Imaging and Diagnostic Testing

Clinical utility of automated assessment of left ventricular ejection fraction using artificial intelligence–assisted border detection

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Background Ejection fraction (EF) calculated from 2-dimensional echocardiography provides important prognostic and therapeutic information in patients with heart disease. However, quantification of EF requires planimetry and is time-consuming. As a result, visual assessment is frequently used but is subjective and requires extensive experience. New computer software to assess EF automatically is now available and could be used routinely in busy digital laboratories (>15 000 studies per year) and in core laboratories running large clinical trials.
We tested Siemens AutoEF software (Siemens Medical Solutions, Erlangen, Germany) to determine whether it correlated with visual estimates of EF, manual planimetry, and cardiac magnetic resonance (CMR).

Methods Siemens AutoEF is based on learned patterns and artificial intelligence. An expert and a novice reader assessed EF visually by reviewing transthoracic echocardiograms from consecutive patients. An experienced sonographer quantified EF in all studies using Simpson's method of disks. AutoEF results were compared to CMR.

Results Ninety-two echocardiograms were analyzed. Visual assessment by the expert (R = 0.86) and the novice reader (R = 0.80) correlated more closely with manual planimetry using Simpson's method than did AutoEF (R = 0.64). The correlation between AutoEF and CMR was 0.63, 0.28, and 0.51 for EF, end-diastolic and end-systolic volumes, respectively.

Conclusion The discrepancies in EF estimates between AutoEF and manual tracing using Simpson's method and between AutoEF and CMR preclude routine clinical use of AutoEF until it has been validated in a number of large, busy echocardiographic laboratories. Visual assessment of EF, with its strong correlation with quantitative EF, underscores its continued clinical utility. (Am Heart J 2008;155:562-70.)

Left ventricular (LV) ejection fraction (LVEF) is an important clinical metric that predicts prognosis of patients with a wide variety of cardiac diseases. In contemporary cardiology practice, clinical decision making involving defibrillator implantation, biventricular pacing for the treatment of congestive heart failure, and access to clinical trials for novel therapies is largely based on ejection fraction (EF). Accordingly, it is important that this index be estimated accurately, reproducibly, and in a timely fashion.

Ejection fraction can be assessed by cardiac magnetic resonance (CMR), cardiac computed tomography, nuclear scintigraphy, contrast ventriculography, and real-time 3-dimensional echocardiography. However, in clinical practice, EF is most frequently assessed by transthoracic 2-dimensional echocardiography because of its availability. Two echocardiographic methods are used to assess LVEF. The first is visual estimation of EF that requires substantial expertise. The second method requires manual tracing of the endocardial contours of the apical 4-chamber and/or the apical 2-chamber views to obtain biplane LV volumes from which EF is calculated. This method is time-consuming and requires expertise to identify endocardial boundaries accurately.

Previous attempts to semiautomate assessment of EF have been confounded by difficulties with endocardial tracking throughout the cardiac cycle because of extreme gain dependence.[1-8] A new biologic application of artificial intelligence based on pattern recognition and database-guided segmentation has become available (AutoEF) that may allow accurate

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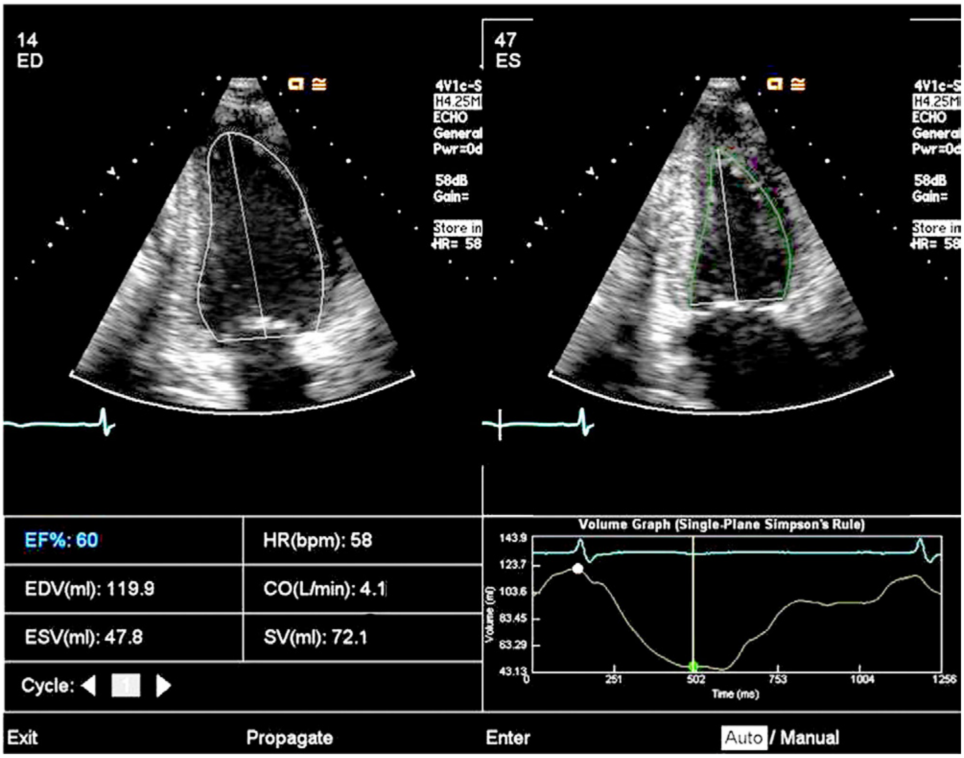
Figure 1



AutoEF output. Representative computer output of AutoEF and instantaneous LV volume.

Table I. Baseline patient characteristics

	Included patients (n = 92)	Excluded patients (n = 19)	All patients (n = 111)
Age (y)	64 ± 16	61 ± 17	63 ± 16
Male	53 (57%)	12 (63%)	65 (58.5%)
BMI (kg/m^2) (n = 70)	27.8± 6.1	30.1± 6.8	28.2± 6.2
Ischemia	17 (18%)	2 (10.5%)	19 (17.1%)
Left ventricular hypertrophy	14 (15%)	5 (26.3%)	19 (17.1%)
Severe right ventricular dilatation	1	0	1
Mitral prosthesis	3	0	3
LV aneurysm	0	0	0

BMI, Body mass index.
Values are mean ± 1SD (range) or number of patients unless otherwise indicated.

Table II. Left ventricular volumes and ejection fraction by manual tracing, expert visual estimation, and AutoEF (n = 92)

	Manual tracing	Expert visual estimation	AutoEF
EDV (mL)	164 ± 63	-	100 ± 51 *
ESV (mL)	94 ± 56	-	51 ± 40 *
EF (%)	45 ± 14	51 ± 16 *	52 ± 15 *

Values are mean ± 1SD.
**P* < .05 vs manual tracing.

and automatic measurement of LV volumes and EF. AutoEF is attractive because it has the advantage of being rapid and user-friendly and does not require human intervention.

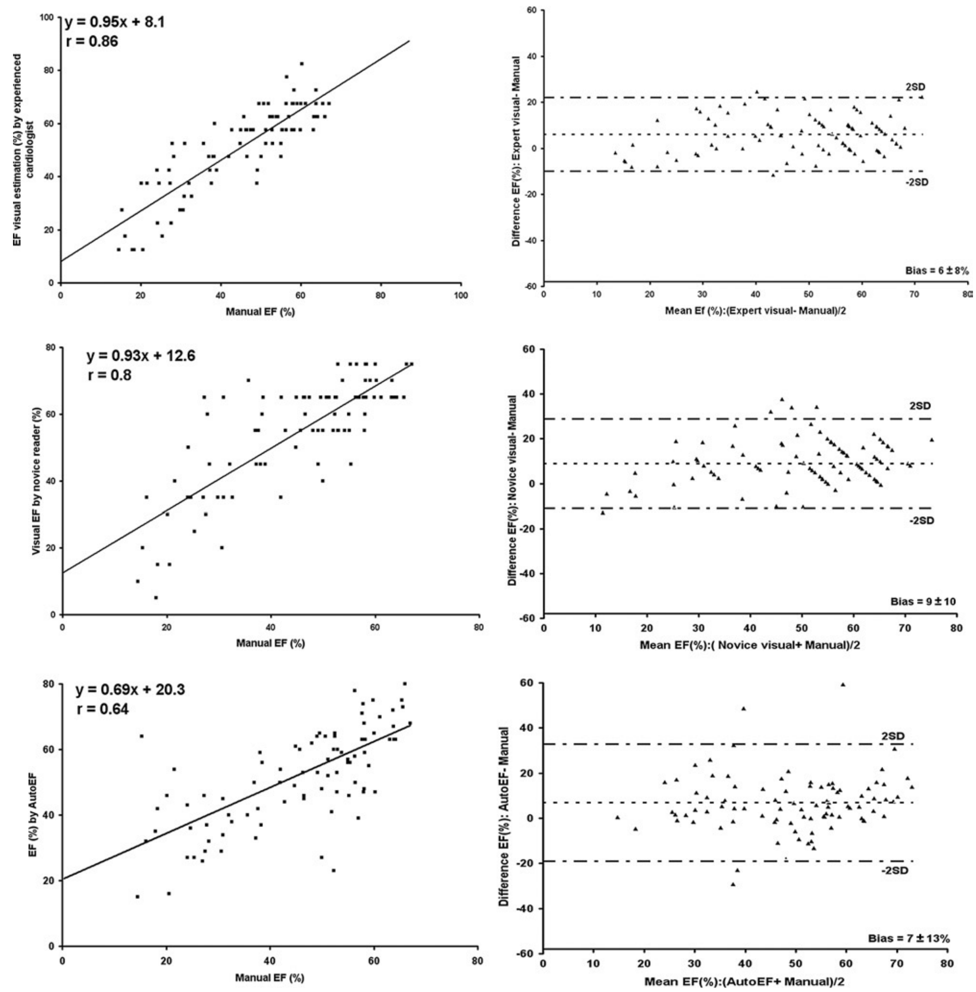
The aim of this study was to compare EF and LV volumes by AutoEF to the conventional echocardiographic methods and to CMR, the acknowledged reference standard for LV volume and EF computations.

Methods

Population

The study population consisted of 111 consecutive patients aged >18 years who had a clinically indicated transthoracic echocardiogram without contrast on a randomly chosen, typical work week from September 1 to 6, 2005. The only predefined echocardiographic exclusion criterion was poor endocardial definition (absence of more than one third of the endocardial perimeter).

Figure 2



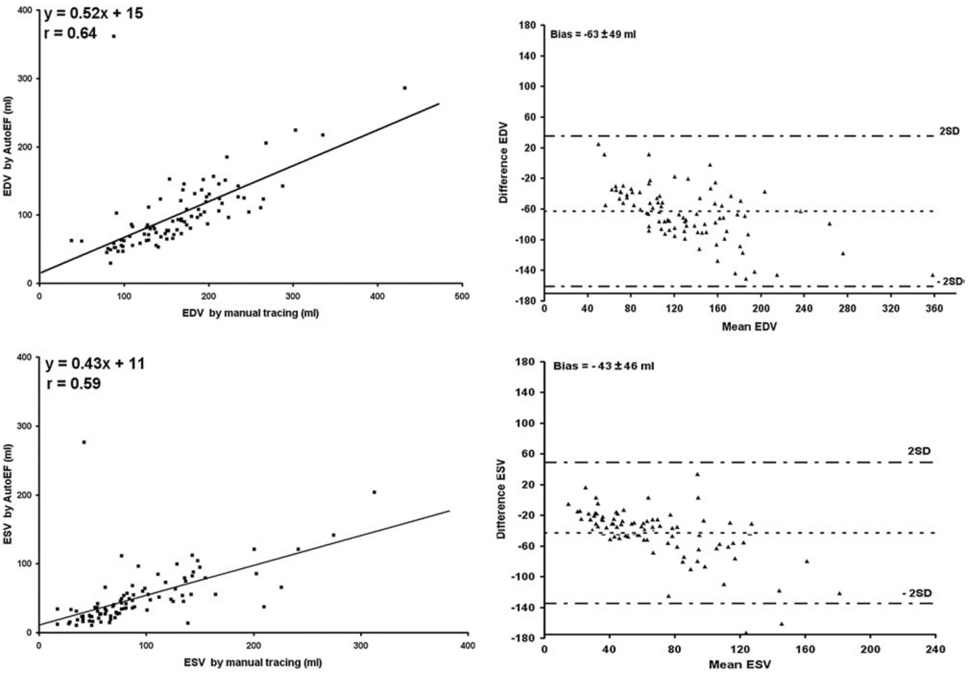
EF by visual assessment and AutoEF vs. manual tracing. Scatter plots with linear regression (left) and Bland-Altman bias plots (right) illustrating agreement in EF measurements between expert visual estimation and manual tracing (top) , novice reader visual estimation and manual tracing (middle), and AutoEF and manual tracing (bottom) measurements. Right, central horizontal line represents mean bias or systematic difference; upper and lower dashed horizontal lines, 95% CI of differences (limits of agreement).

Computer application

This application provides automated border detection and tracking of the LV endocardial contour throughout the cardiac cycle for quantification of volumes and EF. AutoEF uses pattern recognition from a database of 10 000 LV echocardiographic images digitized by experts. The AutoEF application quantifies LV volumes and EF in 3 consecutive steps:

1. Endocardial border detection. The first task is to differentiate the heart from background noise. For every cardiac image, the computer scans the image at all sites where the LV might be located and estimates the probability of each image being the LV. Once the LV is identified, the second task is to detect the endocardial border using segmentation processing. Localization and shape inference is repeated regionally (basal septal, apex, basal lateral, etc) for contour refinement. This process is performed on several frames near end diastole and end systole, and the frame that provides the highest confidence of LV detection and segmentation is used to proceed to the next step of contour propagation to other frames through motion tracking.
2. Motion tracking through the cardiac cycle. The endocardial border is tracked throughout a cardiac cycle, and these boundaries are compared to the recognized endocardial patterns in the database. Statistical fusion techniques are employed to account for factors that constrain heart motion or change LV shape.[9,10]
3. Automated quantification of LV volumes. When the endocardial contours have been detected and tracked, instantaneous LV volumes are quantified using modified Simpson's method from which EF is calculated (Figure 1).

Figure 3



AutoEF vs. manual Simpson's volumes. Scatter plots with linear regression (left) and Bland-Altman bias plots (right) illustrating agreement in EDV measurements between AutoEF and manual tracing (top) and agreement in ESV measurements between AutoEF and manual tracing (bottom). Right, central horizontal line represents mean bias or systematic difference; upper and lower dashed horizontal lines, 95% CI of differences (limits of agreement).

Assessment of EF and volumes

Two-dimensional echocardiograms were recorded on either Philips Sonos 7500 or IE 33 or on Siemens Sequoia 512 (Siemens Medical Solutions, Erlangen, Germany) ultrasound systems with simultaneous electrocardiogram. All echocardiograms were analyzed using the same study protocol and computer software.

Ejection fraction was assessed visually, by manual planimetry, and by AutoEF. End-diastolic (EDVs) and end-systolic volumes (ESVs) were assessed by planimetry and by AutoEF.

Expert visual reading. An expert (level III–trained, American Society of Echocardiography–certified reader) visually estimated the EF blinded to any previous semiquantitative or quantitative assessment. For each patient, the highest quality echocardiographic LV apical images were selected for visual estimation of EF and for measurement of LV volumes. A standard report form was used to monitor quality control of 3 parameters: endocardial definition, adequate visualization of the apex, and whether the apical imaging plane foreshortened true LV cavity length. The image quality of each loop was rated as suboptimal or optimal.

Expert manual tracing/planimetry. Endocardial borders were traced manually in our core laboratory from digital clips according to the American Society of Echocardiography recommendations,[11,12] by a technologist with 25 years of clinical and core laboratory experience of quantitative echocardiography. Left ventricular volumes were calculated using the modified Simpson's method of discs from which EF was derived.

AutoEF. The exact same digital clips were analyzed by a blinded third investigator using AutoEF commercially available software.

Novice visual reading. In addition, a junior cardiology fellow estimated EF visually and by manual tracing at 2 different times (3 weeks apart). Our goal was to test whether the level of expertise influenced the agreement between visual estimation of EF and AutoEF.

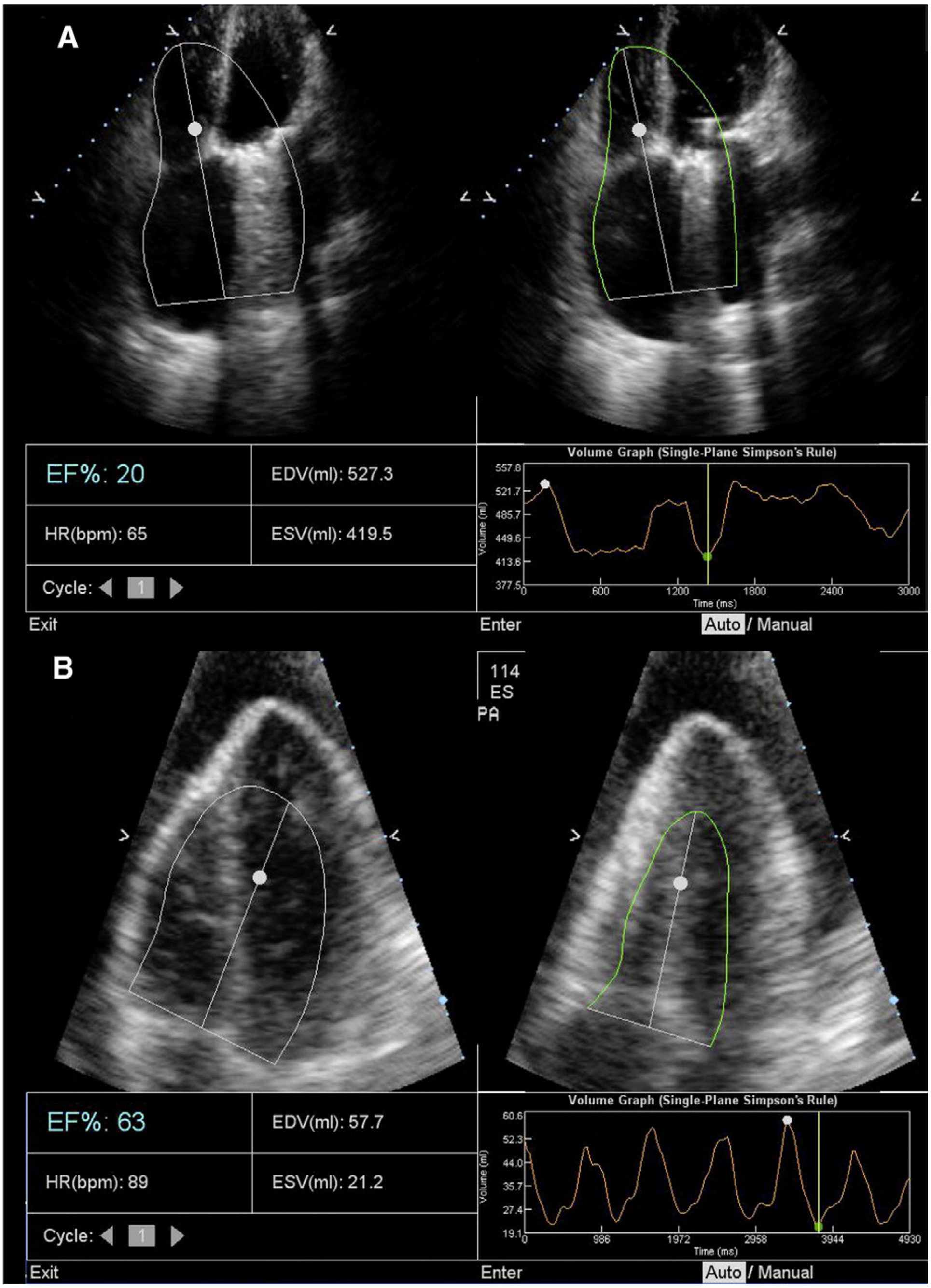
The investigators were blinded to each other's results.

Reproducibility. Intraobserver variability for manual measurement of LVEF and volumes was tested by the same experienced technologist who repeated the analysis of 44 randomly selected echocardiogram after a 5-month interval and was blinded to the results of previous computations.

Magnetic resonance imaging

We assessed the agreement in EF and LV volumes between AutoEF and CMR. We used CMR as a reference standard because of its proven accuracy and reproducibility.[13-15] We selected patients who had a CMR study and an echocardiogram within 48 hours to minimize differences in LV loading condition. The CMR studies were performed with steady-state free procession sequences on GE machines (FIESTA, General Electric

Figure 4



Inappropriate endocardial tracking by AutoEF. Examples of AutoEF output in a patient with mitral prosthesis (**A**) and with pericardial effusion (**B**).

Medical Systems, Milwaukee, WI) and were analyzed using Osirix image analysis software (http://homepage.mac.com/rossetantoine/osirix). TrueFISP sequences on Siemens equipment (Sonata, Siemens Medical Solutions, Erlangen, Germany) were analyzed using the ARGUS image analysis software to calculate EDV, ESV and EF. Cardiac magnetic resonance was limited to subjects with a complete set of breath-hold short axis slices covering the entire left ventricle. Left ventricular volumes were calculated by summing the LV cavity volumes of each slice. Slice thickness was approximately 8 mm (range, 5-8 mm), and the number of slices varied from 7 to 12. End diastole was defined as the first phase of the R wave–triggered sequence, and end systole, as the smallest cavity area. The most basal section to be included had to show a morphology and wall thickness compatible with LV myocardium that extended at least 50% of the circumference of the slice. The LV outflow tract was included up to the level of the aortic valve and the papillary muscles, and trabeculations were included as part of the LV cavity. An investigator blinded to patient data and echocardiographic results analyzed the CMR data.

Statistics

Data were collected in an Excel (Microsoft, Redmond, WA) spreadsheet and analyzed using STATA Statistical Software, release 9.0 (StataCorp LP, College Station, TX). All data are expressed as mean ± SD for descriptive statistics. Correlations between EF and volumes estimated by AutoEF and reference methods were analyzed using linear Pearson correlation. Agreement between the 2 different methods was evaluated using Bland-Altman analysis.[16] The 95% limits of agreement were estimated as the mean difference (bias) ± 2SD of the differences. Intraobserver variability for EF, EDV and ESV for manual tracing was analyzed in 44 randomly selected studies and expressed as absolute difference ± SD. $P < .05$ was considered statistically significant.

This study was approved by the institutional review board at the Hospital of the University of Pennsylvania.

Results

Patient population

One hundred eleven patients' studies were reviewed, and 92 patients comprised the study population. Sixteen studies were recorded on a Philips IE33 (Philips, Inc, Andover, MA) and could not be analyzed by AutoEF because of a fundamental difference in the Digital Imaging and Communications in Medicine format. Three patients had poor-quality images that could not be manually traced. One was obtained early postoperatively and was limited because of bandages and immobility; 1 had foreshortened apical images of the LV, and 1 was obtained during tachycardia of 130 beat/min.

The mean age was 64 ± 16 years. Fifty-three patients (57%) were men. Baseline demographics and LV echocardiographic parameters are shown in Table I. Mean values for LV volumes and EF with SDs are presented in Table II. A representative AutoEF computer output of EF and continuous LV volume from which EDV and ESV were identified is illustrated in Figure 1.

AutoEF versus echocardiographic experts

Ejection fraction

AutoEF versus expert visual estimate. The correlation between AutoEF and visual estimation of EF by the expert echocardiographer was only modest ($r = 0.57$) ($P < .001$).

AutoEF versus manual planimetry. AutoEF correlation with EF derived from manual tracing/planimetry was 0.64 ($P < .001$ for EF) (Figure 2).

Visual versus manual planimetry. There was a significantly closer correlation between visually estimated EF by the expert and the manual tracing ($r = 0.86$) than there was between AutoEF and manual tracing ($r = 0.64$) ($P < .001$ for both). The significantly closer agreement between expert visual estimation and manual tracing was demonstrated by Bland-Altman analysis. The 95% limits of agreement for EF between expert visual estimation of EF and manual tracing varied from −10% to 22% (EF units) and −19% to 33% for AutoEF versus manual tracing (Figure 2).

Volumes. The correlation coefficient between AutoEF and manual tracing for EDV and ESV was 0.64 and 0.59 respectively. The 95% limits of agreement for EDV and ESV between manual tracing and AutoEF were −161 to 35 and −135 to 49 mL, respectively (Figure 3).

These differences were not confined to any individual patient subgroup, such as those with dilated hearts, severe LV dysfunction, normal hearts, or hearts with abnormal LV cavity shape.

Interestingly, in the presence of a mechanical mitral prosthetic valve or significant pericardial effusion, AutoEF failed at the first stage of the pattern recognition process and did not recognize the LV. Thus, endocardial borders were not identified. In these circumstances, tracking algorithm identified structural interfaces outside the LV (Figure 4).

Level of expertise

The novice reader's estimates of EF correlated closely with both expert visual estimation and with manual tracing ($r = 0.86$ and 0.80, respectively). Bland-Altman analysis demonstrated close agreement between the novice reader's visual estimation of EF and expert visual estimation (Figure 2). The 95% limits of agreement for EF between novice reader's visual estimation of EF and manual tracing varied from −11% to 29% (EF units).

AutoEF versus MRI

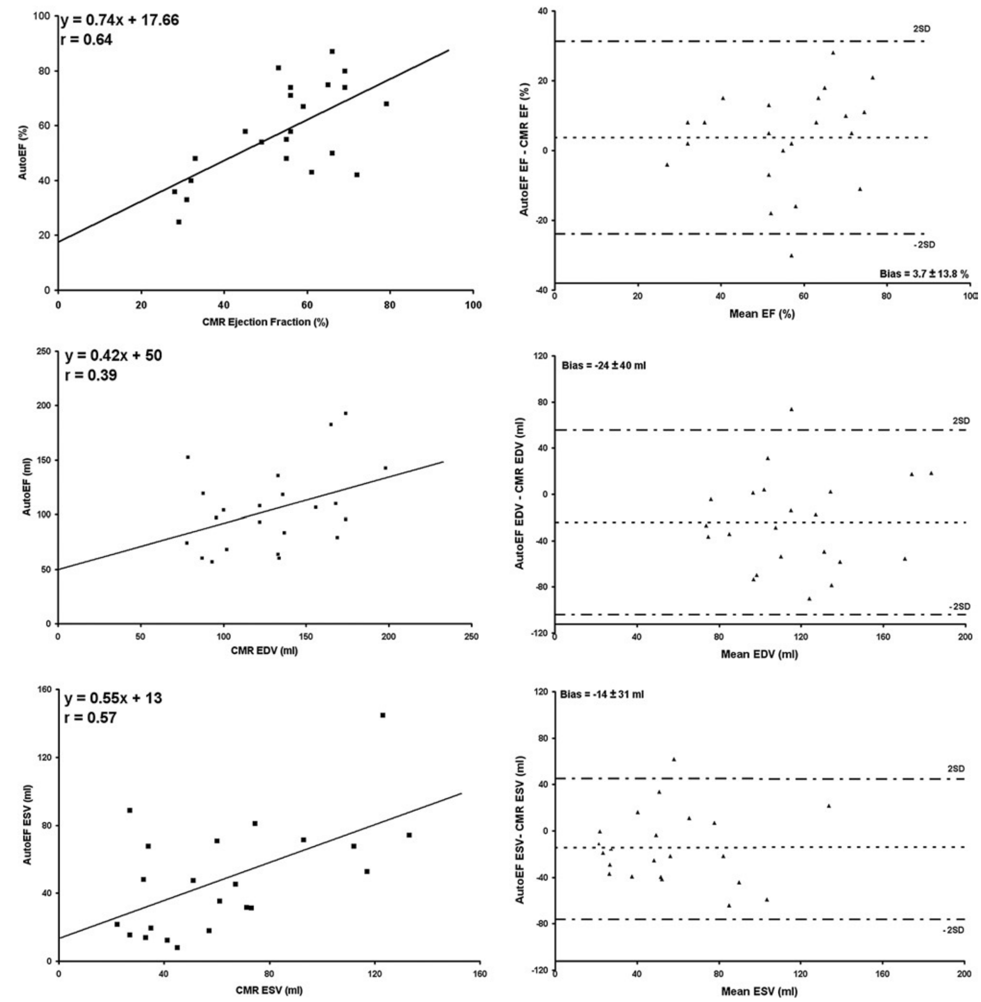
Twenty-two patients had a CMR study within 48 hours of the echo study. Mean values for LV volumes and EF are presented in Table III. The 95% limits of agreement between CMR and AutoEF were −23.9% to 31.3% (EF units) for EF and −104 to 56 mL for EDV and −76 to 45 mL for ESV (Figure 5), indicating that although there were modest correlations between AutoEF and EF by CMR,

Table III. Left ventricular volumes and ejection fraction by MRI and AutoEF (n = 22)

	MRI	AutoEF
EDV (mL)	129 ± 35	104 ± 38*
ESV (mL)	63 ± 33	48 ± 33*
EF (%)	53 ± 15	57 ± 17

MRI, Magnetic resonance imaging.
Values are mean ± 1SD.
* $P < .05$ versus MRI.

Figure 5



AutoEF vs. cardiac magnetic resonance imaging. Scatter plots with linear regression (left) and Bland-Altman bias plots (right) illustrating agreement in EF (top), EDV (middle), and ESV (bottom) between AutoEF and cardiac magnetic resonance imaging. Right, central horizontal line represents mean bias or systematic difference; upper and lower solid horizontal lines, 95% CI of differences (limits of agreement).

AutoEF consistently underestimated LV volumes (EDV and ESV) compared to those by CMR (Table III).

Reproducibility

AutoEF was 100% reproducible. The reproducibility of the manual tracing of 44 randomly selected echocardiograms on 2 separate occasions was (r = 0.94 for EF; r = 0.96 for EDV and r = 0.98 for ESV). The limits of agreement for EF were −8.86 to 11% with a bias of 1%, −29 to 32 mL for EDV with a bias of 1.3 mL, and −19.8 to 21.8 mL for ESV with a bias of 1 (Figure 6 and Table IV).

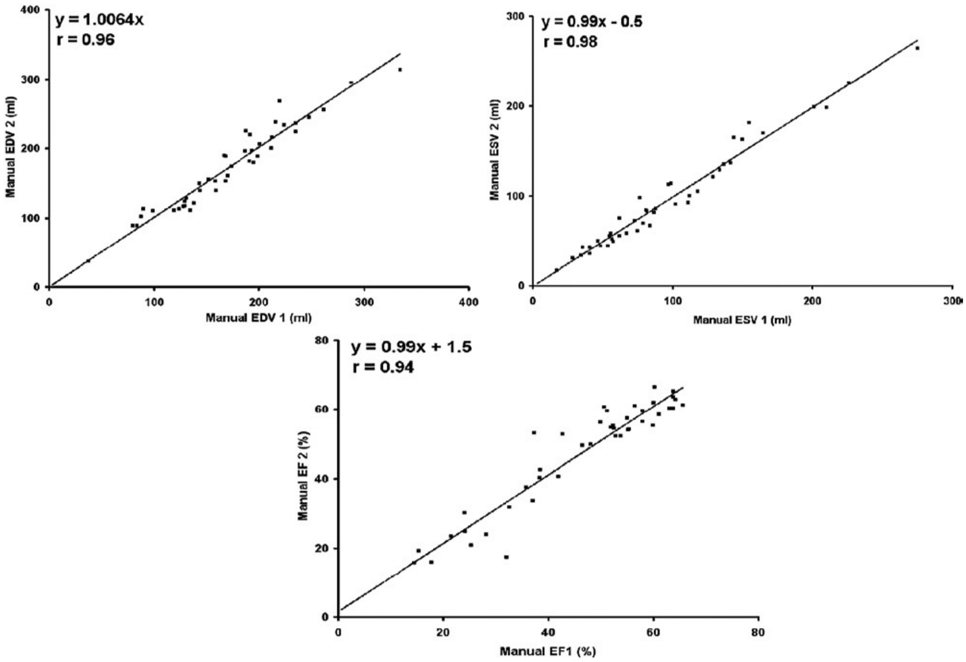
Discussion

Estimation of LV volumes and EF is important because it is used routinely to stratify risk, predict clinical outcome, and determine suitability for novel pharmacologic and device therapies.[17]

There are 2 echocardiographic methods used to estimate EF: visual assessment and quantitation by manual tracing of the endocardial borders. Visual assessment of EF is based on the recognition of patterns of LV contraction and wall motion from different imaging planes of the heart and is highly dependant on reader expertise. By contrast, manual tracing is dependant on accurate definition of the endocardial borders to calculate LV volumes. Manual tracing is time-consuming, varies with image quality, and tends to underestimate LV volumes and overestimates EF.

Thus, there is a compelling need for an accurate and reproducible method for calculating EF and volumes quickly and ideally from all or almost all 2-dimensional

Figure 6



Intraobserver reproducibility of manual tracing. Scatter plot with linear regression illustrating intraobserver agreement for EF (bottom), EDV (left), and ESV (right) (n = 44).

transthoracic echocardiograms. Previous attempts to generate EF and volumes automatically have been confounded by gain dependence and inconsistent endocardial border tracking algorithms.[1,2,5,6] AutoEF analysis system is an innovative potential solution based on the concept of artificial intelligence and pattern recognition. Pattern recognition is broadly used in many fields from automatic recognition of handwritten postal codes to the automatic recognition of images of human faces. In biomedical imaging, programs are already in use for automatic tumor detection, screening for diabetic retinopathy by analysis of retinal images, and recognition of morphological lesions in the urinary tract.

The principle behind using artificial intelligence/ pattern recognition in estimating volumes and EF is to reproduce a new image of a complete endocardial surface aided by interaction with a large number of previously traced LV endocardial silhouettes in the database. Image processing by segmentation and subsequent linkage assigns heart shape and regional wall motion/contraction. Artificial intelligence (AutoEF) appears to be a promising new method for calculating EF that will make automatic quantification of LV function available to all medical practitioners.

In our study of a randomly selected patient cohort, AutoEF did not correlate closely with EF by manual tracing in our core laboratory nor did AutoEF correlate with an expert's visual estimation of EF. AutoEF did not improve upon the accuracy of a novice reader's estimation of EF. However, visual estimates of EF by the expert correlated closely with EF derived from manual tracing. We were unable to demonstrate the same high degree correlations between AutoEF and visual estimation of EF recently reported[18] (r = 0.64 vs. r = 0.98), although we used a similar protocol. This different result between the 2 studies was likely due to their use of manual editing of the endocardial tracking in 23% of the cases. Our aim was strategically different from that of the previous study.[18] We were interested in testing AutoEF as a completely automatic assessment of EF since the incremental value of artificial intelligence resides in its complete independence from human intervention while

Table IV. Reproducibility of manual measurements (n = 44)

	Intraobserver variability
EDV (mL)	12 ± 10
ESV (mL)	8 ± 6
EF (%)	3.7 ± 3.5

Values are mean ± 1SD.

providing precise and reproducible measurements. However, similar to Cannesson et al[18] we found that AutoEF systematically underestimated LV volumes assessed by CMR.

We attempted to elucidate the unanticipated differences in EF between AutoEF, visual estimates, and manual tracing. To achieve this, the study population was divided into subgroups—those with normal heart size, LV dilatation, and extent of LV dysfunction. Subgroup analysis did not reveal any divergence in EF between AutoEF, visual estimates, and manual tracing. Similarly, there was no difference in EF in patients with optimal quality echocardiograms versus those with suboptimal quality so that the discrepancy between EF could not be explained solely by image quality.

An alternative explanation for the discrepancies between AutoEF and our estimations of EF may be due to the limitations of the database. The artificial intelligence based on pattern recognition technology requires an extensive repertoire of LV shapes and sizes. Although AutoEF has a database of 10 000 images, these were largely from normal hearts, and to our knowledge, there was a paucity of cardiac pathology. This resulted in an inappropriate endocardium tracking and underestimation of LV volumes. Inappropriate tracking was exemplified in the presence of either a mitral mechanical prosthesis or pericardial effusion (Figure 4). Increase in the number of abnormal hearts in the database should reduce the discord between AutoEF and EF derived from manual tracing.

In conclusion, AutoEF is theoretically an attractive proposition because it eliminates problems with inter-reader variability and makes automatic assessment of EF universally available. However, AutoEF in its present form does not perform as well as visual estimation of EF either by an expert or a novice reader and did not reproduce the EF results obtained by CMR or by manual tracing. Artificial intelligence and pattern recognition is an important part of future quantitative cardiac imaging. AutoEF needs more extensive validation and database expansion before release to clinicians at large.

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