Journal of Cardiology 61 (2013) 281–288

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Evaluation of automated measurement of left ventricular volume by novel real-time 3-dimensional echocardiographic system: Validation with cardiac magnetic resonance imaging and 2-dimensional echocardiography

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ARTICLE INFO

Article history:
Received 27 July 2012
Received in revised form
12 November 2012
Accepted 26 November 2012
Available online 5 March 2013

Keywords:
Echocardiography
Transthoracic
Ejection fraction
Magnetic resonance imaging
Ventricular function

ABSTRACT

Background: Traditional 3-dimensional echocardiography (3DE) with volumetric scanning technique requires several heart cycles for full-volume acquisition and complicated manual contouring of left ventricular (LV) endocardium. The new real-time 3DE (RT3DE) system allows acquisition of an instantaneous full-volume dataset in a single heart cycle and automated measurement of LV volume by the algorithm software. However, it has not been evaluated adequately whether automated measurement by RT3DE has better agreement with cardiac magnetic resonance imaging (CMR) than 2-dimensional echocardiography (2DE) with CMR.
Purpose: This study aimed to evaluate the accuracy of automated measurement of LV volume using RT3DE compared with 2DE and CMR.
Methods and results: Forty-four consecutive patients who underwent RT3DE, 2DE, and CMR were evaluated in this study. The feasibility of automated measurement by RT3DE was 93.2% and the mean operation time was 6 min. LV volume and ejection fraction (EF) from semi-automated measurement [end-diastolic volume: $r = 0.96$, limits of agreement (LOA) −30.5 to 39.3 ml; end-systolic volume: $r = 0.97$, LOA −22.6 to 32.7 ml; EF: $r = 0.90$, LOA −16.1 to 14.2%, respectively] had better agreement with CMR than those from 2DE ($r = 0.87$, LOA −50.5 to 72.2 ml; $r = 0.93$, LOA −34.1 to 65.2 ml; $r = 0.89$, LOA −20.9 to 10.0%, respectively).
Conclusion: Semi-automated measurement by RT3DE has better agreement with CMR than 2DE in LV volume and EF. In addition, it is simple to operate and acceptable in feasibility for the clinical setting although there may be room for further learning required to incorporate small hypertrophic LV into the automated algorithm software.

Introduction

Left ventricular (LV) volume and ejection fraction (EF) are the most widely used fundamental measurements to assess global LV function for deciding treatment, clinical follow-up, prevalence of heart disease and predictors of long-term survival [1–5]. Currently, LV volumetric measurement by conventional 2-dimensional echocardiography (2DE) is mainly used in routine clinical practice [6,7]. However, the measurement by 2DE has several limitations such as the need for geometric assumptions and the risk of underestimating volumes in foreshortened views [8–10]. On the other hand, 3-dimensional echocardiography (3DE) with volumetric scanning technique has been developed to overcome these limitations in clinical settings. Some studies have demonstrated acceptable feasibility and accuracy of 3DE with volumetric scanning for LV volume assessment [11–17].

However, traditional 3DE with volume scanning has two major limitations, such as stitch noise due to multi-beat acquisition and complex processing due to manual tracing for LV volume measurement. Thus, successful automated measurement based on a 3-dimensional (3D) dataset needs a single heartbeat and automated contour detection.

The recent advent of the real-time 3DE (RT3DE) system has allowed the acquisition of an instantaneous full-volume image of the entire heart in a single heartbeat and the automated measurement of LV volume. A previous validation study demonstrated that

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http://dx.doi.org/10.1016/j.jjcc.2012.11.005

automated measurements of LV end-diastolic volume, end-systolic volume, and EF by this system showed excellent correlation with the corresponding measurements obtained from cardiac magnetic resonance images (CMR) (r = 0.90, 0.96, and 0.98, respectively), and 2DE (r = 0.94, 0.94, and 0.91, respectively) [18]. However, the relative merits between 2DE compared with CMR and semi-automated measurement by the new RT3DE compared with CMR have not been evaluated adequately. The objectives of this study were for the first time to compare semi-automated measurement by RT3DE and 2DE with CMR for LV volume and EF.

Methods

Study population

Forty-four consecutive patients with sinus rhythm who underwent RT3DE, 2DE, and CMR were enrolled in this study. Subjects with atrial fibrillation, incompatible metallic implants or devices, and refractory claustrophobia were not enrolled because they could not undergo LV volume measurement by CMR. In each patient, CMR was recorded first to determine LV volume, and then RT3DE and 2DE were recorded within 3 days of CMR study. In patients with post-percutaneous coronary intervention after acute myocardial infarction, RT3DE, 2DE, and CMR were performed within 6 h. Two patients were subsequently excluded from the study because LV endocardium could not be visualized in 3DE imaging, and one patient was also excluded due to an enlarged heart that exceeded the pyramidal acquisition window.

This study was approved by the human ethics committee at the Sakakibara Heart Institute. Informed consent regarding participation in the study was obtained from all subjects.

RT3DE

RT3DE images were acquired using the ACUSON SC2000 volume imaging ultrasound system (Siemens Medical Solutions USA, Inc., Mountain View, CA, USA) with a 4Z1c volume imaging transducer. This system required one single heart cycle for full-volume image acquisition of the entire heart. All full-volume imaging of $90^\circ \times 90^\circ$ at a depth of 16 cm was achieved at more than 15 frames per second.

The RT3DE datasets were analyzed on off-line Syngo® SC2000 Workplace (eSie LVA, Siemens AG, Munich, Germany) to measure LV end-diastolic volume (EDV), LV end-systolic volume (ESV) and LVEF. The automated algorithm of this software used the knowledge which was gained from large, expert-annotated training database of volume data combined with 3D discriminative model to match relevant image features of the given LV volume to the database. Firstly, automated volumetric analysis for LV volume measurement was achieved by fully automatic alignment and extraction of standard views, 2- and 4-chamber views and short-axis view, from a full-volume 3D data set and fully automatic delineation of the LV endocardium throughout the cardiac cycle. Then, the voxel count inside the endocardial surface was used to calculate EDV and ESV automatically, and EF was calculated from ESV and EDV using the standard formula (fully automated measurement; Fig. 1) [19]. Following fully automated measurement, the LV volume manipulation and the delineation of the LV endocardium without trabecular were modified in all patients (semi-automated measurement). EDV was selected by the algorithm using the peak R-wave from the electrocardiography signal. ESV was selected from the systolic frame with the minimal volume.

2DE

Traditional 2D transthoracic echocardiographic images were acquired using same equipment with a 4V1c vector array transducer separately from full-volume datasets. EDV, ESV, and EF were calculated by the biplane Simpson's rule from the apical 2-chamber and 4-chamber views.

CMR

CMR studies were performed with the Magnetom Sonata 1.5-T MR scanner (Siemens Medical Solutions, Erlangen, Germany) using a 6-channel phased-array body and spine coil. All images were acquired by electrocardiogram-gated breath-hold technique.

Steady-state free-precession cine images were acquired in three long-axis views and five short-axis views covering the LV from base to apex. Image parameters were as follows: slice thickness 8 mm, TR (repetition time) 56.8 ms, TE (echo time) 1.21 ms, and flip angle 50–60°, with 20 phases per cardiac cycle. LV function analysis was performed with Argus Function VA30 (Siemens Medical Solutions). Epicardial and endocardial borders were manually traced on each cine image to obtain LV EDV, ESV, and EF. The papillary muscles and LV trabeculae were excluded from the endocardium and the mitral valve plane was included in the analysis.

Inter- and intraobserver variabilities

Two blinded observers independently measured LV volume and EF by RT3DE. For estimation of reproducibility of RT3DE, manual contour corrections by semi-automated measurement were also undertaken following fully automated measurement.

For intraobserver variability, one of two observers repeated the analysis of 8 random patients after a 5-month interval. Interobserver variability was measured by analyzing 8 random patients in these two observers.

Statistical analysis

Data are presented as mean ± standard deviation for continuous variables, or as a number with percentage for categorical variables. RT3DE- and 2DE-derived measurements of EDV, ESV, and EF were compared with the corresponding CMR reference values using linear regression with Pearson's correlation coefficients and Bland–Altman analyses to assess the bias and limits of agreement (LOA), mean difference ± 2 standard deviation, with the CMR reference. Wilcoxon signed-rank test was used to compare the difference between CMR and other methods, and two-tailed probability values less than 0.01 were considered statistically significant. Interobserver and intraobserver variability were evaluated by LOA and interclass coefficient of correlation. Statistical analysis was performed using the SPSS 17.0 software (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics

Table 1 presents the clinical characteristics of 41 patients (30 men; 63 ± 11 years). Fourteen (34%) patients had global wall motion abnormality due to dilated cardiomyopathy or valvular heart disease. Fourteen (34%) patients with regional wall motion abnormality underwent revascularization due to coronary artery disease. The infarct-related artery was the right coronary artery in 9 (22%) patients, the left anterior descending coronary artery in 11 (27%) patients, and the left circumflex coronary artery in 2 (5%) patients. Multivessel coronary artery disease was present in 5 (12%) patients. One (2%) patient with regional wall motion abnormality

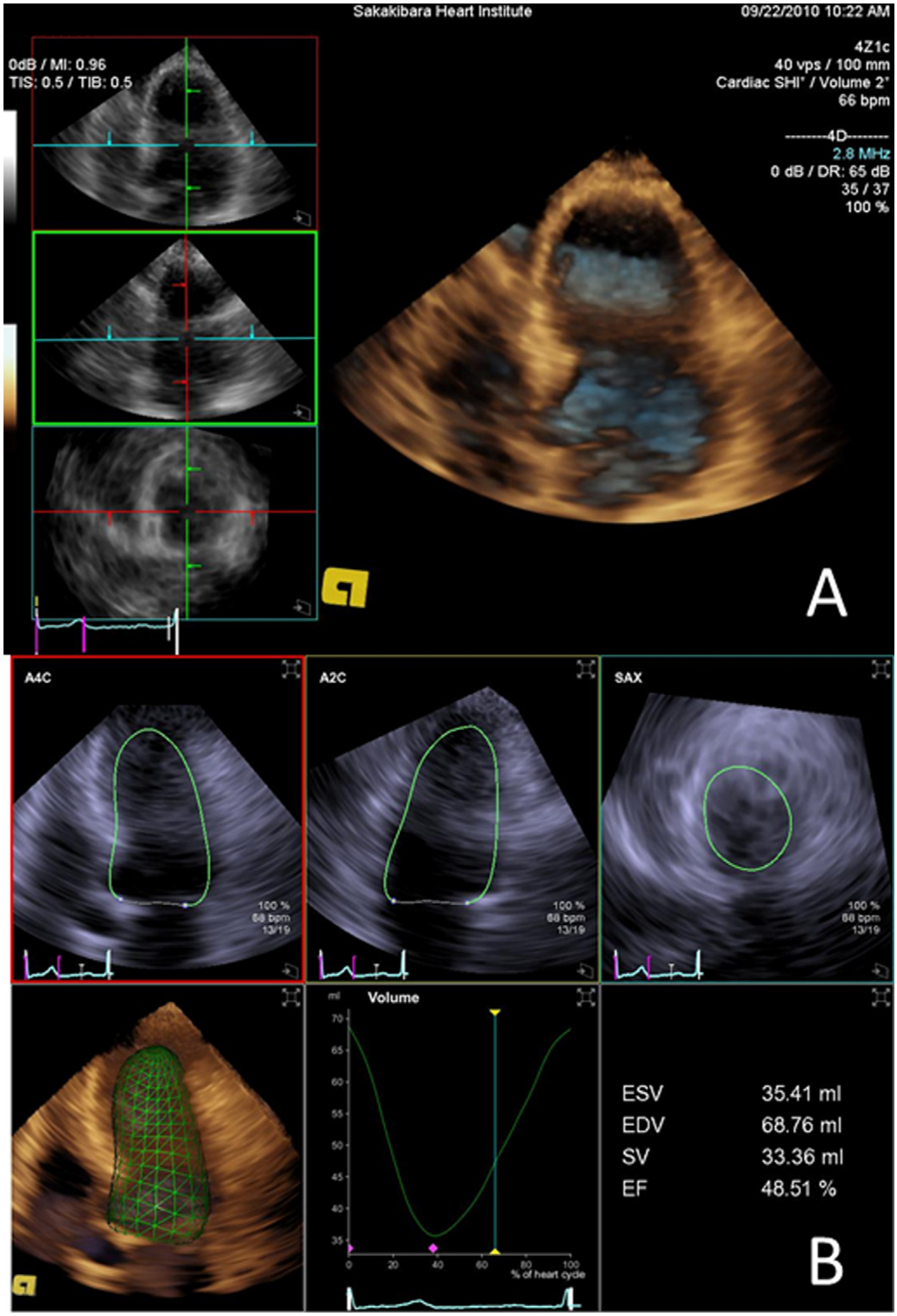

Fig. 1. Left ventricular volume measurement by the ACUSON SC2000 volume imaging ultrasound system. Automatic alignment and extraction of standard views from a full-volume 3D dataset (A) and automatic delineation of the left ventricular endocardium (B) throughout the cardiac cycle.

underwent percutaneous transluminal septal myocardial ablation for hypertrophic obstructive cardiomyopathy.

Measurements of LV volume and EF

The results of EDV, ESV, and EF measurements by RT3DE, 2DE, and CMR are summarized in Table 2. Both EDV and ESV from fully automated measurement by RT3DE were underestimated compared with CMR. On the other hand, both EDV and ESV by semi-automated measurement were similar to those by CMR.

In the present study, the feasibility of automated measurement by RT3DE was 93.2% (41/44). The mean frame rate was $22 \pm 7\,s^{-1}$. In 12 randomly selected patients, the mean times of fully automated measurement and semi-automated measurement from opening the dataset to completion were 37 ± 8 s and 371 ± 116 s, respectively.

Table 1
Clinical characteristics of study patients ($n = 41$).

Age (years)	63 ± 11
Men	30 (73%)
Height (cm)	163 ± 9
Weight (kg)	60 ± 14
Body mass index (kg/m^2)	22 ± 4
Disease	
None	12 (29%)
Valvular heart disease	2 (5%)
DCM	12 (29%)
HCM after PTSMA	1 (2%)
Myocardial infarction	14 (34%)
Acute	3 (7%)
Old	11 (27%)
Culprit vessels	
RCA	9 (22%)
LAD	11 (27%)
LCX	2 (5%)
Multivessel coronary artery disease	5 (12%)
With regional wall motion abnormality	15 (37%)

DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; PTSMA, percutaneous transluminal septal myocardial ablation; RCA, right coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery.

Table 2
Left ventricular volumes determined by CMR, RT3DE and 2DE in study patients ($n = 41$).

	EDV (ml)	ESV (ml)	EF (%)
CMR	131 ± 60	81 ± 55	44 ± 17
RT3DE			
Fully automated	109 ± 42*	63 ± 34*	45 ± 12
Semi-automated	127 ± 54	76 ± 50	45 ± 16
2DE	120 ± 43	65 ± 38*	49 ± 15*

CMR, cardiac magnetic resonance imaging; RT3DE, real-time three-dimensional echocardiography; 2DE, two-dimensional echocardiography; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction.
* Comparison with CMR, $p < 0.01$.

Comparison of LV volume and EF among RT3DE, 2DE, and CMR

Linear regression analysis was used to determine the correlation of RT3DE and 2DE with CMR for EDV, ESV and EF measurements (Figs. 2–4). EDV, ESV, and EF calculated from semi-automated measurements by RT3DE had better agreement with those from CMR for EDV ($r = 0.96$, LOA −30.5 to 39.3 ml; ESV: $r = 0.97$, LOA −22.6 to 32.7 ml; EF: $r = 0.90$, LOA −16.1 to 14.2%, respectively) than those from 2DE ($r = 0.87$, LOA −50.5 to 72.2 ml; $r = 0.93$, LOA −34.1 to 65.2 ml; $r = 0.89$, LOA −20.9 to 10.0%). From fully automated measurements, the corresponding correlation coefficients for EDV, ESV, and EF were 0.80, 0.85, and 0.54, respectively. On the Bland–Altman analysis, the biases and LOA for those were −50.9 to 95.2 ml, −46.2 to 82.2 ml, and −24.5 to 22.0%, respectively.

Observer variability

For fully automated and semi-automated measurement by RT3DE, both intraobserver and interobserver variabilities for EDV, ESV, and EF are shown in Table 3. The reliability was high for those in fully automated and semi-automated measurements.

Discussion

The main finding of this study is that semi-automated measurement by the new RT3DE system had better agreement with CMR than 2DE with CMR in LV volume and EF. Semi-automated measurement by RT3DE had excellent agreement with CMR, good feasibility (93%), and acceptable operation time (6 min) for clinical practice, which was consistent with a previous study [20]. Additionally, the reproducibility by RT3DE was similar to that by 2DE and the operation time of semi-automated measurement was not longer than that of 2DE (5 min).

3DE with volume scanning technique was developed to overcome the limitations of 2DE in clinical settings, such as geometric assumption. Feasibility and validation of 3DE for clinical assessment of LV volume have been demonstrated in previous studies [11–17,21,22]. Gutiérrez-Chico et al. showed that the correlation between 3DE and CMR for LV volumes (EDV: $r = 0.995$; ESV: $r = 0.997$) was better than that between 2DE and CMR (EDV: $r = 0.779$; ESV: $r = 0.864$), and the LOA between 3DE and CMR (EDV MD: −45.9 to 20.9 ml, ESV MD: −34.2 to 15.2 ml) were less variable than those between 2DE and CMR (EDV MD: −158.7 to 108.8 ml, ESV MD: −125.4 to 83.9 ml) [15]. However, traditional 3DE with volume scanning has needed to record four to seven heart cycles for full-volume acquisition and time-consuming manual tracing of contour of LV endocardium throughout [23,24]. Therefore, successful automated measurement based on a 3D data set of a single beat will be superior to traditional 3DE, that is, it could achieve 3D full-volume data without stitch noise and simplify complex procedures in all patients at all times.

Recently, the new RT3DE has been developed to allow acquisition of instantaneous full-volume image of the entire heart in a single heart cycle as well as automated measurement of LV volume and EF. There were two previous validation studies with regard to this new RT3DE system [18,20]. Firstly, Chang and colleagues reported that semi-automated measurements of EDV, ESV, and EF by RT3DE showed excellent correlations ($r = 0.94$, 0.91, and 0.91, respectively) and reasonable LOA (−41.0 to 25.2 ml, −77.9 to −4.9 ml, and −21.0 to 4.5%) with the corresponding measurements obtained from CMR in 91 patients [20]. However, the correlation between the new RT3DE and conventional 2DE remained unclear. The second validation study by Thavendiranathan and colleagues demonstrated that LV volume and EF derived by fully automated contouring of RT3DE and 2DE showed excellent correlation for EDV, ESV, and EF ($r = 0.94$, LOA −30 to 34 ml; $r = 0.94$, LOA −22 to 30 ml; $r = 0.91$, LOA −10 to 6%, respectively) in 24 patients with atrial fibrillation [18]. However, it has not been evaluated adequately whether or not semi-automated measurement by RT3DE has better agreement with CMR than 2DE. Thus, we aimed for the first time to compare semi-automated measurement by the new RT3DE and 2DE with CMR for LV volume and EF.

The accuracy of semi-automated measurement using the new RT3DE in our results had excellent agreement with CMR and better agreement with CMR than 2DE; however, fully automated measurements showed significant underestimation compared with CMR, which was similar to previous studies [19,20]. The main cause of the underestimation compared with CMR in fully automated measurement using RT3DE was the spatial resolution of 3D imaging which was insufficient to provide clear definition of endocardial trabeculae [18]. In addition, Chang and colleagues described in the first validation paper that this software algorithm was not very effective in patients with particular LV geometry, especially small hypertrophic LV [20]. The reason was that this automated algorithm, which detects the endocardial surface from expert-annotated training databases, does not include a large enough number of the small hypertrophic LV patterns, and it could not delineate the true endocardial border excluding LV trabeculae, particularly in sharp-pointed LV apex. On the other hand, the second validation study for American patients demonstrated that fully automated measurement by this RT3DE had excellent agreement with CMR. It was thought that the discrepancy of fully automated measurement among the previous and present studies resulted strongly from the difference of study population. The study population in the first validation study and our study have consisted of East Asian people including Japanese, whose heart was small

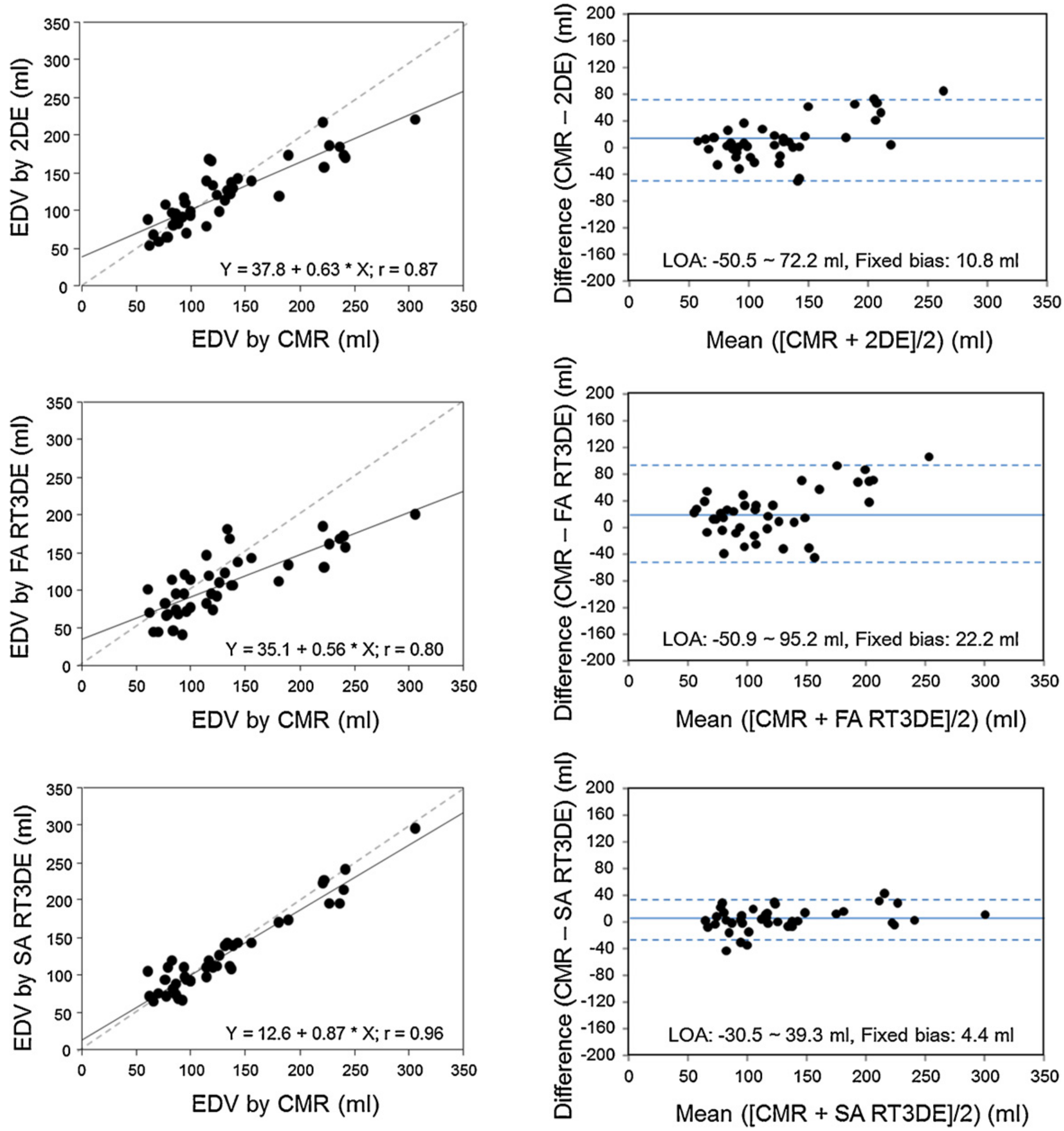

Fig. 2. Linear regression and analysis of agreement between RT3DE, 2DE, and CMR for EDV ($n = 41$). CMR, cardiac magnetic resonance imaging system; RT3DE, real-time three-dimensional echocardiography; FA, fully automated measurement; SA, semi-automated measurement; 2DE, two-dimensional echocardiography; EDV, end-diastolic volume; LOA, limits of agreement.

Table 3
Intraobserver and interobserver variability in automated measurement by RT3DE.

Characteristics ($n = 8$)	Intraobserver variability				Interobserver variability			
	LOA	ICC	95% CI	*p*	LOA	ICC	95% CI	*p*
2DE								
EDV (ml)	−36.2 to 48.9	0.88	0.56–0.97	<0.01	−24.8 to 43.8	0.89	0.58–0.97	<0.01
ESV (ml)	−21.4 to 26.1	0.94	0.77–0.98	<0.01	−12.6 to 21.9	0.96	0.83–0.99	<0.01
EF (%)	−5.7 to 8.5	0.97	0.86–0.99	<0.01	−7.2 to 10.7	0.95	0.81–0.99	<0.01
Fully automated								
EDV (ml)	−0.2 to 0.3	>0.99	0.98–0.99	<0.01	−36.9 to 21.9	0.92	0.67–0.98	<0.01
ESV (ml)	−0.1 to 0.1	>0.99	0.97–0.98	<0.01	−24.7 to 16.2	0.94	0.74–0.99	<0.01
EF (%)	−0.1 to 0.2	>0.99	0.97–0.99	<0.01	−6.6 to 7.7	0.95	0.79–0.99	<0.01
Semi-automated								
EDV (ml)	−40.3 to 18.1	0.93	0.71–0.99	<0.01	−34.0 to 34.5	0.95	0.78–0.99	<0.01
ESV (ml)	−36.6 to 18.1	0.9	0.63–0.98	<0.01	−23.1 to 13.5	0.98	0.89–0.99	<0.01
EF (%)	−7.8 to 13.1	0.84	0.44–0.97	<0.01	−7.9 to 15	0.92	0.62–0.98	<0.01

LOA, limits of agreement; ICC, interclass coefficient of correlation; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction.

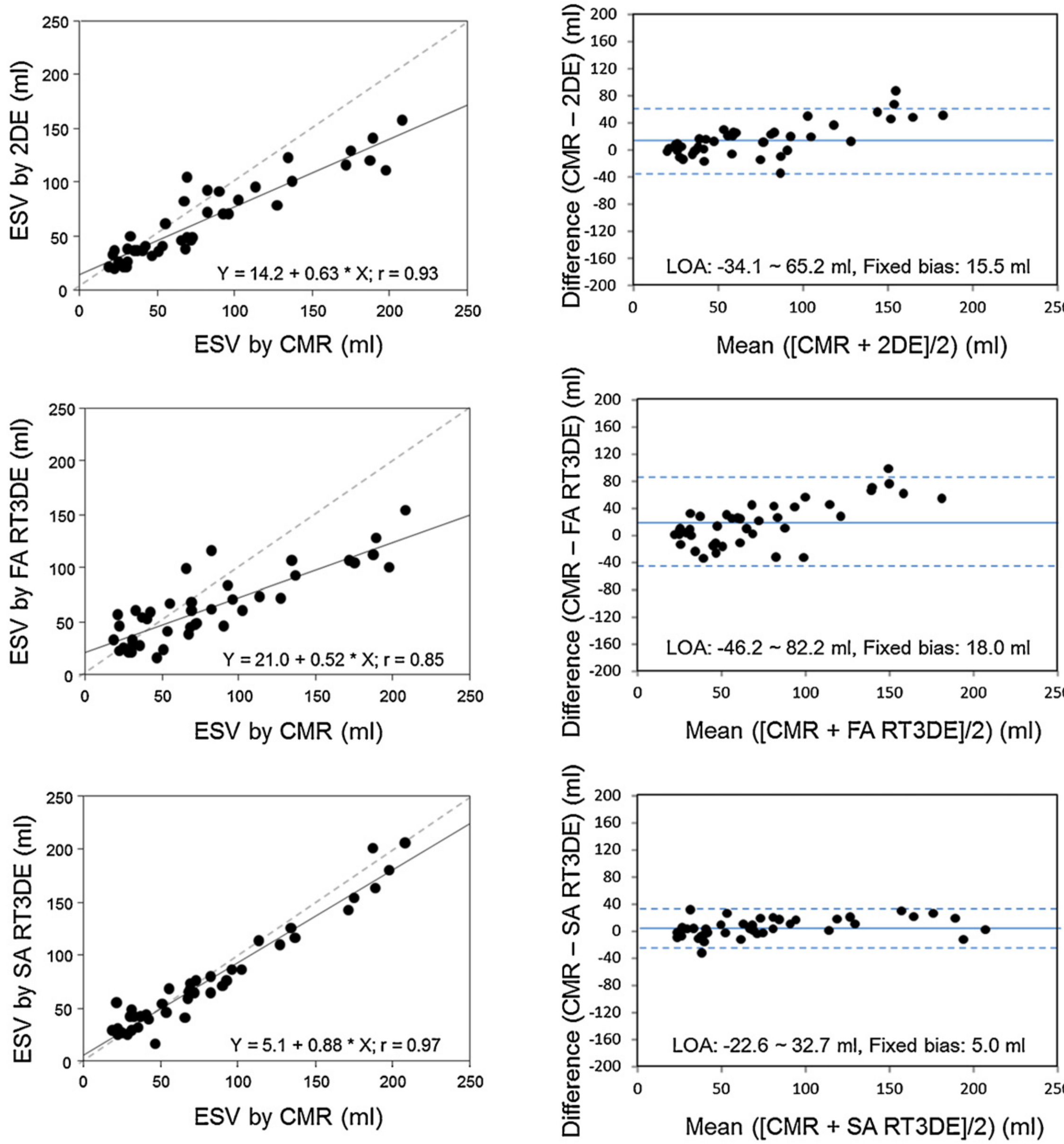

Fig. 3. Linear regression and analysis of agreement between RT3DE, 2DE, and CMR for ESV ($n = 41$). CMR, cardiac magnetic resonance imaging system; RT3DE, real-time three-dimensional echocardiography; FA, fully automated measurement; SA, semi-automated measurement; 2DE, two-dimensional echocardiography; ESV, end-systolic volume; LOA, limits of agreement.

compared with the reference values in the guidelines from the American Society of Echocardiography [25,26]. Therefore, the study population in the first validation study and our study had smaller LV volume (EDV by CMR 137 ml and 131 ml, ESV by CMR 39 ml and 81 ml, respectively) than the second validation study (EDV by CMR 171 ml, ESV by CMR 93 ml) [18,20]. Consequently, Chang and colleagues reported that only 11% of study subjects were successfully analyzed with no additional manual manipulation; and among our study subjects, 27% needed the major outward modification to the real endocardial border in LV apex because of small hypertrophic LV.

Successful automated measurement by RT3DE with single-beat full-volume capture will allow any clinical practice, such as exercise stress echocardiography, in any patients with arrhythmias [22]. In addition, it will ensure good reproducibility with any observers. In the present study, our results demonstrated that automated measurement by the new RT3DE is acceptable in the accuracy and feasibility for the clinical setting, although there may be room for further learning required to incorporate small hypertrophic LV into the automated algorithm software.

Study limitations

Our study has several limitations. First, the study population was relatively small. A larger number of patients should be examined in future investigations. Second, we did not analyze patients with arrhythmias because of the possibility of using multiple-beat gated CMR. However, there is merit in using RT3DE in these patients. Third, there was an interval of up to three days between echocardiography and CMR, although echocardiography and CMR were performed within 6 h of each other in patients with acute myocardial infarction.

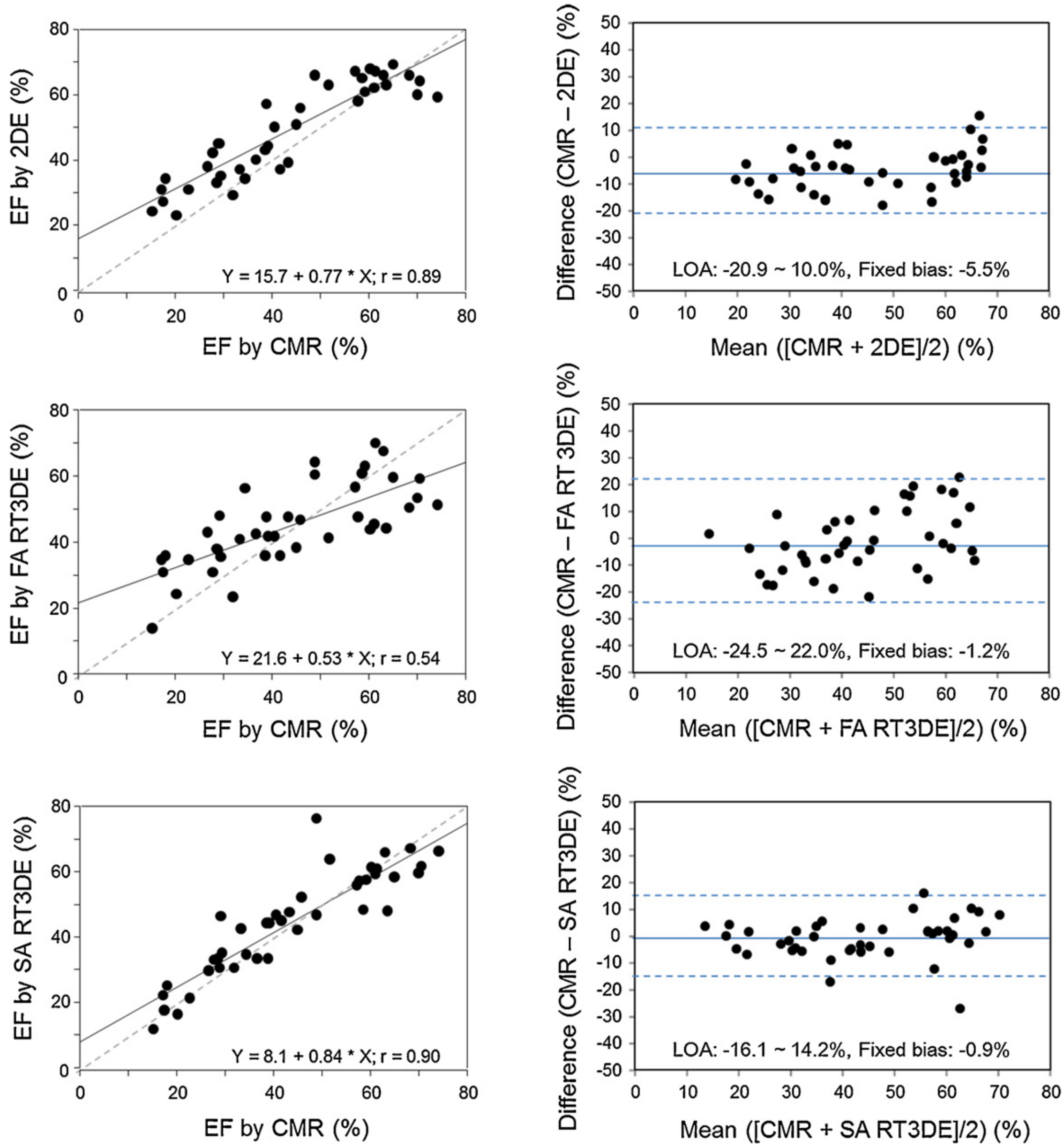

Fig. 4. Linear regression and analysis of agreement between RT3DE, 2DE, and CMR for EF ($n = 41$). CMR, cardiac magnetic resonance imaging system; RT3DE, real-time three-dimensional echocardiography; FA, fully automated measurement; SA, semi-automated measurement; 2DE, two-dimensional echocardiography; EF, ejection fraction; LOA, limits of agreement.

Conclusion

Semi-automated measurement by RT3DE has better agreement with CMR than 2DE in LV volume and EF. It is simple to operate and acceptable in feasibility for the clinical setting although there may be room for further learning required to incorporate various LV geometrical patterns, particularly small hypertrophic LV, into the automated algorithm software.

Conflict of interest

None.

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