to reflect the confounding effects of the endocardial trabeculae on endocardial identification and tracking, which have not been resolved in the transition from 2D to 3D imaging. Also, RT3DE measurements of RV volumes are affected by multiple additional factors, including gain settings as well as thickness and disk orientation during disk summation (2,17). In addition, the disk summation approximation, which is an extension of a fundamentally 2D technique, fails to take full advantage of the RT3DE images that contain the entire ventricle because the ability to accurately identify the RV outflow tract in individual planes and include it in the RV cavity is limited by the same factors that have been affecting the multiplane 2D method of disks.

Another potential source of discordance with CMR reference is that the complex 3D shape of the RV may affect the ability of CMR to accurately quantify RV volumes. Similar to echocardiographic cut-planes, the identification of the RV boundaries near the RVOT may be quite challenging from short-axis slices acquired perpendicular to the long axis of the left ventricle, which is the standard for CMR acquisition. We hypothesized that a different acquisition strategy is necessary for accurate RV volume measurements, including separate acquisition of RV short-axis slices perpendicular to the long axis of the RV and the use of coronal slices that offer better delineation of the RVOT.

This study was designed in an attempt to address these issues by testing the recently developed volumetric analysis technique across the 3 most commonly used cardiac imaging modalities. Similar to a recent report (8), we found that this technique is feasible, relatively simple, and not time-consuming. Because there is no perfect "gold-standard" reference technique to measure RV volume in vivo, we first used RV-shaped phantoms with known volumes to determine the accuracy of this volumetric analysis with each of the 3 imaging modalities. These in vitro measurements showed that: 1) the volumetric approach was more accurate than the DS technique, when applied to CMR images, likely because of the limited ability of the latter technique to accurately incorporate the RV outflow tract; 2) the volumetric analysis of CMR images yielded the most accurate measurements among the 3 imaging modalities; 3) CCT volume measurements showed slight (4%) but consistent overestimation; and 4) RT3DE volume measurements showed small underestimation, but had considerably wider margins of error, probably due to the relatively low spatial resolution.

The results of the human protocol showed that both RT3DE and CCT measurements correlated highly with the CMR reference, with correlation coefficients similar to those recently reported (7). We found that CCT measurements were overestimated by a higher percentage of the measured RV volumes, compared with the phantoms. Similarly, RT3DE measurements in humans showed a larger percent of underestimation than in vitro. These differences can be probably attributed to the effects of endocardial trabeculae that did not exist in the phantoms, but are quite prominent in human RVs. This factor was found to play an important role in the intermodality discordances in left ventricular volume measurements (18), and could certainly be expected to affect RV measurements even more, since the RV is more heavily trabeculated. This is because these measurements rely on the visualization of the endocardial boundary, which varies widely among modalities depending on their spatial resolution that determines the ability to differentiate trabeculae from the myocardium or blood pool (18). In this regard, computed tomography is the best, followed by CMR, with RT3DE being the worst, thus resulting in different degrees of inward displacement of the detected endocardial boundary. Nevertheless, since the true volumes in the human RVs were unknown and based on the accuracy of the CMR in vitro measurements, CMR was used as a reference, despite the fact that its accuracy in humans may be questioned due to the presence of heavy trabeculation. Also, the limited number of phases of the cardiac cycle in the CCT data could have played a role in the overestimation of ESV (19), but would not explain the overestimation of EDV, since changes in ventricular volume toward end-diastole are minimal.

It is likely that the higher spatial resolution in CCT contributed toward the higher reproducibility of CCT compared with RT3DE measurements. The reproducibility of CMR measurements in this study was lower than that of either CCT or RT3DE, in agreement with the recent study (7). This may be explained by the fact that CMR is only 1 of the 3 imaging modalities that is not truly 3D, and that the definition of the RV outflow tract for this modality depends on a single coronal view. Importantly, despite the wide margin of error in vitro, the reproducibility of RT3DE-derived RV volume measurements was within clinically acceptable 15% range. Of note, the variability of CMR evaluation of RV volumes and EF in our study was higher than that reported in several previous publications (20,21) that focused on healthy volunteers. It is likely that in our patients with a wide range of RV geometries, accurate quantification of RV volumes may be more challenging and thus less reproducible.

CONCLUSIONS

This multimodality study tested the newly developed approach of volumetric quantification of RV volume, which was tested on CMR, CCT, and RT3DE images. We found that this analysis overcomes many of the known hurdles that impeded accurate assessment of this geometrically complex chamber in the past, and can be used with all 3 imaging modalities. However, our results also showed that RV volume measurements are not interchangeable between modalities and, therefore, serial evaluations should preferably be performed using the same modality.

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Key Words: right ventricle ■ 3-dimensional echocardiography ■ cardiac magnetic resonance ■ multidetector computed tomography.