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Echocardiography

Reproducibility and Accuracy of Echocardiographic Measurements of Left Ventricular Parameters Using Real-Time Three-Dimensional Echocardiography

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OBJECTIVES We sought to determine whether assessment of left ventricular (LV) function with real-time (RT) three-dimensional echocardiography (3DE) could reduce the variation of sequential LV measurements and provide greater accuracy than two-dimensional echocardiography (2DE).

BACKGROUND Real-time 3DE has become feasible as a standard clinical tool, but its accuracy for LV assessment has not been validated.

METHODS Unselected patients (n = 50; 41 men; age, 64 ± 8 years) presenting for evaluation of LV function were studied with 2DE and RT-3DE. Test-retest variation was performed by a complete restudy by a separate sonographer within 1 h without alteration of hemodynamics or therapy. Magnetic resonance imaging (MRI) images were obtained during a breath-hold, and measurements were made off-line.

RESULTS The test-retest variation showed similar measurements for volumes but wider scatter of LV mass measurements with M-mode and 2DE than 3DE. The average MRI end-diastolic volume was 172 ± 53 ml; LV volumes were underestimated by 2DE (mean difference, −54 ± 33; $p < 0.01$) but only slightly by RT-3DE (−4 ± 29; p = 0.31). Similarly, end-systolic volume by MRI (91 ± 53 ml) was underestimated by 2DE (mean difference, −28 ± 28; $p < 0.01$) and by RT-3DE (mean difference, −3 ± 18; p = 0.23). Ejection fraction by MRI was similar by 2DE (p = 0.76) and RT-3DE (p = 0.74). Left ventricular mass (183 ± 50 g) was overestimated by M-mode (mean difference, 68 ± 86 g; $p < 0.01$) and 2DE (16 ± 57; p = 0.04) but not RT-3DE (0 ± 38 g; p = 0.94). There was good inter- and intra-observer correlation between RT-3DE by two sonographers for volumes, ejection fraction, and mass.

CONCLUSIONS Real-time 3DE is a feasible approach to reduce test-retest variation of LV volume, ejection fraction, and mass measurements in follow-up LV assessment in daily practice. (J Am Coll Cardiol 2004;44:878–86) © 2004 by the American College of Cardiology Foundation

Left ventricular (LV) mass, volume, and ejection fraction (EF) are important prognostic factors (1) and are frequently requested for serial testing (2,3). However, although two-dimensional echocardiography (2DE) is widely available for LV assessment, it has limited test-retest reliability (3,4). Repeated EF measurements may differ because of poor image quality, geometric issues related to volume calculations, and the performance of off-axis cuts and variations in ventricular loading (5). Subjective visual assessment of LV EF, widely used because of these limitations of quantitation, is effective for single assessments but insufficiently reliable for sequential use. Consequently, cardiac magnetic resonance imaging (MRI) has been proposed as a more desirable alternative for LV assessment, especially in trials (2), although the cost and availability of MRI are problematic for routine clinical evaluation.

A number of advances may make the echocardiographic assessment of volumes, EF, and mass more consistent in the presence of constant load. Harmonic imaging has greatly improved image quality, and LV opacification with contrast has enabled improvements in endocardial border detection. Three-dimensional echocardiography (3DE) may overcome the geometric limitations of 2DE. Existing work with three-dimensional reconstruction, based on external localization of transducer angle in space, shows good correlation with MRI and autopsy volumes (6,7), superior to 2DE. Real-time (RT) 3DE may be more feasible for clinical use, as it is not based on an external transducer registration system, and a shorter scanning time may avoid problems arising from the use of multiple cycles such as breathing, variable R-R intervals, and patient movement.

Because both MRI and RT-3DE are three-dimensional techniques, we hypothesized that they may produce comparable results. Therefore, the objectives of this study were to: 1) compare LV volume, mass, and EF by RT-3DE and MRI; 2) determine if the test-retest variability of RT-3DE is clinically acceptable; and 3) compare RT-3DE to similar results from 2DE and M-mode (MM) to demonstrate the improvement achieved.

METHODS

Patient selection. We prospectively recruited 60 patients (48 men, age 63 ± 11 years) referred to the echocardiography laboratory for measurement of LV volume, mass, and

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Abbreviations and Acronyms

EF	= ejection fraction
LV	= left ventricle/ventricular
LVEDV	= left ventricular end-diastolic volume
LVESV	= left ventricular end-systolic volume
MM	= M-mode
MRI	= magnetic resonance imaging
RT	= real-time
2DE	= two-dimensional echocardiography
3DE	= three-dimensional echocardiography

EF. After exclusion of seven patients with technically inadequate echocardiographic images, one with inability to perform a breath-hold, and two patients who were unable to undergo MRI due to claustrophobia, a study group of 50 patients remained who underwent 2DE, RT-3DE, and MRI. The investigations were approved by the ethics committee of the Princess Alexandra Hospital, and all patients gave informed consent.

Study design. Data for test-retest variability were obtained by discharging patients from the laboratory and repeating their imaging within 1 h with no intervening therapy. A subgroup ($n = 20$) was studied for inter-observer variability, which was determined by using the same set of three-dimensional and two-dimensional images measured by two separate sonographers. The same group was tested for intra-observer variability. Intra-observer repeated measures were performed on average one week apart, and the order of repeated analysis was randomized before analysis.

2DE. An experienced sonographer acquired apical views of the LV, using harmonic imaging with a transthoracic 3-MHz phased array transducer (Sonos 7500, Philips Medical Systems, Andover, Massachusetts). Measurements of left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and EF were obtained using the software installed on the ultrasound machine, with LVEDV measurements at the time of mitral valve closure and LVESV measured on the image with the smallest LV cavity. The papillary muscles were excluded from the volumes. Biplane Simpson's rule volumes were obtained from the apical four- and two-chamber views (8); LV mass calculations were made by MM, 2DE, and 3DE, in accordance with the American Society of Echocardiography guidelines (9). Contrast was not given in this study.

RT-3DE. Real-time 3DE images were obtained from an apical window with the patient in the same position. Images were also gathered over four cardiac cycles using a matrix array ultrasonographic transducer (×4 transducer, Philips Sonos 7500 system, Andover, Massachusetts).

Measurements of RT-3DE volumes and masses were performed off-line (4D analysis, Tomtec Gmbh, Unterslessheim, Germany). Frames for LVEDV and LVESV measurement were identified by the same method as 2DE, and endocardial contours were marked in 12 slices (i.e., 15 degrees per slice). Contour tracing was performed with semi-automatic border detection—after first identifying the apex and mitral annulus on each slice, a pre-configured ellipse was fitted to the endocardial borders of each frame and adjusted as required. The LVEDV and LVESV were measured from the resulting three-dimensional volume (Fig. 1A). For RT-3DE, an ellipse was also traced around the epicardial border in end-diastole to give a three-dimensional volume. The endocardial volume was then subtracted from the epicardial volume and multiplied by the specific gravity of heart muscle.

MRI. Cardiac magnetic resonance images were obtained using a Sonata 1.5-T scanner (Siemens, Erlangen, Germany). Left ventricular anatomy and function images were acquired in horizontal and vertical long- and short-axis views using free induction, steady state precession imaging during a breath-hold. Acquisition time for cardiac magnetic resonance images was approximately 40 to 50 min. Off-line calculation of the LVEDV, LVESV, and EF were performed using Cardiac Image Modeling software (CIM version 4.2, Auckland University, Auckland, New Zealand). The LV volume calculation with this method is analogous to that used for 3DE and has previously been described (10). Using two long-axis and six or more short-axis views, markers were placed on the right ventricle and LV annulus, and the endocardial border was detected automatically (Fig. 1B). The same method was utilized to detect the epicardial border in the long- and short-axis views. Left ventricular mass was calculated by the same method as used with 3DE.

Statistical analysis. Results for LVEDV, LVESV, EF, and mass are represented as mean and standard deviation. Correlations were performed between echocardiography and MRI measurements, and agreement was expressed according to the method of Bland and Altman (11,12). A value of $p < 0.05$ was considered to be significant. Z transformations were performed between each group to see if there was any significant difference between correlations (12). Data analyses were performed using SPSS statistical software (version 10, SPSS Inc., Chicago, Illinois).

RESULTS

Patient characteristics. Results of MRI, RT-3DE, and 2DE were analyzed in 50 patients (41 males, 64 ± 8 years). Table 1 summarizes the presence and etiology of LV dysfunction in each group; the majority had regional wall motion abnormalities.

Test-retest variation of 2DE and RT-3DE. Test-retest variation was assessed in all 50 patients (Table 2). The correlation between sequential EF measurements was superior for RT-3DE compared with 2DE ($Z = 5.5$, $p < 0.01$), and variation was slightly less with RT-3DE (Fig. 2). Sequential volume measurements by each echocardiography technique also correlated well, but the correlation between measurements was superior for RT-3DE compared with 2DE for both LVEDV ($Z = 4.9$, $p < 0.01$) and LVESV ($Z = 6.8$, $p < 0.01$) (Table 2). Similarly, sequential LV mass

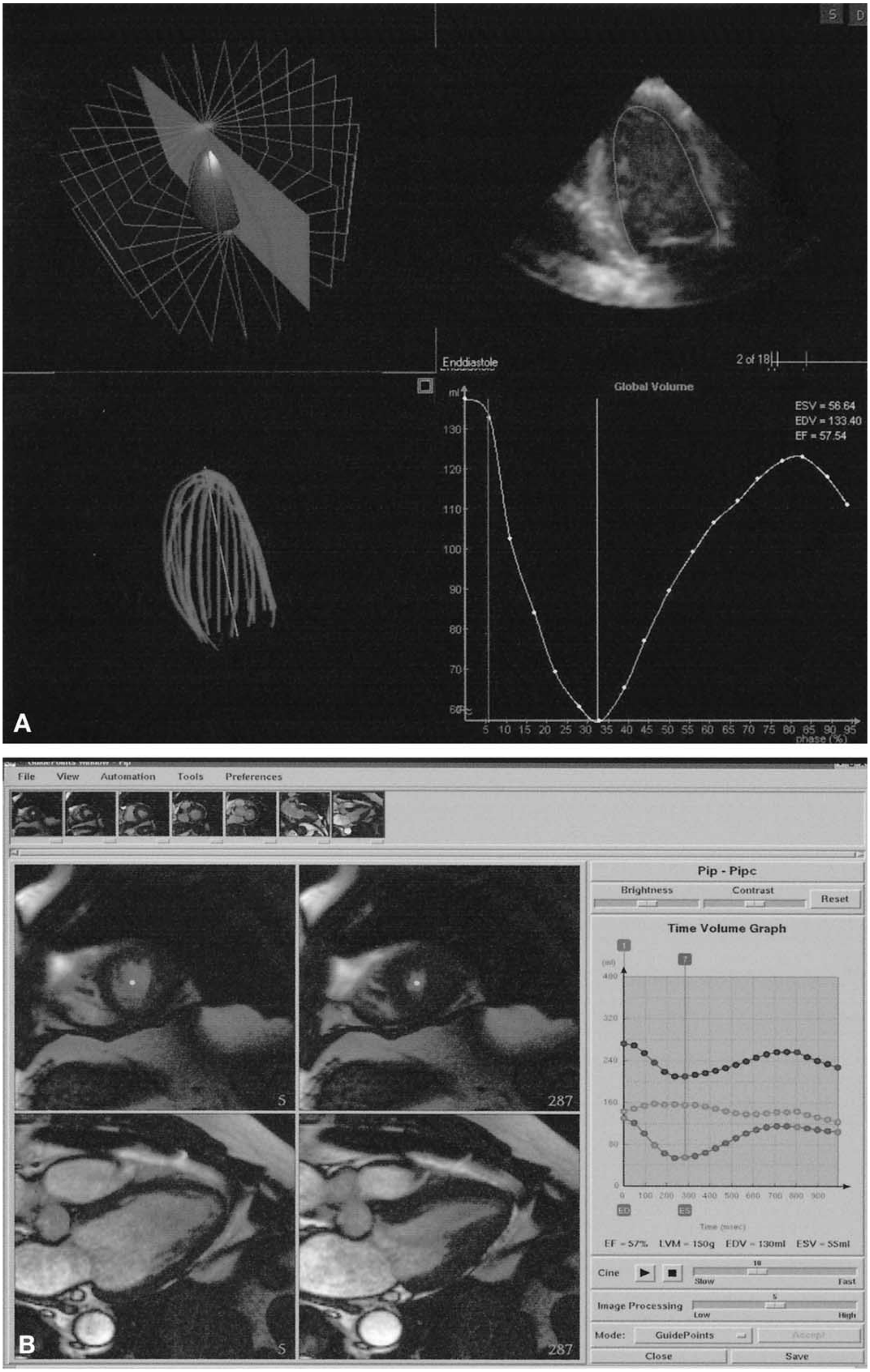

Figure 1. **(A)** Analysis of left ventricular (LV) volume using three-dimensional echocardiography. The figure demonstrates selection of one image **(upper right)**, automated contour-tracing **(upper left)**, superimposition of all contours in three-dimensional space **(lower left)**, and the resulting time-volume curve **(lower right)**. **(B)** Analysis of LV volume using magnetic resonance imaging. The position of apex and base is shown on the longitudinal plane images, and endocardial and epicardial borders are traced in the short-axis views. EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; LVM = left ventricular mass.

Table 1. Clinical Characteristics of the Study Patients

	Test-Retest Correlation/ MRI Validation (n = 50)	Interobserver/ Intraobserver Reproducibility (n = 20)
Age (yrs)	64 ± 8	57 ± 12
Males	41	13
Etiology		
Regional WMA	41	18
Global LV dysfunction		
Hypertension	2	1
Normal	7	1

LV = left ventricular; MRI = magnetic resonance imaging; WMA = wall motion abnormalities.

measurements with RT-3DE showed less difference than with 2DE (Z = 0.53, p = 0.6) (Fig. 3), and both were superior to MM measurement of LV mass (Z = 1.97, p < 0.05).

Inter- and intra-observer variation of RT-3DE and 2DE. For all parameters, inter-observer agreement for RT-3DE exceeded that obtained with 2DE (Table 3). The widest discrepancy in inter-observer variability was with MM measurement of LV mass (mean difference, 8 ± 39 g; R = 0.52; p < 0.01), with RT-3DE being superior to 2DE. There were significant differences between MM and 2DE and RT-3DE (Z = 3.0, p < 0.01 and Z = 10.43, p < 0.01).

Similar findings were made with intra-observer variation (Table 4). Real-time 3DE showed significantly better intra-observer agreement than 2DE measurement of EF (Z = 10.5, p < 0.01), LVEDV (Z = 6.28, p < 0.01), and LVESV (Z = 7.65, p < 0.01). Again, the greatest intra-observer variation concerned LV mass (mean difference, 4 ± 26 g; R = 0.77; p < 0.01), and agreement was better with RT-3DE than 2DE (Z = 5.5, p < 0.01) as well as MM (Z = 7.05, p < 0.01). Two-dimensional echocardiography and MM were not significantly different (Z = 1.5, p = 0.13).

Validation with MRI. The mean differences of the echocardiographic techniques from MRI techniques are summarized in Table 5. Of the echocardiographic methods for EF measurement, the use of RT-3DE gave the smallest measurement error and closest correlation to MRI (Fig. 4). The correlation of EF between MRI and the echocardiography techniques is summarized in Figure 5. Although LV mass was underestimated by RT-3DE and overestimated by both 2DE techniques, the greatest difference from MRI mass was MM-derived mass (mean difference, 68 ± 86 g; p < 0.01).

Feasibility. Table 6 summarizes the scanning times to acquire apical and parasternal views by 2DE and apical RT-3DE. Scanning time for RT-3DE was taken for multiple full volume datasets; acquisition time during each breath hold was approximately 10 s. The time required for calculation of LV volumes and mass from cardiac magnetic resonance images ranged from 10 to 15 min.

DISCUSSION

The results of this study indicate that three-dimensional imaging of the LV with either MRI or RT-3DE do indeed produce comparable results in patients with suitable echocardiography image quality. Real-time 3DE also provides low test-retest variation and high reproducibility of LV measurements between observers.

Test-retest variation. In contrast with the more widely reported parameters of intra- and inter-observer variability, which relate to the repeated measurement of a single dataset, test-retest variation involves repetition of the entire acquisition and analysis. This parameter assumes particular importance in the use of a follow-up test. Both physiologic and imaging factors are contributors to variations in LV measurements in time. Standard parameters for LV assessment are strongly influenced by differences in loading conditions over time, and we sought to minimize these by repeating the study over a short time frame and without any treatment changes, so that the main source of variation related to imaging considerations.

Previous work found significant variations between sonographers with respect to both the angulation and displacement of 2DE imaging planes, with foreshortening of >90% of apical views (13). The limitations of standard echocardiographic measurements of LV mass have been highlighted in several studies (2,14), and they pose a critical issue if LV mass is used to help make decisions about initiating or altering treatment in hypertensive subjects. The degree of test-retest variation of volume measurements in this study was less than anticipated, probably because of the avoidance of variation of loading conditions due to the relatively short time between repeat testing. Nonetheless,

Table 2. Correlation and Mean Difference Between the Sequential ("Test-Retest") Studies With 2DE and RT-3DE (n = 50)*

	RT-3DE		2DE		Difference in Test-Retest Correlation for RT3D and 2DE	
End-diastolic volume (ml)	r = 0.98†	0 ± 5	r = 0.92†	2 ± 8	Z = 4.9	p < 0.01
End-systolic volume (ml)	r = 0.99†	1 ± 4	r = 0.93†	1 ± 8	Z = 6.8	p < 0.01
Ejection fraction (%)	r = 0.92†	0 ± 2	r = 0.66†	−2 ± 6	Z = 5.5	p < 0.01
LV mass (g)	r = 0.87†	0 ± 13	r = 0.85†	0 ± 17	Z = 0.5	p = 0.6

*The correlations between sequential measures were greater with RT-3DE than 2DE techniques; †p < 0.01.
LV = left ventricular; RT-3DE = real-time three-dimensional echocardiography.

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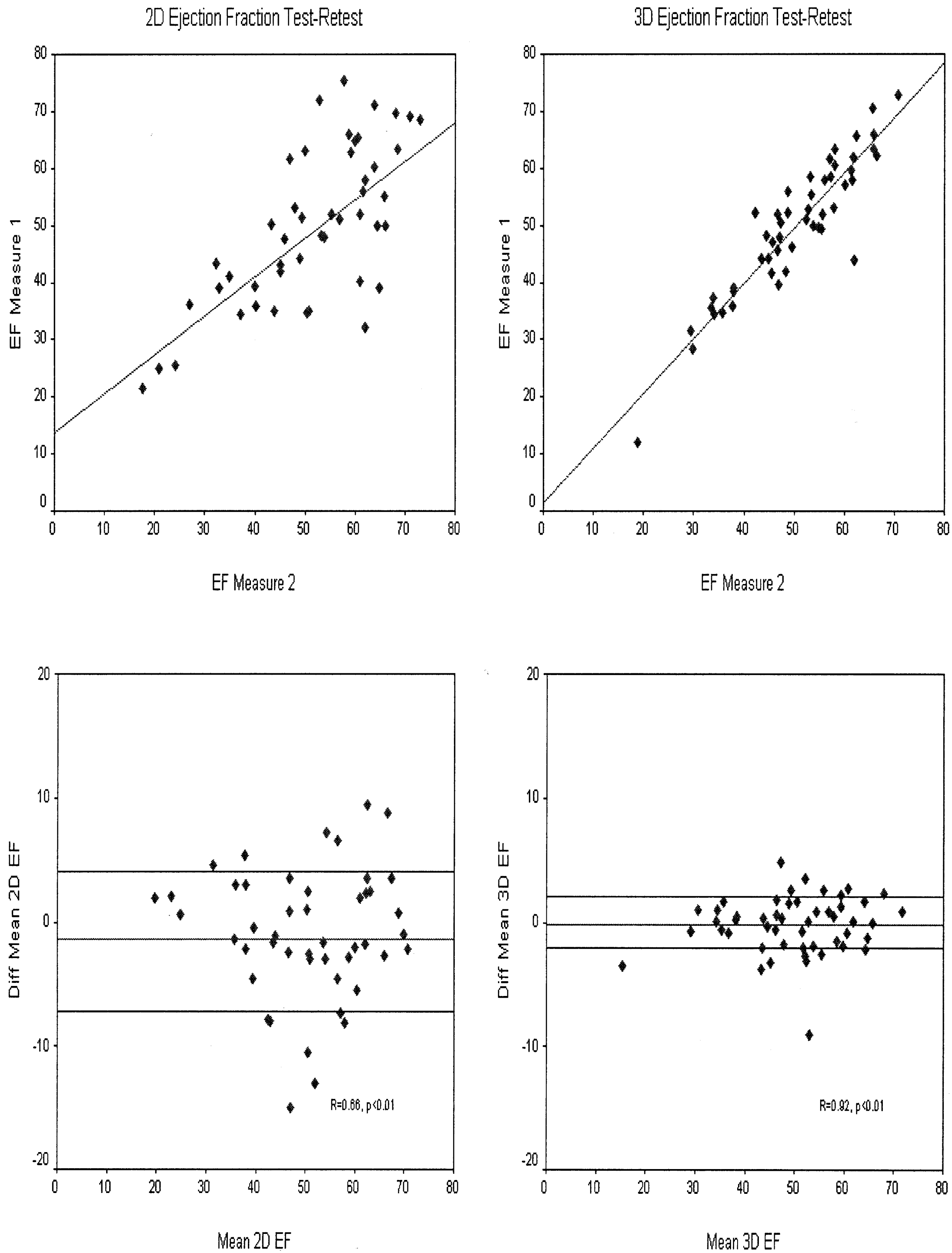

Figure 2. Test-retest comparisons of sequential ejection fraction (EF) for two-dimensional (2D) echocardiography **(left panels)** and real-time three-dimensional (3D) echocardiography **(right panels)** (n = 50).

while test-retest variability may be minimized by a skilled observer, the use of three-dimensional techniques may reduce the likelihood of variation being due to different cut-plane angulations.

Inter- and intra-observer variation. Previous studies of volumetric and reconstructed 3DE (3–5) have shown that this technique shows higher reproducibility than 2DE. In particular, the use of a three-dimensional dataset is the most important aspect of minimizing variation, irrespective of the technique (echocardiography or MRI) (13).

In this study, inter-observer variation was optimized by the use of RT-3DE. While this likely reflects minimization of error derived by the selection of different 2DE cycles, it also reflects the use of a semi-automated edge-detection

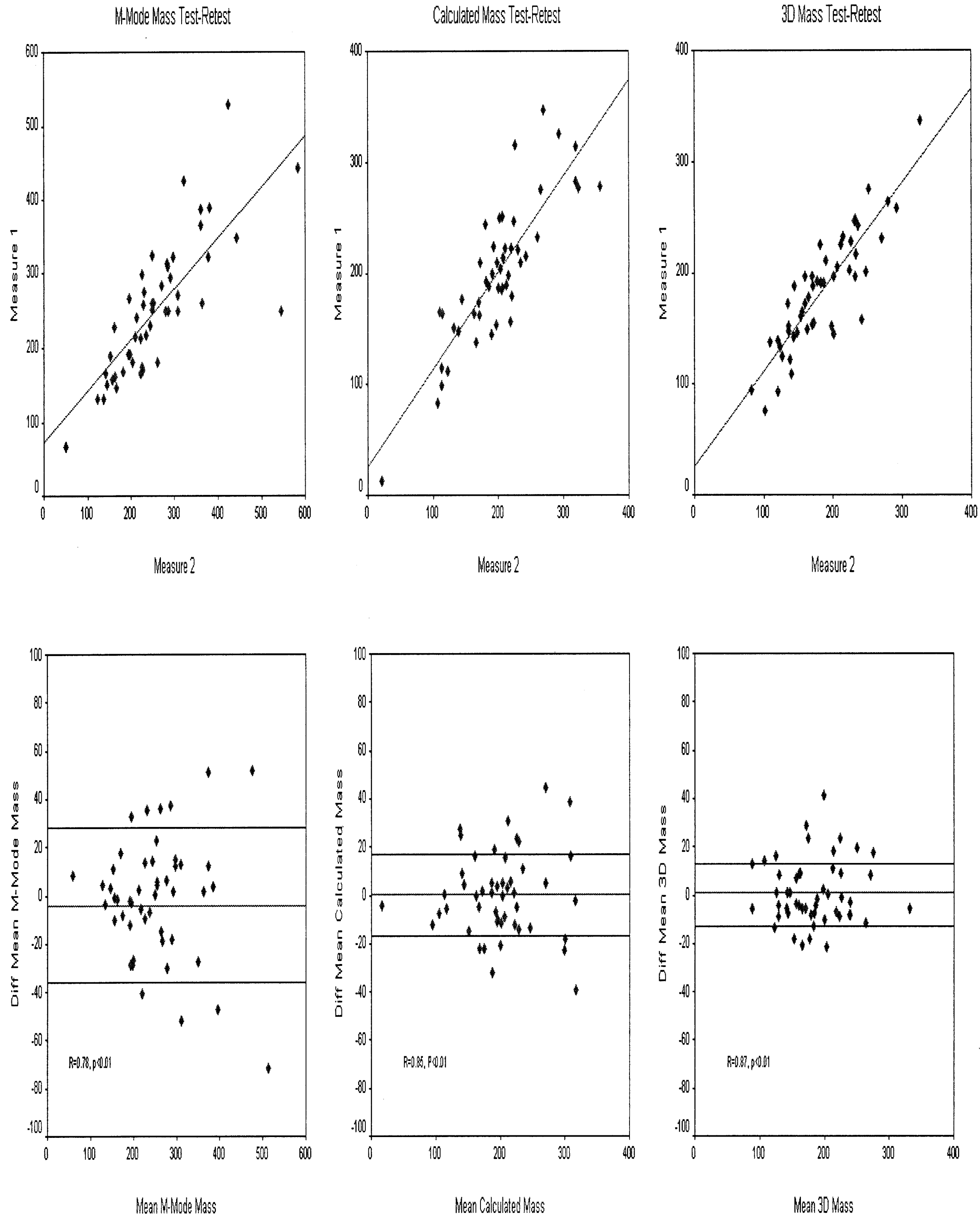

Figure 3. Test-retest comparisons of sequential mass measurements for M-mode **(left panels)**, two-dimensional echocardiography **(center panels)**, and real-time three-dimensional (3D) echocardiography **(right panels)** (n = 50).

technique for LV volume and mass measurement. The importance of a standard approach to partition between the wall and cavity to minimizing variation is reinforced by the more favorable intra-observer results, implying that measurement (rather than acquisition) problems reflect different criteria for tracing the LV myocardium.

Validation of RT-3DE. Although previous studies have validated the use of reconstructed and volumetric 3DE, we are unaware of an existing comparison of RT-3DE and 2DE with MRI. In this study of normal and abnormal ventricles, the majority of which showed regional wall motion abnormalities, volumes were underestimated by

Table 3. Inter-Observer Agreement With 2DE and RT-3DE (n = 20) Showing Correlations and Mean Difference Between the Studies

	RT-3DE		2DE		Difference in Interobserver Agreement for RT-3DE and 2DE	
End-diastolic volume (ml)	r = 0.95*	−3 ± 10	r = 0.76*	13 ± 17	Z = 6.4	p < 0.01
End-systolic volume (ml)	r = 0.97*	−2 ± 6	r = 0.79*	−9 ± 13	Z = 7.8	p < 0.01
Ejection fraction (%)	r = 0.88*	0 ± 3	r = 0.61†	2 ± 8	Z = 5.1	p < 0.01
LV mass (g)	r = 0.96*	−1 ± 11	r = 0.75*	−5 ± 23	Z = 7.4	p < 0.01

*p < 0.01; †p < 0.03.
2DE = two dimensional echocardiography; other abbreviations as in Table 2.

Table 4. Intra-Observer Agreement With 2DE and RT-3DE (n = 20) Showing R Values and Mean Difference Between the Studies

	RT-3DE		2DE		Difference in Intraobserver Agreement for RT-3DE and 2DE	
End-diastolic volume (ml)	r = 0.98*	−1 ± 6	r = 0.90*	−5 ± 9	Z = 6.3	p < 0.01
End-systolic volume (ml)	r = 0.98*	−2 ± 6	r = 0.86*	0 ± 10	Z = 7.7	p < 0.01
Ejection fraction (%)	r = 0.97*	1 ± 2	r = 0.61†	−2 ± 6	Z = 10.5	p < 0.01
LV mass (g)	r = 0.96*	−5 ± 8	r = 0.84*	−12 ± 24	Z = 5.5	p < 0.01

*p < 0.01; †p < 0.03.
Abbreviations as in Tables 2 and 3.

Table 5. Mean Difference Between Echocardiographic and MRI Measurements (n = 50)

	RT-3DE		2DE		Difference in Variance Between MRI and RT-3DE or 2DE	
End-diastolic volume (172 ± 53 ml)	−4 ± 29	p = 0.31	−54 ± 33	p < 0.01	F = 1.31	p = 0.17
End-diastolic volume (91 ± 53 ml)	−3 ± 18	p = 0.23	−28 ± 28	p < 0.01	F = 2.38	p = 0.001
Ejection fraction (50 ± 14%)	0 ± 7	p = 0.74	−1 ± 13	p = 0.76	F = 3.82	p < 0.0001
LV mass (183 ± 50 g)	0 ± 38	p = 0.94	16 ± 57	p = 0.04	F = 2.25	p < 0.003

MRI = magnetic resonance imaging; other abbreviations as in Tables 2 and 3.

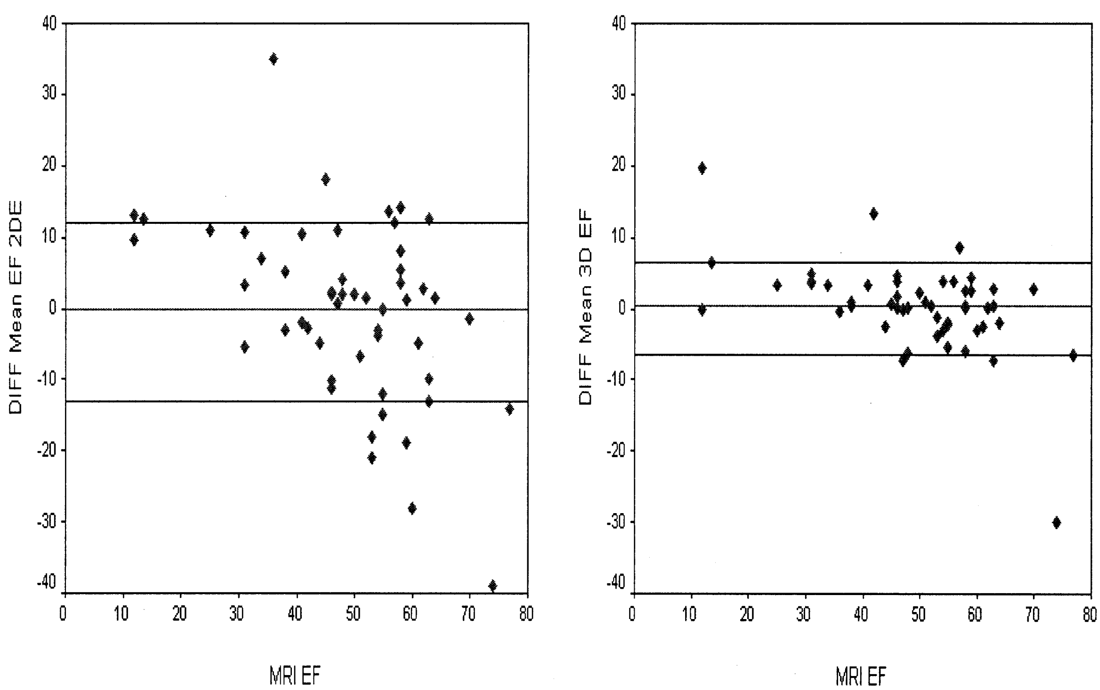

Figure 4. Magnetic resonance imaging (MRI) comparisons with two-dimensional echocardiography (2DE) **(left panel)** and real-time three-dimensional (3D) echocardiography **(right panel)** for ejection fraction (EF) (n = 50).

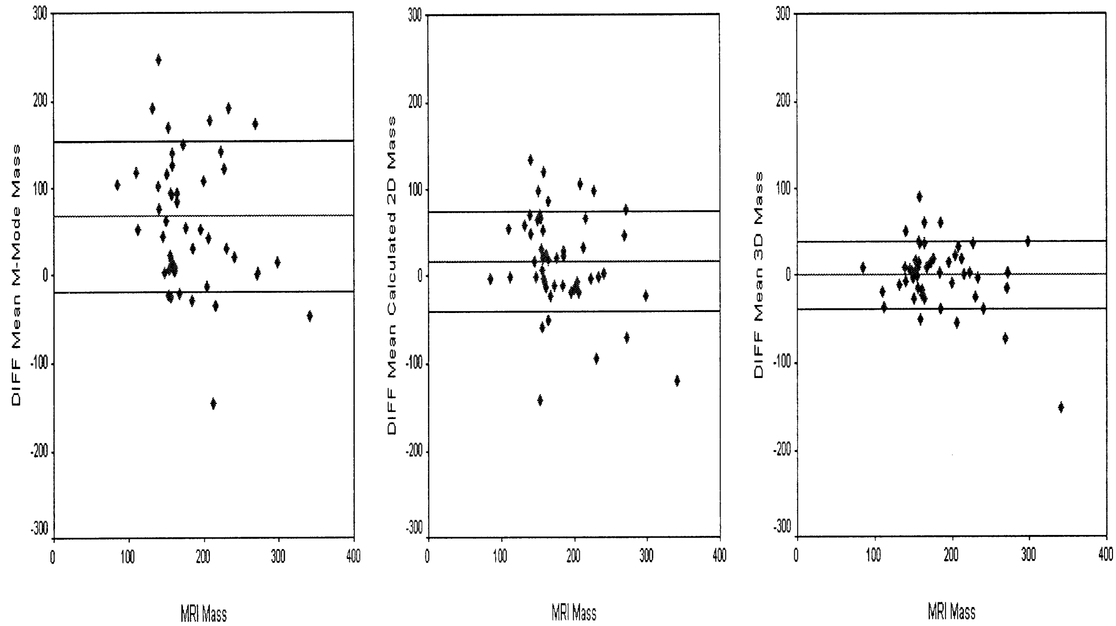

Figure 5. Magnetic resonance imaging (MRI) comparisons with M-mode **(left panel)**, two-dimensional (2D) echocardiography **(center)**, and real-time three-dimensional (3D) echocardiography **(right)** for mass (n = 50).

echocardiography—although less with RT-3DE than with any other technique. This systematic underestimation may, in part, reflect the correspondence between the "bright blood" MRI technique with ventriculography (both filling the space between trabeculations) and, in part, reflect the failure of the 2DE biplane method to depict the LV outflow tract (15).

Conclusions. A clinically feasible echocardiographic approach to sequential assessment of LV volumes and mass would be of value in many settings, including the management of hypertension and heart failure and the follow-up of regurgitant valves. Despite its accuracy in clinical studies, MRI has yet to fill this role because of cost, availability, and more minor issues regarding device incompatibilities and patient tolerance. The development of RT-3DE has made the echocardiographic approach more feasible, although the analysis time remains longer than with MRI. The results of this study indicate that RT-3DE is a feasible approach to reduce test-retest variation and improve accuracy of LV volume, EF, and mass measurements in follow-up LV assessment in daily practice.

Table 6. Mean Acquisition and Calculation Times (n = 20)

	RT-3DE	2DE
Acquisition time (s)	50 ± 19	120 ± 60
Volume calculation (s)	630 ± 60	90 ± 27
Mass calculation (s)	360 ± 50	M-mode −30 + 10 2DE −42 + 10

Abbreviations as in Tables 2 and 3.

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