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ORIGINAL RESEARCH

Transthoracic 3D Echocardiographic Left Heart Chamber Quantification Using an Automated Adaptive Analytics Algorithm

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ABSTRACT

OBJECTIVES The goal of this study was to test the feasibility and accuracy of an automated algorithm that simultaneously quantifies 3-dimensional (3D) transthoracic echocardiography (TTE)-derived left atrial (LA) and left ventricular (LV) volumes and left ventricular ejection fraction (LVEF). Conventional manual 3D TTE tracings and cardiac magnetic resonance (CMR) images were used as a reference for comparison.

BACKGROUND Cardiac chamber quantification from 3D TTE is superior to 2D TTE measurements. However, integration of 3D quantification into clinical practice has been limited by time-consuming workflow and the need for 3D expertise. A novel automated software was developed that provides LV and LA volumetric quantification from 3D TTE datasets that reflect real-life manual 3-dimensional echocardiography measurements and values comparable to CMR.

METHODS A total of 159 patients were studied in 2 separate protocols. In protocol 1, 94 patients underwent 3D TTE imaging (EPIQ, iE33, X5-1, Philips Healthcare, Andover, Massachusetts) covering the left atrium and left ventricle. LA and LV volumes and LVEF were obtained using the automated software (HeartModel, Philips Healthcare) with and without contour correction, and compared with the averaged manual 3D volumetric measurements from 3 readers. In protocol 2, automated measurements from 65 patients were compared with a CMR reference. The Pearson correlation coefficient, Bland-Altman analysis, and paired Student *t* tests were used to assess inter-technique agreement.

RESULTS Correlations between the automated and manual 3D TTE measurements were strong ($r = 0.87$ to 0.96). LVEF was underestimated and automated LV end-diastolic, LV end-systolic, and LA volumes were overestimated compared with manual measurements. Agreement between the automated analysis and CMR was also strong ($r = 0.84$ to 0.95). Test-retest variability was low.

CONCLUSIONS Automated simultaneous quantification of LA and LV volumes and LVEF is feasible and requires minimal 3D software analysis training. The automated measurements are not only comparable to manual measurements but also to CMR. This technique is highly reproducible and timesaving, and it therefore promises to facilitate the integration of 3D TTE-based left-heart chamber quantification into clinical practice. (J Am Coll Cardiol Img 2016;9:769–82)

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ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

3D = 3-dimensional

3DE = 3-dimensional echocardiography

CMR = cardiac magnetic resonance

CT = computed tomography

LA = left atrium

LAV = left atrial volume

LV = left ventricle

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVES = left ventricular end-systole

LVESV = left ventricular end-systolic volume

TTE = transthoracic echocardiography

Multiple studies have demonstrated the advantages of using 3-dimensional echocardiography (3DE). Specifically, 3-dimensional (3D) transthoracic echocardiographic (TTE) measurements of left ventricular (LV) and left atrial (LA) volumes are superior in accuracy and reproducibility to 2-dimensional (2D) techniques, due to avoidance of geometric assumptions and foreshortened views (1–3). These findings have led to guidelines supporting the clinical use of 3DE in LV volume assessment (4,5). In addition, 2D and 3DE datasets can now be acquired by using a single transducer, allowing the integration of 3DE into routine practice.

Despite these demonstrated benefits, however, widespread use of 3D TTE for LA and LV volume assessments has not become a clinical reality. This scenario is likely due to the time and training required to obtain accurate and reproducible 3DE volumetric measurements (1,6,7). The availability of a reasonably accurate and reproducible, automated cardiac chamber quantification technique, which would require minimal or no manual correction of endocardial borders, would potentially allow integration of 3DE volumetric LV and LA measurements into routine practice.

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Novel automated software has been developed that provides LV and LA volumetric quantification. Because 3DE-derived volumes are known to be smaller than those obtained from cardiac magnetic resonance (CMR) images, the program was designed to provide 2 types of 3DE LV and LA volumes: values reflective of real-life manual 3DE measurements (3DE model) and values comparable to CMR (CMR model). The present study was designed to: 1) validate automated LV and LA measurements obtained by using the 3DE model against manual 3DE measurements and those obtained using the CMR model against the CMR reference; 2) examine the relationship between LV and LA measurements obtained by using these techniques; and 3) compare the reproducibility and analysis time of the 3DE model with those of the conventional manual 3DE measurements.

METHODS

All studies were performed at the University of Chicago Medical Center. The institutional review board approved the protocol. Written informed consent was obtained for each patient. 3DE imaging was performed using an EPIQ/iE33, X5 transducer (Philips Healthcare, Andover, Massachusetts) with the patient in the left lateral decubitus position. Wide-angled acquisition using "full-volume" mode over 4 consecutive cardiac cycles was used during a single breath-hold. Care was taken to include the entire LA and LV cavity within the 3D volume. Imaging settings were optimized for endocardial visualization. The highest possible frame rate was obtained by minimizing imaging depth and sector width.

PROTOCOL 1: 3DE MANUAL REFERENCE STANDARD. To validate the automated 3DE model, we compared left ventricular end-systolic volumes (LVESV), left ventricular end-diastolic volumes (LVEDV), left ventricular ejection fraction (LVEF), and left atrial volumes (LAV) at left ventricular end-systole (LVES) obtained from the automated 3DE program versus 3D manual measurements. Patients were included if they were in sinus rhythm and agreed to participate. Patients were excluded if they had poor endocardial visualization on 2D echocardiography of ≥3 contiguous segments using a 17-segment model or complex congenital heart disease.

We screened 104 consecutive patients who were referred for 2D TTE for assessment of LV function and had no history of mitral valve replacement or right heart enlargement. After excluding 10 patients because of poor image quality, 94 patients were studied. Two independent investigators analyzed the 3DE datasets using the prototype-automated software, and their results were averaged.

Three additional independent expert investigators manually measured the 3DE datasets to obtain LVESV, LVEDV, LVEF, and LAV at LVES. Manual measurements were then averaged and used as a manual reference standard that was not biased by an individual measurement style but reflected real-world variability. Individuals involved in the development of the program did not participate in the analysis of the validation datasets.

PROTOCOL 2: CMR REFERENCE STANDARD. To validate the automated CMR model against a CMR reference standard, 69 nonconsecutive patients referred for CMR evaluation, who agreed to undergo transthoracic 3DE within 24 h of the CMR study, were recruited by using inclusion and exclusion criteria identical to those in protocol 1. Of the 69 patients, 4 were excluded because of poor TTE image quality. In the remaining 65 patients, LV and LA automated 3DE measurements were compared with CMR values. In addition, as in protocol 1, 3 independent expert investigators manually measured the 3DE datasets to obtain LVESV, LVEDV, LVEF, and LAV at LVES. The

manual measurements were then averaged and compared with the CMR reference standard.

AUTOMATED 3DE MEASUREMENTS. For both models (3DE and CMR), derivation datasets involving 30 to 50 patients were initially examined. The results of the validation datasets are presented in the current paper.

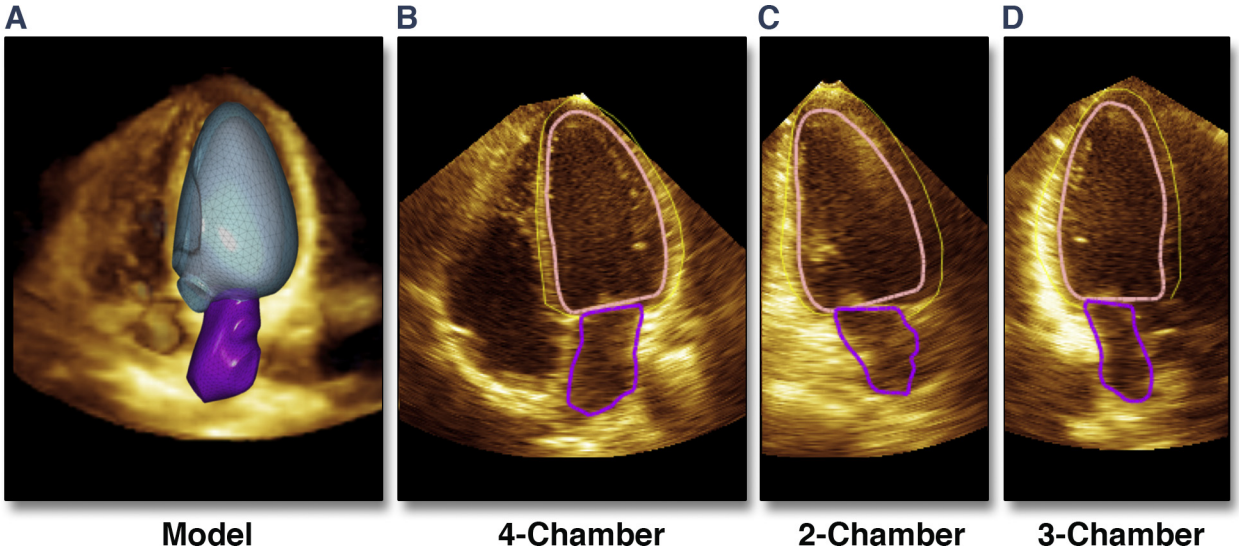
3DE model. The prototype 3DE software involves an automated analysis that simultaneously detects LV and LA endocardial surfaces by using an adaptive analytics algorithm. First, the program identifies LV end-diastole using the electrocardiogram and determines global cardiac shape orientation. LVES is then determined by using motion analysis to identify the smallest LV cavity. Preliminary end-systolic and end-diastolic LV and LA models are then built by using automatic endocardial surface detection in conjunction with information from a 3DE database, which consists of LA and LV end-diastolic and end-systolic shapes from approximately 1,000 3D TTE datasets of varying image quality in patients with a wide range of function and morphologies (i.e., normal, dilated cardiomyopathy). The program matches features from the LV volume being analyzed to selected shapes in the database. This selected model is then locally adapted to the patient's LV volume by using a series of adaptations.

The algorithm adjusts to various imaging conditions, including variations in dropout, acoustic clutter, ventricular shape, and dataset orientation. However, similar to manual measurements, a minimum number of visible endocardial border segments (approximately 14 to 15 of 17 LV segments) are necessary for a reasonable estimation of chamber volumes. Lastly, when re-analyzing the same dataset, the algorithm has a deterministic convergence response, thus yielding zero variability when repeating the analysis on the same dataset. Once the final model has been fitted, the LA and LV contours are displayed on end-diastolic and end-systolic 4-, 3-, and 2-chamber cut-planes derived from the 3DE datasets (Figure 1). If the user is not satisfied with the contours displayed, they can be manually edited.

CMR model. This model differs from the 3DE model in that the end-systolic and end-diastolic LV and LA values are adjusted with information from a 3DE CMR database. Thus, whereas the automated program LA and LV contours displayed on 2D cut-planes derived from the 3DE datasets reflect the 3DE data, the values produced are adjusted with knowledge of the relationship between the 3DE and CMR data. Again, if the user is not satisfied with the displayed contours, they can be edited.

Automated program use. The investigator first recorded the LV and LA measurements without contour adjustment. Values were then recorded allowing contour adjustment if deemed necessary. LV border adjustment could be performed by using 2 different

FIGURE 1 Automated Program LA and LV Endocardial Shells



Three-dimensional (3D) left atrial (LA) and left ventricular (LV) shells are displayed on the 3D volume cropped to a **(A)** 4-chamber view. The contours are also displayed on **(B to D)** 2-dimensional cut-planes derived from the 3D dataset.

approaches. The first option was to globally scale the border by a user-determined amount; the second option was to adjust a specific region of the endocardial border. The user could employ both approaches or a single approach to improve endocardial tracings. LA contours could be adjusted by altering the locations of the 2 basal and 1 apical reference points.

MANUAL 3DE MEASUREMENTS. LV volumes and LVEF, as well as LAV at LVES, were measured using commercially available software (QLAB-3DQ, Philips Healthcare) by 3 experienced echocardiographers blinded to the results of the automated program and the CMR results. The end-diastolic and end-systolic frames analyzed by the automated program and confirmed by an echocardiographer not performing the manual measurements were provided to the individuals performing the manual measurement. The following steps were performed on the end-diastolic and end-systolic frames. First, the users aligned the multiplanar view to maximize the LV cavity long- and short-axes in the 2- and 4-chamber views. Four mitral annular and 1 apical point were then placed on the left ventricle as landmarks in each of the views. The endocardial border was then manually edited where needed, and the final LVESV, LVEDV, and LVEF were then recorded. The long-axis of the left atrium was identified at LVES in the 2- and 4-chamber views, and the blood-tissue interface was traced manually to allow biplane LAV calculation.

CMR IMAGING AND ANALYSIS. CMR images were obtained using a 1.5-T scanner (Achieva, Philips Healthcare) with a phased-array cardiac coil. Steady-state free precession dynamic gradient-echo cine loops were obtained using retrospective electrocardiographic gating and parallel imaging sensitivity encoding during approximately 5-s breath-holds (30 frames per cardiac cycle). Cine loops of 6-mm thick short-axis slices with 2-mm gaps and 2.0 × 2.0-mm in-plane spatial resolution were obtained from above the left atrium to below the apex. Images were analyzed using commercial software (ViewForum, Philips Healthcare).

An investigator experienced in CMR analysis who had no knowledge of the echocardiographic measurements performed all tracings (W.T.). LV analysis included the first basal slice that exhibited at least 50% of the circumference of the LV cavity surrounded by myocardial tissue to the last apical slice that showed the LV cavity. The basal and apical slices were confirmed on long-axis views. The end-systolic and end-diastolic LV endocardial boundary were manually traced with the papillary muscles and trabeculae included in the LV cavity. LVESV and LVEDV were calculated using the disk area summation method. LVEF was calculated from the LVESV and LVEDV using the standard formula. LAV was determined at LVES. In each short-axis slice, the endocardial LA border was manually traced. The LA appendage and pulmonary veins were not included in the LAV. LAV was calculated by adding up the volumes from each slice.

REPRODUCIBILITY. LA and LV volume measurement reproducibility using the automated 3DE model program without contour adjustment was performed in all 94 patients. The same loops were re-analyzed without contour adjustment 1 week later by the same investigator who was blinded to all previous measurements.

Test-retest reproducibility was assessed in all 94 patients. After the initial 3DE dataset was obtained, the sonographer removed the probe from the patient's chest and after 5 min repositioned the transducer to obtain a second dataset. Image and frame rate optimization were performed in a manner similar to the initial acquisition. LV and LAV measurements were obtained using the automated 3DE program with and without contour adjustment.

Interobserver LV and LAV measurement reproducibility using the automated 3DE model program with contour adjustment was performed in 30 patients. Two investigators independently analyzed the same 3DE loops. These investigators were blinded to each other's results and all other previous measurements.

Intraobserver and interobserver variability for the 3D manual measurements was assessed in 94 patients. Two investigators measured the same 3DE loops, and 1 of the investigators repeated the analysis 4 weeks later.

Intraobserver variability of CMR-derived LA and LV volume measurements were assessed in a subgroup of 15 patients. CMR images were re-analyzed using the same method at least 4 weeks after the initial analysis.

EXAMINATION LENGTH ANALYSIS. One reader recorded the time required to manually measure LVEDV, LVESV, LVEF, and LAV at LVES from 30 3DE-datasets. The timer was paused when the reader switched between images and was restarted with re-initiation of further measurements. One week later, the same reader recorded the time required to repeat the analysis using the 3DE-model automated program without contour adjustment; after another week, the reader recorded the time needed when using the 3DE-model automated program with contour adjustment.

STATISTICAL ANALYSIS. The automated 3DE-derived values of LVEDV, LVESV, LVEF, and LAV were compared with the corresponding manual 3D TTE or CMR reference values using linear regression with Pearson correlation coefficients and Bland-Altman analysis to assess the bias and limits of agreement. Biases and SDs between automated and manual 3DE or CMR LVEDV, LVESV, and LVEF were also obtained for the following subgroups: 1) reference LVEF ≥50%, reference LVEF <50% due to global reduction, and reference LVEF <50% due to regional wall motion abnormalities; and 2) volume rate <15 Hz and ≥15 Hz. To verify the significance of the biases, paired Student *t* tests were performed. Values of $p < 0.05$ were considered significant. Measurement variability was expressed as the absolute difference of the corresponding pair of repeated measurements in percentage of their mean in each patient and then averaged over the entire study group.

RESULTS

Baseline characteristics are presented in Table 1. The average 3DE volume rate was 16 ± 6 Hz (median 15 Hz; interquartile range: 11 to 21 Hz). Twelve (8%) datasets had a volume rate <10 Hz.

3DE MODEL VERSUS MANUAL MEASUREMENTS. There was good correlation between the automated 3DE model and the manual 3DE measurements of LVEDV, LVESV, LVEF, and LAV (Table 2). The automated 3DE model LVESV and LAV measurements without contour adjustment were larger than the averaged manual 3DE measurements (Figure 2). However, LVEF measured using the automated 3DE program without contour adjustment had a small negative bias compared with the manual 3DE values.

TABLE 1 Baseline Demographic Characteristics

	Protocol 1 (n = 94)	Protocol 2 (n = 65)
Age, yrs	57 ± 19	50 ± 17
Female	50 (53)	34 (52)
Race		
White	18 (19)	34 (52)
Non-white	76 (81)	31 (48)
BSA, m^2	1.8 ± 0.2	1.9 ± 0.2
3D manual LVEF, %	41 ± 18	–
LVEF <50%	56 (60)	–
Ischemic	23 (41)	–
Nonischemic	33 (59)	–

Values are mean ± SD or n (%). Protocol 1 is a comparison against a manual 3DE reference standard. Protocol 2 is a comparison against a CMR reference standard.

3D = 3-dimensional; 3DE = 3-dimensional echocardiography; BSA = body surface area; CMR = cardiac magnetic resonance; LVEF = left ventricular ejection fraction.

TABLE 2 3DE Model Comparison Versus Manual 3D Measurements

	Averaged Automated 3DE Program	Averaged Manual 3DE Reference Standard	Correlation	Bias	LOA (2 SDs)
LVEF, %					
No contour adjustment	40 ± 16	46 ± 16*	0.87	-6	16
With contour adjustment	42 ± 16	46 ± 16*	0.92	-4	12
LVEDV, ml					
No contour adjustment	163 ± 73	161 ± 71	0.96	2	40
With contour adjustment	173 ± 75	161 ± 71*	0.97	12	36
LVESV, ml					
No contour adjustment	105 ± 67	95 ± 66*	0.95	10	40
With contour adjustment	108 ± 70	95 ± 66*	0.96	13	36
LAV at LVES, ml					
No contour adjustment	85 ± 34	76 ± 31*	0.95	10	20
With contour adjustment	93 ± 37	76 ± 31*	0.96	17	24

Values are mean ± SD. *p < 0.001 compared with automated 3DE program.

LAV = left atrial volume; LOA = limits of agreement; LVEDV = left ventricular end-diastolic volume; LVES = left ventricular end-systole; LVESV = left ventricular end-systolic volume; other abbreviations as in Table 1.

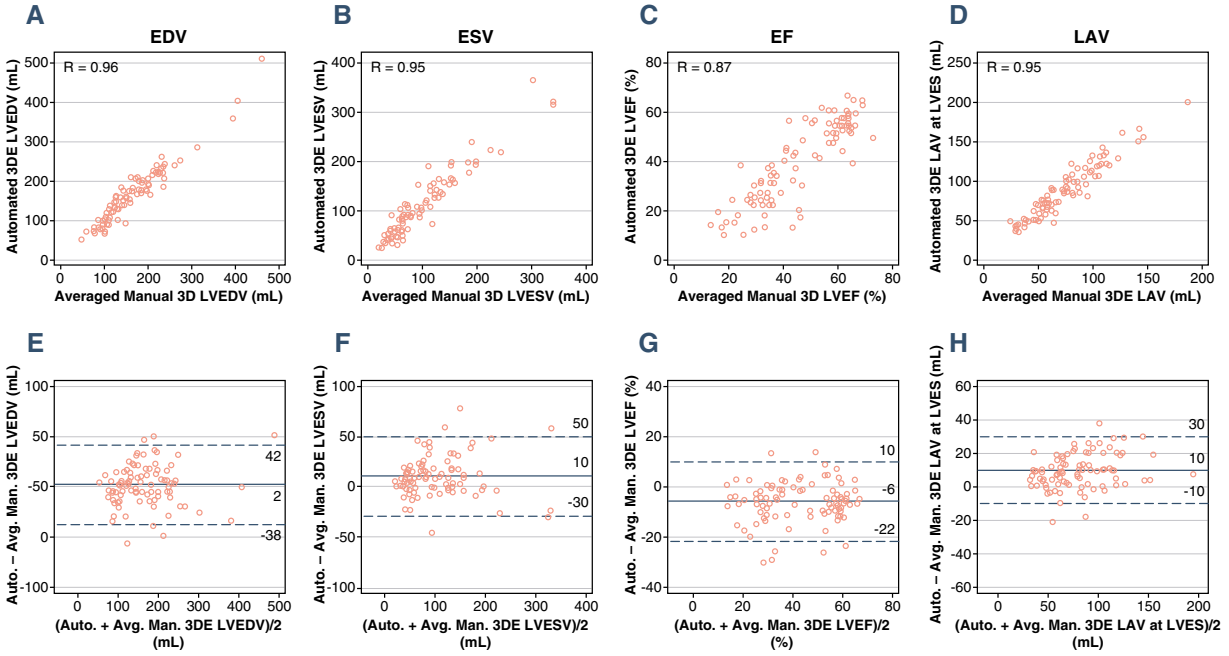
With contour adjustment, the LVEF inter-technique bias was reduced but not eliminated (Table 2, Figure 3). In contrast, LVEDV and LVESV measurements were overestimated. Overall, alteration of the contours minimally altered LV volumes. The average differences between the automated measurements with and without contour adjustments were as follows: LVEDV, 10 ± 5 ml; LVESV, 3 ± 6 ml; LVEF, 2 ± 3%; and LAV, 8 ± 4 ml. In addition, the absolute difference between observers was small. The average difference in final adjusted volumes between observers was as follows: LVEDV, -5 ± 6 ml; LVESV, -2 ± 6 ml; LVEF, -1 ± 3%; and LAV, -2 ± 6 ml. Due to this small difference, only a single observer was used to obtain automated program measurements with contour adjustment when compared with the CMR reference.

Repeating the analysis, while accounting for LVEF and regional wall motion abnormalities, we found no differences in the LVEF bias or limits of agreement with or without contour adjustment (Table 3). For LVEDV and LVESV, the bias and limits of agreement were largest in patients with reduced LVEF and regional wall motion abnormalities when contour adjustment was performed.

When the impact of 3DE volume rate was assessed, no significant changes in LVEF bias or limits of agreement were found, regardless of whether contour adjustment was performed (Table 4). Biases and limits of agreement were larger for LV volumes obtained from patients with volume rates <15 Hz.

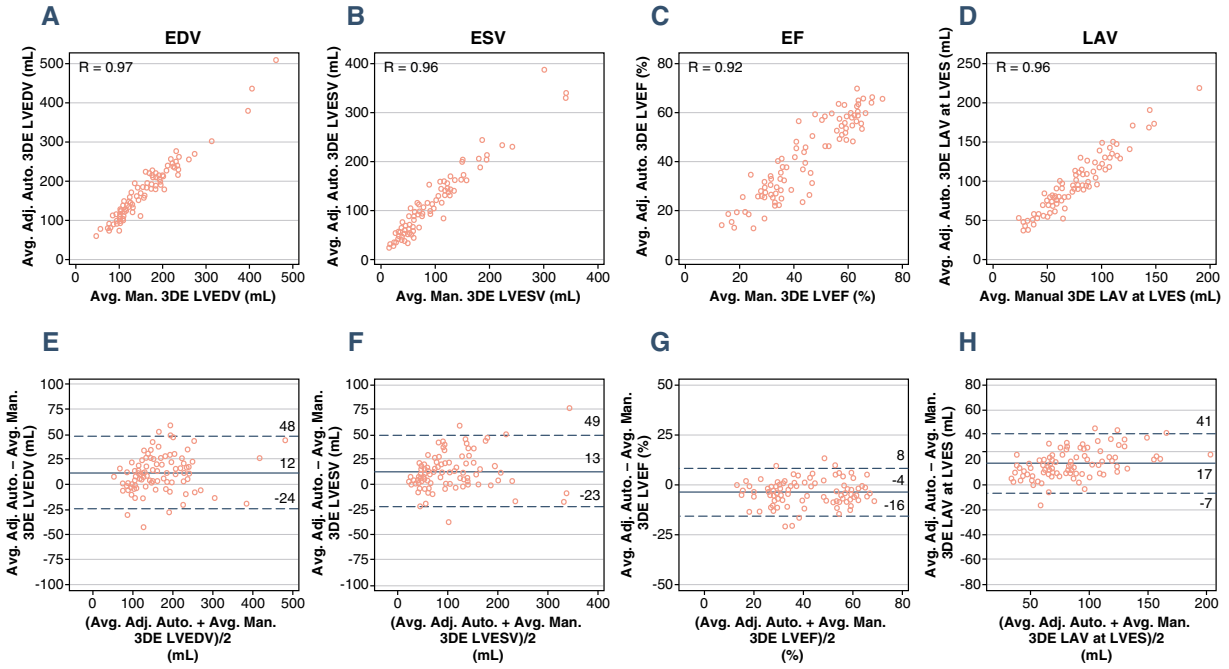
CMR MODEL VERSUS CMR. Overall, there was strong correlation between the automated 3DE CMR model

FIGURE 2 Validation of the Automated 3DE Model Without Contour Adjustment Against Averaged Manual Measurements



Correlation and Bland-Altman analysis of **(A, E)** left ventricular end-diastolic volume (LVEDV), **(B, F)** left ventricular end-systolic volume (LVESV), **(C, G)** left ventricular ejection fraction (LVEF), and **(D, H)** left atrial volume (LAV) at left ventricular end-systole (LVES). 3DE = 3-dimensional echocardiography; Auto. = automated; Avg. = averaged; Man. = manual.

FIGURE 3 Validation of the Automated 3DE Model With Contour Adjustment Against Averaged Manual Measurements



Correlation and Bland-Altman analysis of averaged **(A, E)** LVEDV, **(B, F)** LVESV, **(C, G)** LVEF, and **(D, H)** LAV. Adj. = adjusted; other abbreviations as in Figure 2.

without contour adjustment and CMR-derived measurements (Table 5, Figure 4). Compared with CMR values, LVEF measured using the automated 3DE CMR model program without contour adjustment had a negligible bias, and there was no significant difference between LVEF values obtained by these 2 imaging modalities. For volume measurements, LVEDV, LVESV, and LAV obtained by the automated 3DE CMR model program without contour adjustment were smaller than those obtained by CMR. However, LVEDV, LVESV, and LAV obtained by the automated 3DE CMR model program without contour adjustment were larger than those obtained by manual measurements.

With contour adjustment of the automated 3DE CMR model values, the bias for LVEF compared with CMR remained at -2% (Table 5, Figure 5). However, the biases for LVEDV and LVESV were both reduced. LVEDV remained significantly smaller than CMR values, but no difference between the automated 3DE CMR model and CMR LVESV were found.

When the averaged 3DE manual measurements were compared versus the CMR values, good correlations were found (Table 5, Figure 6). However, the 3D manual measurements resulted in significantly smaller LVEDV, LVESV, and LAV compared with CMR, reflected by a negative bias that was larger than with the automated program (CMR model) with and without contour adjustment. When the analysis was repeated by dividing the study group according to LVEF and the presence of regional wall motion abnormalities, LV volume biases and limits of agreement with or without contour adjustment were largest in those with reduced LVEF (Table 6).

When the impact of volume rate was again assessed, there was no significant effect on the measured biases (Table 7). However, limits of agreement were larger for LV volumes from patients with volume rates ≥15 Hz regardless of whether contour adjustments were performed.

REPRODUCIBILITY. Reproducibility results are presented in Table 8. Measurement variability of the automated 3DE model for the same 3DE datasets that were initially analyzed was 0 ± 0% for all parameters. Test-retest variability of the automated program by using a different dataset was higher but did not change significantly whether contour adjustment was performed. The interobserver coefficient of variation when using the automated program with contour adjustment on the same dataset was similar to the test-retest values with contour adjustment. Intraobserver and interobserver variability for the 3D manual measurements was greater than automated values with or without contour adjustment. Lastly, CMR intraobserver variability was low.

TABLE 3 Effect of Wall Motion and Ejection Fraction on Measurements From the 3DE Model Compared With Manual 3DE Measurements

	N	Averaged Automated 3DE Program	Averaged Manual 3DE Reference Standard	Bias	LOA (2 SDs)
LVEF, %					
No contour adjustment					
LVEF >50%	42	54 ± 6	61 ± 5*	-7	14
LVEF <50%, global reduction	34	28 ± 13	34 ± 10†	-5	20
LVEF <50%, regional wall motion	18	26 ± 8	32 ± 7†	-6	12
With contour adjustment					
LVEF >50%	42	57 ± 6	61 ± 5*	-5	10
LVEF <50%, global reduction	34	31 ± 12	34 ± 10†	-3	16
LVEF <50%, regional wall motion	18	28 ± 7	32 ± 7†	-4	12
LVEDV, ml					
No contour adjustment					
LVEF >50%	42	125 ± 43	120 ± 35	4	34
LVEF <50%, global reduction	34	194 ± 92	197 ± 87	-3	44
LVEF <50%, regional wall motion	18	194 ± 42	190 ± 49	4	44
With contour adjustment					
LVEF >50%	42	133 ± 45	120 ± 35*	12	34
LVEF <50%, global reduction	34	206 ± 92	197 ± 87†	10	38
LVEF <50%, regional wall motion	18	206 ± 44	190 ± 49†	16	42
LVESV, ml					
No contour adjustment					
LVEF >50%	42	57 ± 23	47 ± 16*	10	26
LVEF <50%, global reduction	34	143 ± 78	135 ± 76	9	52
LVEF <50%, regional wall motion	18	144 ± 39	130 ± 44†	14	44
With contour adjustment					
LVEF >50%	42	58 ± 23	47 ± 16*	11	26
LVEF <50%, global reduction	34	148 ± 81	135 ± 76†	13	46
LVEF <50%, regional wall motion	18	149 ± 41	130 ± 44†	19	40

Values are mean ± SD. *$p < 0.001$ compared with automated 3DE program. †$p < 0.05$ compared with automated 3DE program.

Abbreviations as in Tables 1 and 2.

EXAMINATION DURATION. The use of the automated 3DE model program without contour adjustment significantly reduced the average time per patient compared with manual analysis ($p < 0.0001$) (Figure 7). When contour adjustment was performed with the automated program, the time required per patient increased significantly compared with the automated analysis without contour adjustment ($p < 0.0001$) but was still significantly shorter than using manual analysis ($p < 0.0001$).

DISCUSSION

The present study showed that automated chamber quantification analysis can provide accurate, simultaneous measurements of LVEDV, LVESV, LVEF, and LAV. The use of this prototype program resulted in

TABLE 4 Effect of Volume Rate on Measurements From the 3DE Model Compared With Manual 3DE Measurements

	N	Averaged Automated 3DE Program	Averaged Manual 3DE Reference Standard	Bias	LOA (2 SDs)
LVEF, %					
No contour adjustment					
Volume rate <15 Hz	41	31 ± 15	38 ± 14*	-7	20
Volume rate ≥15 Hz	53	46 ± 14	51 ± 14*	-6	12
With contour adjustment					
Volume rate <15 Hz	41	34 ± 14	38 ± 14*	-4	14
Volume rate ≥15 Hz	53	48 ± 14	51 ± 14*	-4	12
LVEDV, ml					
No contour adjustment					
Volume rate <15 Hz	41	193 ± 89	194 ± 85	-1	46
Volume rate ≥15 Hz	53	139 ± 46	136 ± 45	3	38
With contour adjustment					
Volume rate <15 Hz	41	206 ± 90	194 ± 85*	12	40
Volume rate ≥15 Hz	53	148 ± 48	136 ± 45*	12	34
LVESV, ml					
No contour adjustment					
Volume rate <15 Hz	41	138 ± 77	126 ± 77*	12	50
Volume rate ≥15 Hz	53	79 ± 44	70 ± 42*	9	30
With contour adjustment					
Volume rate <15 Hz	41	142 ± 80	126 ± 77*	16	46
Volume rate ≥15 Hz	53	82 ± 46	70 ± 42*	11	28
LAV at LVES, ml					
No contour adjustment					
Volume rate <15 Hz	41	102 ± 32	92 ± 32*	10	20
Volume rate ≥15 Hz	53	72 ± 29	62 ± 24*	9	20
With contour adjustment					
Volume rate <15 Hz	41	112 ± 36	92 ± 32*	19	22
Volume rate ≥15 Hz	53	78 ± 31	62 ± 24*	16	24

Values are mean ± SD. *$p < 0.001$ compared with automated 3DE program.
Abbreviations as in Tables 1 and 2.

reproducible values, and it reduced the duration of the examination. Overall, this program provides larger volumes than manual measurements, slightly smaller values than CMR without contour adjustment, and similar values to CMR after contour adjustment.

SOFTWARE DEVELOPMENT RATIONALE. CMR is currently considered the gold standard in evaluating cardiac chamber volumes. However, in clinical practice when 3DE data are analyzed, the results reflect the 3DE data under study, not CMR values. We therefore developed a 3DE model based on 3DE tracings and compared it with a 3DE manual reference standard. We also studied a CMR model that is a CMR-tuned version because if automated analysis becomes integrated into practice, measurements should be comparable to the CMR gold standard. Ideally, patients could have their cardiac chambers evaluated using any imaging modality and have comparable results between modalities. Potentially, this approach would allow for a single set of cutoff reference values regardless of the imaging modality used.

The automated software uses a unique adaptive analytics algorithm that works in 3 stages. First, knowledge-based identification is used, in which an echocardiographic atlas of cardiac chamber shapes is screened and, based on the overall morphological size, shape, curvature, and volume of the 3DE data under study, the best "matching" shapes are selected. Second, patient-specific adaptation occurs using scaling and affine transformation until the best border is achieved that is consistent with the chosen shape and the echo data under analysis. This stage combines knowledge of ultrasound beam-forming behaviors with computer vision processing of the anatomical targets to adapt the model to the patient's data. Third, a confidence engine examines border signal strength and overall fit to determine algorithm confidence in the final model. Finally, an editing tool is provided that allows not only regional but global editing.

AUTOMATED LV ANALYSIS. Compared with previous studies (8–10), the software used in the present study does not require any input once the 3D TTE dataset has loaded to automatically perform the measurements. Previously studied algorithms required the investigators to review the LV endocardial contours for 3 to 5 cardiac cycles before recording values from the "best cycle" and the application of fixed correction factors to improve the accuracy compared with CMR results (9).

Beyond simplicity of use, automated LVEF measurement with this software was accurate compared with CMR and similar to publications using semi-automated LV software (9,11). LV volume measurements using this program were similar to CMR measurements for LVESV but slightly underestimated for LVEDV. The LVEDV and LVESV biases using the automated CMR model without contour adjustment are on the smaller side of those reported for semi-automated programs. These biases range from -18 to -67 ml and -8 to -41 ml for LVEDV and LVESV, respectively (1,8,9). One reason for this consistent underestimation is the poor differentiation between the compacted myocardium and trabeculae on TTE, especially during systole, that results in less precise endocardial border identification compared with CMR (1,2,12,13).

With contour adjustment, the automated CMR model program's LVEDV and LVESV biases from the present study were smaller than in previous publications. This outcome results from algorithmic adjustments that account for the relationship between 3DE and CMR contours, which is further

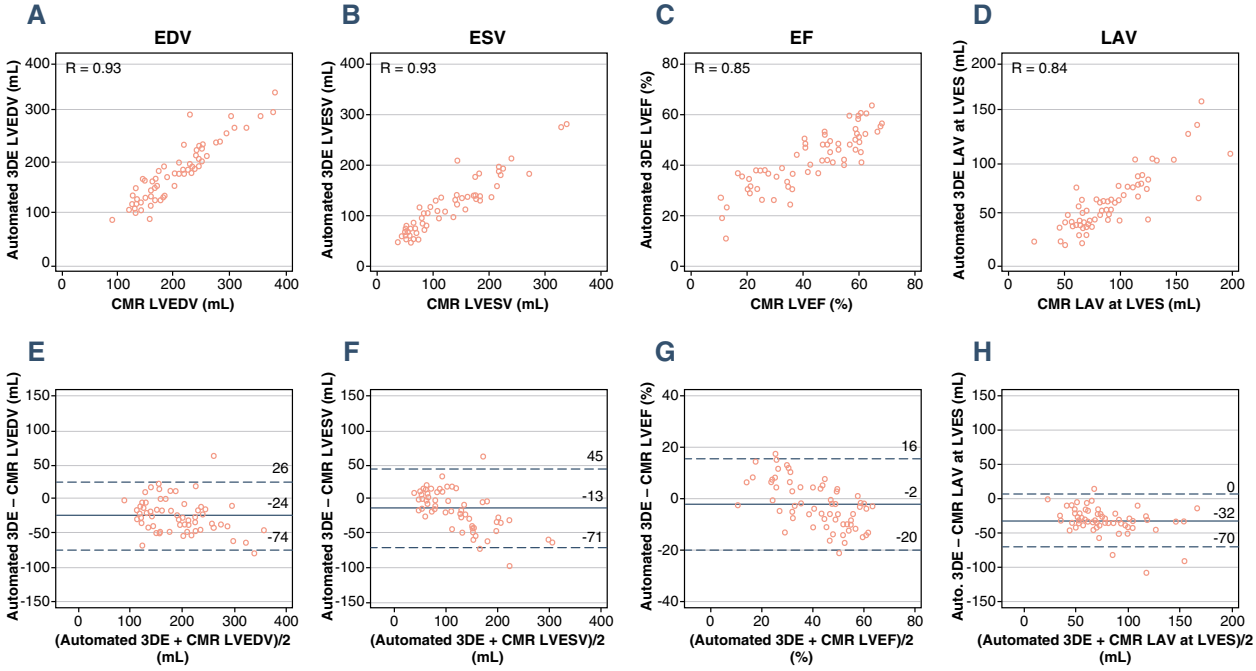
TABLE 5 3DE-Derived CMR Model Comparison Versus CMR Measurements

	Parameter	CMR Reference Standard	Correlation With CMR	Bias With CMR	LOA (2 SDs)
LVEF, %					
Averaged manual 3DE	45 ± 13	43 ± 16	0.89	2	16
Automated program with no contour adjustment	41 ± 11	43 ± 16	0.85	−2	18
Automated program with contour adjustment	41 ± 12	43 ± 16	0.91	−2	16
LVEDV, ml					
Averaged manual 3DE	146 ± 53	201 ± 66*	0.95	−54	46
Automated program with no contour adjustment	177 ± 58	201 ± 66*	0.93	−24	50
Automated program with contour adjustment	190 ± 64	201 ± 66*	0.95	−10	44
LVESV, ml					
Averaged manual 3DE	85 ± 49	122 ± 71*	0.96	−37	56
Automated program with no contour adjustment	108 ± 53	122 ± 71*	0.93	−13	58
Automated program with contour adjustment	118 ± 60	122 ± 71	0.95	−4	46
LAV at LVES, ml					
Averaged manual 3DE	61 ± 26	94 ± 35*	0.80	−33	42
Automated program with no contour adjustment	61 ± 28	94 ± 35*	0.84	−32	38
Automated program with contour adjustment	83 ± 34	94 ± 35*	0.88	−10	34

Values are mean ± SD. *$p < 0.001$ compared with automated 3DE program.
Abbreviations as in Tables 1 and 2.

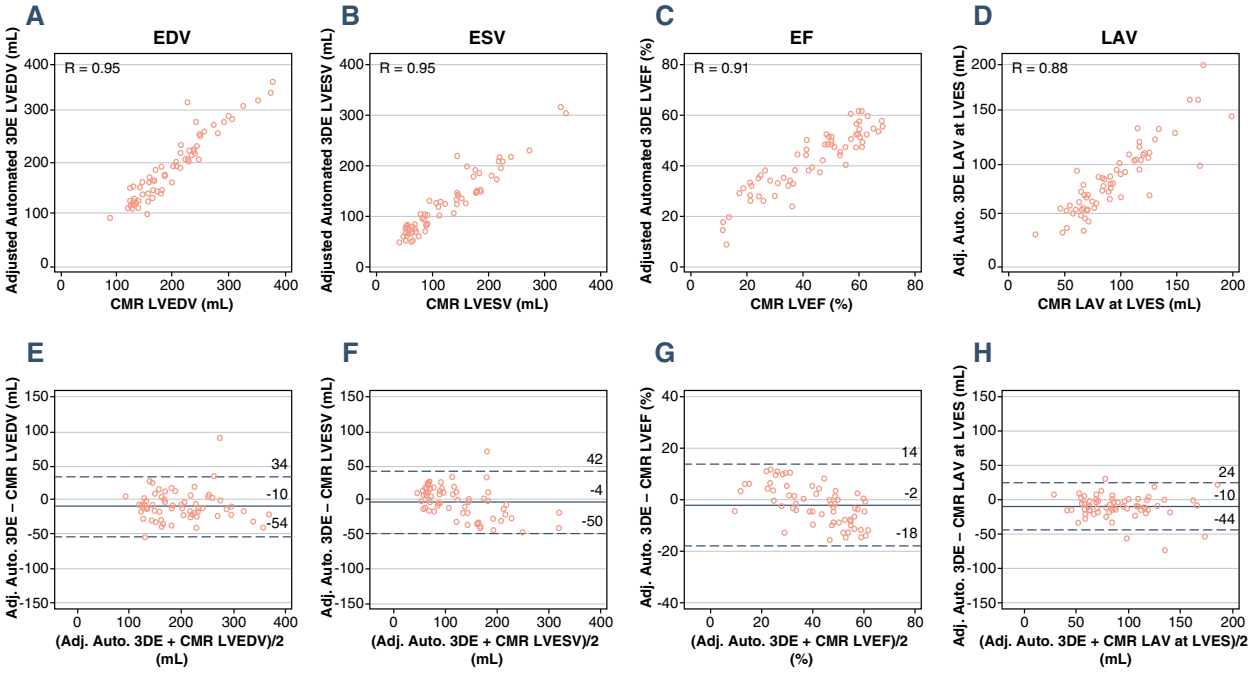
improved when the 3DE contours are perfected. This approach differs from previous solutions used by other investigators to address the underestimation of 3DE volumes. They automatically added a variety of different fixed end-systolic volume and end-diastolic volume values to the tracked border to "artificially" enlarge the final volumes (9). Although this approach results in smaller biases compared

FIGURE 4 Validation of the Automated CMR Model Without Contour Adjustment Against CMR



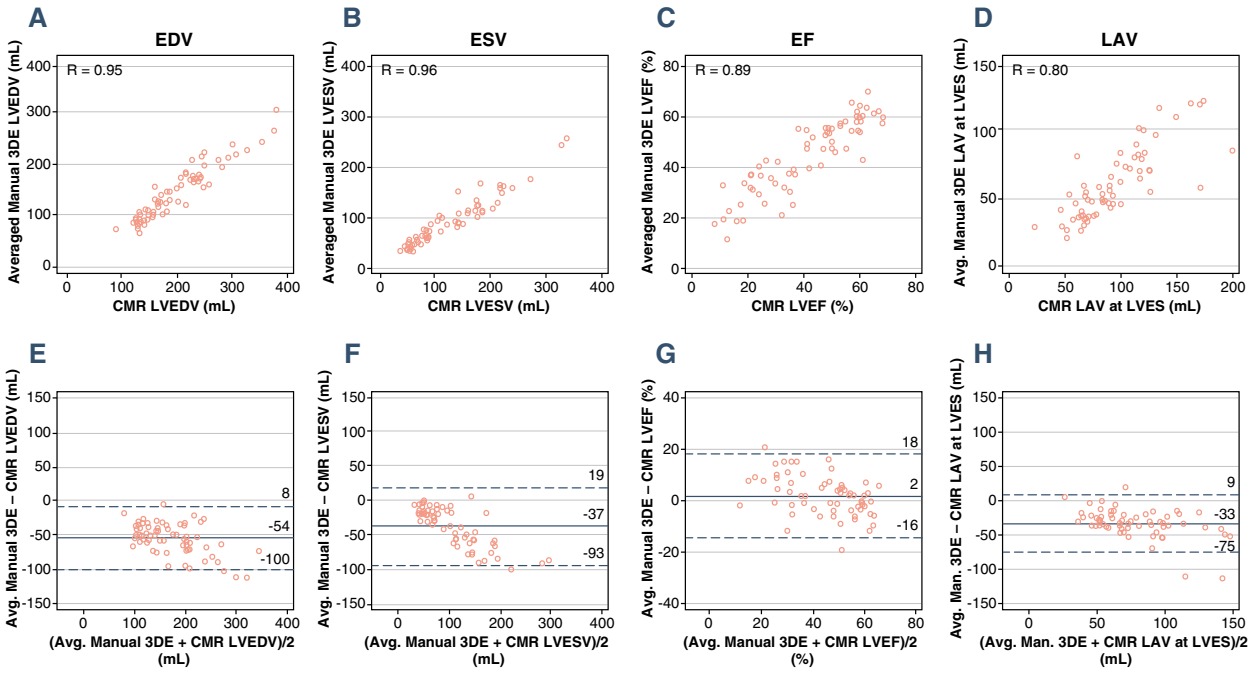
Correlation and Bland-Altman analysis of **(A, E)** LVEDV, **(B, F)** LVESV, **(C, G)** LVEF, and **(D, H)** LAV. CMR = cardiac magnetic resonance; other abbreviations as in Figure 2.

FIGURE 5 Validation of the Automated CMR Model With Contour Adjustment Against CMR



Correlation and Bland-Altman analysis of **(A, E)** LVEDV, **(B, F)** LVESV, **(C, G)** LVEF, and **(D, H)** LAV. Abbreviations as in Figures 2 and 4.

FIGURE 6 Manual 3DE Measurements Compared With CMR



Correlation and Bland-Altman analysis of **(A, E)** LVEDV, **(B, F)** LVESV, **(C, G)** LVEF, and **(D, H)** LAV. Abbreviations as in Figures 2 and 4.

TABLE 6 Effect of Wall Motion and Ejection Fraction on Measurements From the 3DE-Derived CMR Model Compared With CMR Measurements

	N	Parameter	CMR Reference Standard	Bias With CMR	LOA (2 SDs)
LVEF, %					
Automated program with no contour adjustment					
LVEF >50%	28	50 ± 6	59 ± 5*	-9	10
LVEF <50%, global reduction	22	34 ± 10	32 ± 12	2	14
LVEF <50%, regional wall motion	15	36 ± 9	32 ± 12	4	16
Automated program with contour adjustment					
LVEF >50%	28	51 ± 5	59 ± 5*	-8	10
LVEF <50%, global reduction	22	34 ± 10	32 ± 12	2	12
LVEF <50%, regional wall motion	15	34 ± 11	32 ± 12	2	14
LVEDV, ml					
Automated program with no contour adjustment					
LVEF >50%	28	135 ± 34	154 ± 34*	-18	44
LVEF <50%, global reduction	22	212 ± 64	240 ± 72*	-27	54
LVEF <50%, regional wall motion	15	201 ± 37	231 ± 43*	-30	50
Automated program with contour adjustment					
LVEF >50%	28	146 ± 37	154 ± 34†	-8	38
LVEF <50%, global reduction	22	226 ± 72	240 ± 72†	-14	50
LVEF <50%, regional wall motion	15	221 ± 47	231 ± 43	-10	42
LVESV, ml					
Automated program with no contour adjustment					
LVEF >50%	28	69 ± 19	63 ± 16†	6	26
LVEF <50%, global reduction	22	146 ± 60	169 ± 74†	-24	60
LVEF <50%, regional wall motion	15	129 ± 32	162 ± 49*	-33	58
Automated program with contour adjustment					
LVEF >50%	28	72 ± 20	63 ± 16*	9	24
LVEF <50%, global reduction	22	155 ± 67	169 ± 74†	-13	50
LVEF <50%, regional wall motion	15	148 ± 42	163 ± 49†	-15	44

Values are mean ± SD. *$p < 0.001$ compared with automated 3DE program. †$p < 0.05$ compared with automated 3DE program.
Abbreviations as in Tables 1 and 2.

with CMR values, identification of the different correction values were determined with knowledge of the CMR values post hoc. Also, different correction values were required for patients with normal LVEF versus those with LVEF <50% and for end-systolic versus end-diastolic measurements. Given that the correction factors varied from 0.5 to 1.0 mm, and it has been shown that changes of 1 mm to the endocardial border can result in an 11% change in measured volumes, prospective studies are required to validate this approach (1). It remains to be proven whether this method could address inaccurate measurements due to regional dilation rather than trabecular tracking. The algorithmic approach used here addresses inaccurate measurements due to suboptimal identification of compacted versus noncompacted myocardium and difficulties with regional dilation.

PROGRAM REPRODUCIBILITY. Reproducibility of LV volumes was excellent with the automated program, as interobserver variability in our study was zero (1). This finding has significant clinical implications because it has been shown that 3D TTE LV volumes have the greatest reproducibility during follow-up (14). Thus, in echocardiographic laboratories with multiple readers, use of this program could potentially reduce reader measurement variability, allowing true changes in LV volume to be detected.

LAV MEASUREMENTS. Recent guidelines have highlighted the importance of routinely measuring and reporting LAV (5). The study program is the first automated technique designed to quantify LAV from 3DE datasets. We found that the automated LAV values from the 3DE model were slightly larger than those obtained with manual measurements. However, with the CMR model, automated program measurements were similar to manual measurements but smaller than CMR measurements. This finding is consistent with reported biases ranging from 0 to -23 ml (3,15,16) and may be related to differences in

TABLE 7 Effect of Volume Rate on Measurements From the 3DE-Derived CMR Model Compared With CMR Measurements

	N	Parameter	CMR Reference Standard	Bias With CMR	LOA (2 SDs)
LVEF, %					
Automated program with no contour adjustment					
Volume rate <15 Hz	25	40 ± 13	43 ± 18	−3	18
Volume rate ≥15 Hz	40	42 ± 10	44 ± 15	−2	20
Automated program with contour adjustment					
Volume rate <15 Hz	25	40 ± 13	43 ± 67	−3	14
Volume rate ≥15 Hz	40	42 ± 11	44 ± 15	−2	16
LVEDV, ml					
Automated program with no contour adjustment					
Volume rate <15 Hz	25	190 ± 67	215 ± 81*	−24	46
Volume rate ≥15 Hz	40	168 ± 52	192 ± 53*	−24	52
Automated program with contour adjustment					
Volume rate <15 Hz	25	202 ± 73	215 ± 81*	−13	32
Volume rate ≥15 Hz	40	183 ± 60	192 ± 53†	−9	48
LVESV, ml					
Automated program with no contour adjustment					
Volume rate <15 Hz	25	121 ± 66	134 ± 89†	−13	52
Volume rate ≥15 Hz	40	100 ± 42	114 ± 58†	−14	62
Automated program with contour adjustment					
Volume rate <15 Hz	25	129 ± 74	134 ± 89	−5	40
Volume rate ≥15 Hz	40	111 ± 50	114 ± 58	−4	50
LAV at LVES, ml					
Automated program with no contour adjustment					
Volume rate <15 Hz	25	65 ± 28	98 ± 37*	−33	32
Volume rate ≥15 Hz	40	59 ± 29	91 ± 34*	−32	42
Automated program with contour adjustment					
Volume rate <15 Hz	25	89 ± 32	98 ± 37†	−9	26
Volume rate ≥15 Hz	40	80 ± 34	91 ± 34*	−12	38

Values are mean ± SD. *$p < 0.001$ compared with automated 3DE program. †$p < 0.05$ compared with automated 3DE program.
Abbreviations as in Tables 1 and 2.

spatial resolution between imaging techniques (16). However, one confounding factor in relating these biases to the current results is that previous studies used 3DE software designed to measure LV volumes. Geometric assumptions needed to obtain LV volumes introduce inaccuracies when applied to the left atrium. LAV reproducibility was better than previously published interobserver variability (3). This finding is important, as poor reproducibility would adversely impact the clinical use of LAV.

CLINICAL IMPACT. In this study, the use of automated analysis software significantly reduced the time required to obtain LVEF, LVEDV, LVESV, and LAV. This outcome is important: in a clinical laboratory in which 40 echocardiographic studies are interpreted per day, if on average it requires 140 s to

TABLE 8 Reproducibility

	Automated 3DE Program Variability Without Contour Adjustment	Automated 3DE Program Test-Retest Without Contour Adjustment	Automated 3DE Program Test-Retest With Contour Adjustment	Automated 3DE Program Interobserver With Contour Adjustment	Intraobserver 3D Manual	Interobserver 3D Manual	Intraobserver CMR
LVEDV	0 ± 0%	6 ± 6%	5 ± 5%	9 ± 4%	10 ± 4%	15 ± 12%	4 ± 6%
LVESV	0 ± 0%	8 ± 7%	9 ± 9%	10 ± 4%	12 ± 4%	18 ± 18%	8 ± 8%
LVEF	0 ± 0%	8 ± 9%	8 ± 8%	9 ± 6%	11 ± 12%	21 ± 18%	8 ± 7%
LAV at LVES	0 ± 0%	12 ± 14%	5 ± 8%	8 ± 8%	8 ± 4%	17 ± 16%	3 ± 3%

Values are mean ± SD.
Abbreviations as in Tables 1 and 2.

measure these data from one 2DE study, then in 1 day, >90 min are spent performing these measurements. With the use of this automated program, this time is decreased to 10 min per day with the added benefit of enhanced accuracy and reproducibility. Ultimately, with future advances, which will allow acquisition of larger 3DE pyramidal data with higher volume rates, this software would aim to simultaneously quantify both the LA and right atrial and ventricular chambers.

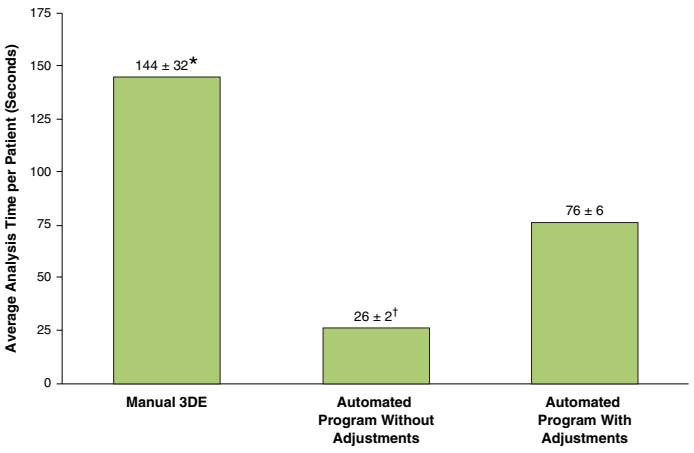
STUDY LIMITATIONS. First, only patients in sinus rhythm were studied. These results cannot be extrapolated to patients with irregular rhythms. Second, automated detection of LVES depends on 3D volume rate. For patients with dilated cardiomyopathy, to fit the entire left ventricle into a single pyramidal volume, a large sector is needed, which reduces the 3D volume rate. This limitation can now be overcome with the development of improved acquisition algorithms that allow faster sampling with large acquisition sectors; this option was not available during the present study. Third, although the initial analysis was automated, upon visual inspection, a number of patients required regional adjustment of the generated endocardial contours. Although this method did not greatly change the volumes, it affects the largely automated nature of the program. Fourth, patients were excluded if there was poor endocardial visualization. Thus, the accuracy of the algorithm in subjects with poor image quality cannot be determined. Also, the use of echocardiographic contrast agents with this algorithm was not tested.

Lastly, although these findings were smaller than biases reported in the published data (8-10), the unadjusted program still underestimated LA and LV volumes compared with CMR. However, this bias was significantly reduced with the use of contour adjustment. Thus, although this program is extremely promising, limitations remain with respect to its use without contour adjustment. This aspect of the program is expected to improve with continued development of the algorithm.

CONCLUSIONS

This study is the first to demonstrate that automated software which simultaneously measures LA and LV volumes and LVEF from 3DE data with and without manual input is highly feasible, reproducible, and rapid. Because one of the core functions of the echocardiographic laboratory is to assess LV and LA volumes, this program is the logical next step required to integrate 3DE measurements into clinical practice.

FIGURE 7 LA and LV 3DE Analysis Time



3D transthoracic echocardiography (TTE) LA and LV analysis time using the manual method and the automated method with and without contour adjustment. Left atrial and ventricular acquisition and timing. *p < 0.0001 compared with 3D automated program with and without adjustments. †p < 0.0001 compared with 3D automated program with adjustments. Abbreviations as in Figures 1 and 2.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Societal guidelines recommend measurement of LA volumes, LV volumes, and LVEF by using 3D TTE. The use of this automated program to acquire these parameters is not only feasible in clinical practice but improves accuracy and reproducibility while saving time.

TRANSLATIONAL OUTLOOK: Studies on the automation of the 3DE measurements have only been validated in single-center studies. Large multicenter studies with a variety of readers are required to test the true robustness of these automated algorithms.

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