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Comparison between Radionuclide Ejection Fraction and Fractional Area Changes Derived from Transesophageal Echocardiography Using Automated Border Detection

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Background: **Left ventricular fractional area changes (FAC) can be derived from transesophageal echocardiography using an automated border detection system. However, FAC has not yet been compared to left ventricular ejection fraction (EF) evaluated by a reference technique. The aim of this study was to correlate transesophageal echocardiography automated FAC to EF derived from radionuclide angiography to obtain a quantifying method of global left ventricular systolic function at the bedside.**

Methods: **Ten critically ill patients, whose lungs were mechanically ventilated, were included in this prospective study. Patients were scheduled for radionuclide EF evaluation when at least 75% of the endocardium was clearly visualized on transesophageal echocardiography. Patients with esophageal pathology or cardiac dysrhythmia were excluded. Ejection fraction derived from radionuclide angiography was measured using technetium 99m. Echocardiographic data were obtained using an ultrasound system with automated border capabilities. Simultaneous measurements of left ventricular EF and FAC were obtained for each patient, both before and after starting a dobutamine intravenous infusion to modify left ventricular contractility.**

Results: **Mean values for radionuclide EF and transesophageal echocardiography FAC were, respectively: 55% ± 19% (range 19–89%) and 46% ± 18% (range 17–80%). Left ventricular EF and FAC were significantly correlated (r = 0.85, SEE = 9.6%). Variations of EF and FAC, induced by dobutamine, were also correlated (r = 0.70, SEE = 4.9%).**

Conclusions: **Fractional area changes determined by transesophageal echocardiography using automated border detection correlate well with radionuclide EF and may be used at the bedside to quantify left ventricular function in selected intensive care unit patients. (Key words: Heart: left ventricular function. Monitoring: radionuclide angiography. Monitoring, transesophageal echocardiography: edge detection; ejection fraction; fractional area changes.)**

TRANSESOPHAGEAL echocardiography (TEE) provides reliable information about regional and global left ventricular function.[1-3] It allows estimation of left ventricular volume from left ventricular area.[4-7] In addition, transesophageal echocardiographic fractional area changes (FAC), defined as end-diastolic area (EDA) minus end-systolic area (ESA) divided by end-diastolic area (FAC = [EDA − ESA]/EDA), and measured at the level of the mid-papillary muscles, are highly correlated to ejection fraction (EF), defined as end-diastolic volume (EDV) minus end-systolic volume (ESV) divided by end-diastolic volume (EF = [EDV − ESV]/EDV), and derived from radionuclide angiography.[4,7] Nevertheless, in clinical practice, quantitative TEE evaluation of FAC, as an index of global left ventricular systolic function, is time consuming, and requires manual tracing of at least two freeze-frame images. Thus, considerable attention has been dedicated to the development of automated systems capable of quantifying left ventricular function in real-time. A recent technique has been developed to automatically delineate the endocardial border of the left ventricle, allowing a continuous on-line assessment of FAC. Several studies have validated this automated system compared to manual tracing using either transthoracic[8-10] or transesophageal[11] echography. Recent studies[12-14] compared the automated border detection technique to a reference technique, but none of them used TEE. Because TEE generally produces better images than transthoracic echocardiography does, it might generate better automated border detection esti-

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mates. The aim of the current study was to compare real-time evaluation of transesophageal left ventricular FAC, derived from an automated border detection system (automated FAC), to left ventricular EF assessed by radionuclide angiography.

Methods and Materials

Patients Selection

After approval of our Institutional Review Board (Hôpital Henri Mondor, Université Paris XII), and obtaining written informed consent from patients' families, ten critically ill patients, whose lungs were mechanically ventilated, were enrolled in this prospective study. Patients were scheduled for radionuclide EF evaluation when at least 75% of the endocardium was clearly visualized by human eye on TEE. We excluded patients with chronic or acute esophagus pathology, and patients with cardiac dysrhythmia.

Radionuclide Angiography

Radionuclide EF was measured according to the method proposed by Stanck *et al.*[15] Thirty minutes before the first acquisition data period, 5 mg stannous pyrophosphate was injected intravenously. technetium 99m (740 MBq) was injected immediately before the gated pool imaging. A scintillation camera (Low Energy Mobile, Siemens, Paris, France) equipped with a parallel slanthole collimator was then positioned over the patient's chest to obtain a left anterior oblique view that most clearly defined the interventricular septum. Five hundred thousand count images were recorded on a 64 × 64 matrix during a 6–12-min period. The angle of the camera was held fixed throughout the procedure. The photopeak was centered at 140 keV, with application of a 20% energy window. Data were stored on a hard disk for computation.

Transesophageal Echocardiography

After induction of general anesthesia, a 5-MHz transesophageal transverse monoplane probe, connected to an ultrasonograph (Hewlett-Packard Sonos 1000, Andover, MA), was positioned to visualize the transgastric short-axis view of the left ventricle, at the level of the mid-papillary muscles.[16] After a complete TEE examination was performed, short-axis images of the left ventricle were recorded on VHS videotapes (Panasonic AG6200 videocassette recorder, Matsushita, Japan).

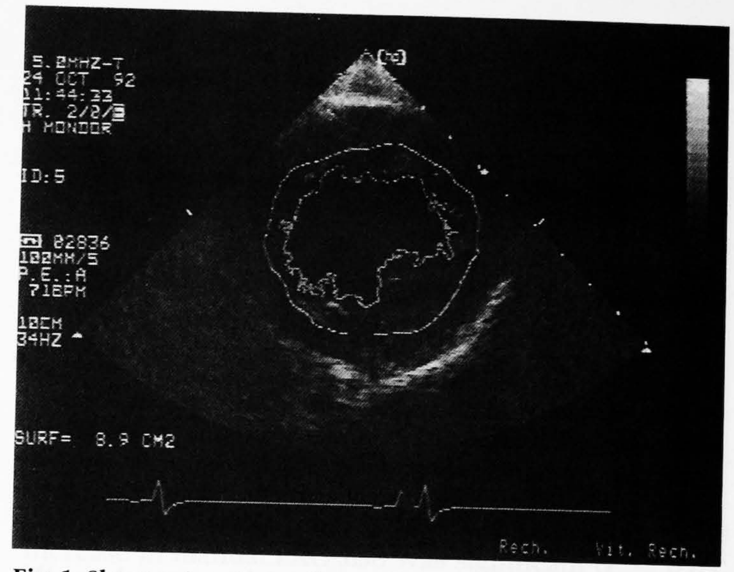

Fig. 1. Short-axis echocardiographic image of the left ventricle at the mid-papillary muscles level, with automated border detection activated. The region of interest has been defined (the white line through the left ventricular myocardium around the left ventricular cavity). The automatically detected endocardial border is shown as the inner dotted line.

The probe was held fixed, scanning the left ventricle at the same level throughout the procedure.

Automated Border Detection System The ultrasonograph made use of the integrated backscatter imaging software.[8-11,17-19] The automated border detection system analyzed each radiofrequency A-line over a 3.2-μs period. The backscatter data along each scan line were used to discriminate the blood-tissue interface of the endocardium. This interface is represented on the two-dimensional image, as a dotted line (fig. 1). The operator adjusted the gain controls to track at least 75% of the circumference of the left ventricle endocardium with the highlighted border indicator. Then, using the trackball of the ultrasonograph, the operator outlined a region of interest that included only the left ventricular cavity. A calculation and graphic software package computed and displayed continuously the area within the region of interest and the derived FAC (fig. 2).

Manual Transesophageal Echocardiography Tracing Left ventricular images were analyzed off-line and by two independent investigators who were unaware of radionuclide EF and automated FAC results. End-diastolic area was measured at the peak of the electrocardiographic R-wave. End-systolic area was defined as the smallest left ventricular cavity determined by visual inspection. Measurements of the left ventricular area were performed over three consecutive cardiac cycles

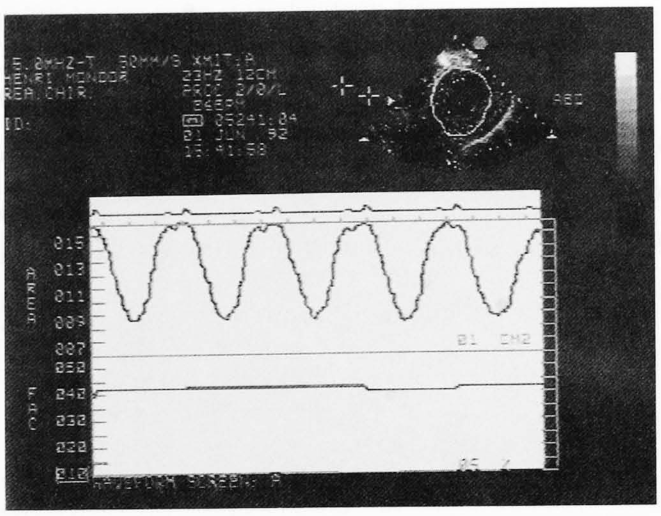

Fig. 2. The small sector in the upper right corner shows the short-axis view after activation of the automated border detection. The upper trace (AREA) shows the cavity area computed and displayed instantaneously with calibration marks (in cm²). The lower trace displays the on-line computed fractional area changes with calibration marks (in %).

for averaging, using the black-white interface.[20] Each left ventricular cross-sectional area measurement considered for manual FAC determination was the mean of the values derived from both independent observers. Fractional area changes were calculated from the following formula: FAC (%) = (EDA − ESA) × 100 / (EDA). Because segmental wall motion abnormalities of the left ventricle could alter the correlation between FAC and EF,[21] these were also reported.

Study Protocol

Transesophageal echocardiography and radionuclide angiography were performed simultaneously in the radionuclide imaging department. Arterial blood pressure, pulse oximetry and 3-lead electrocardiogram were continuously monitored throughout the study protocol. Two sets of left ventricular EF and FAC measurements were obtained for each patient, before and 15 min after starting a 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dobutamine intravenous infusion. The infusion goal was to modify left ventricular contractility, thus testing the ability of the TEE automated system to detect EF variations.

Sequences of Data Acquisition Echocardiographic images were recorded during apnea. Controlled ventilation was maintained during radionuclide angiography because of the lengthy duration of the procedure (6–

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beginning of the procedure, they were not changed during the study protocol period. Fractional area changes determined by automated border detection were sampled at the beginning, middle, and end of the radionuclide angiography acquisition period. The FAC value considered for the comparison with angiographic EF was the average of these three measurements. All echocardiographic and radionuclide angiographic data were collected at two different periods: before and 15 min after starting the dobutamine infusion.

Statistical Analysis

Results are expressed as mean ± standard deviation. Echocardiographic FAC and radionuclide EF, as well as variations before and after dobutamine administration, were compared using linear regression analysis. Intraobserver variability for radionuclide imaging and interobserver variability for TEE manually traced area determinations were expressed as the difference between two measurements divided by the mean value and multiplied by 100. Automated and manually drawn TEE FAC were compared using linear regression and bias analysis.[22] Statistical significance was determined using the Wilcoxon signed rank test for paired data; $P < 0.05$ was considered significant.

Results

Patients

No complication occurred during the study protocol. One patient could not be included in the study because of insufficient endocardial definition on TEE. Patients' demographic characteristics are given in table 1. Six of

Table 1. Patient Demographics

Patient No.	Diagnosis	Age (yr)	Sex
1	Multiple trauma	47	F
2	Septic shock	51	F
3	Pneumonia	92	F
4	Obstructive cardiomyopathy	70	M
5	COPD	79	F
6	Multiple trauma	25	M
7	Septic shock	75	M
8	Mitral valve replacement	62	F
9	Cardiogenic shock	69	M
10	Aortic valve replacement	83	M

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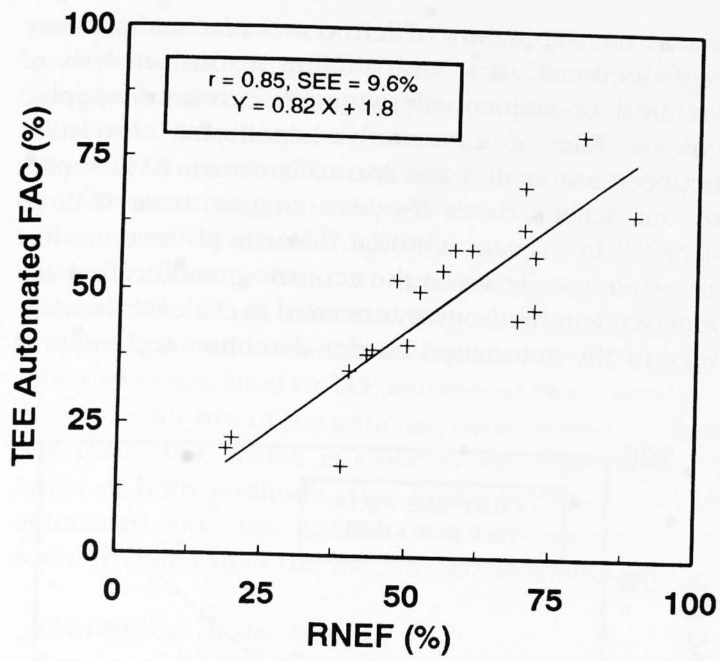

Fig. 3. Comparison between transesophageal automated fractional area changes and radionuclide ejection fraction. Regression line was not statistically different from the identity line ($P = 0.74$).

ten patients had a poor left ventricular function confirmed by a radionuclide EF < 50%. Among those six patients, two documented minor segmental wall motion abnormalities visualized on the short-axis view of the left ventricle, in the anterior and lateral walls and in the posterior wall, respectively. These wall motion abnormalities were not modified by dobutamine infusion. No segmental wall motion abnormality was noted in the four patients having a good left ventricular radionuclide EF (>50%).

Comparison between Automated Fractional Area Changes and Radionuclide Ejection Fraction

Transesophageal echocardiographic automated FAC measurements were performed easily. After the left ventricular short-axis view was visualized, an interval of 1–2 min was necessary to adjust gains and draw the region of interest. The intraobserver variability coefficient for radionuclide EF was 1.0% ± 3.6%. A strong correlation was documented between TEE automated FAC and radionuclide EF (fig. 3). Variations of radionuclide EF before and after dobutamine intravenous infusion were also correlated to automated FAC variations (fig. 4). The mean values of radionuclide EF were, respectively, 51% ± 17% (range 19–72%) before, and 58% ± 21% (range 20–89%) after dobutamine infusion. The increase in radionuclide EF was significant ($P <$ 0.01, Wilcoxon test), and varied from 0% to 17%. The mean values for TEE automated FAC were, respectively, 41% ± 15% (range 17–62%) before, and 51 ± 20% (range 17–80%) after dobutamine infusion. The rise in automated FAC also was significant ($P < 0.01$, Wilcoxon test), and varied from 0% to 18%; however, this increment was less than 10% for five patients.

Comparisons between Manually Traced Fractional Area Changes and Radionuclide Ejection Fraction

The mean values of TEE manual FAC were, respectively, 44% ± 14% (range 23–69%) before, and 54% ± 18% (range 26–75%) after dobutamine infusion. The increase in manual FAC also was significant ($P < 0.01$, Wilcoxon test), and varied from 1% to 32%. A high correlation also was documented between TEE manual FAC and radionuclide EF (fig. 5).

Comparison between Manually Traced and Automated Fractional Area Changes

Interobserver variability for TEE manual FAC was 6.5% ± 15.4%. A significant correlation was documented between FAC obtained from manually drawn

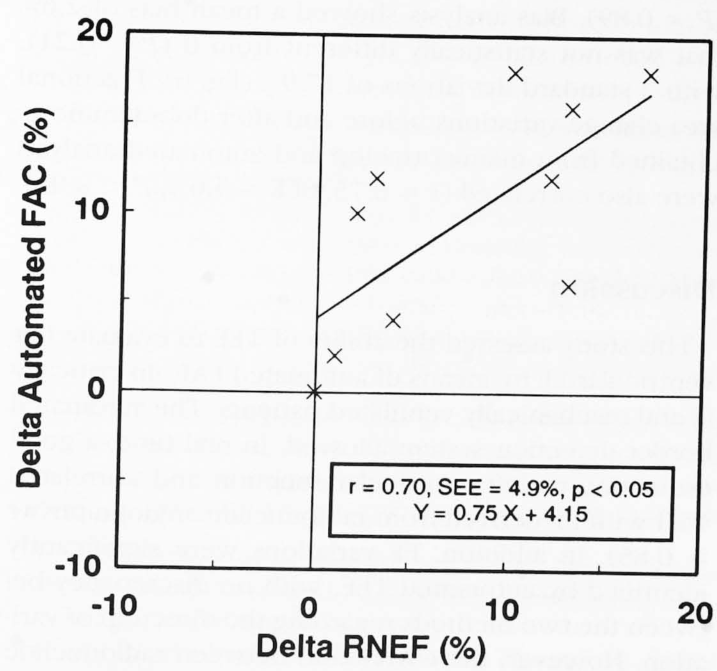

Fig. 4. Linear regression analysis comparing variations of radionuclide ejection fraction and variations of TEE automated fractional area changes before and after dobutamine infusion. Regression line was not statistically different from the identity line ($P = 0.37$).

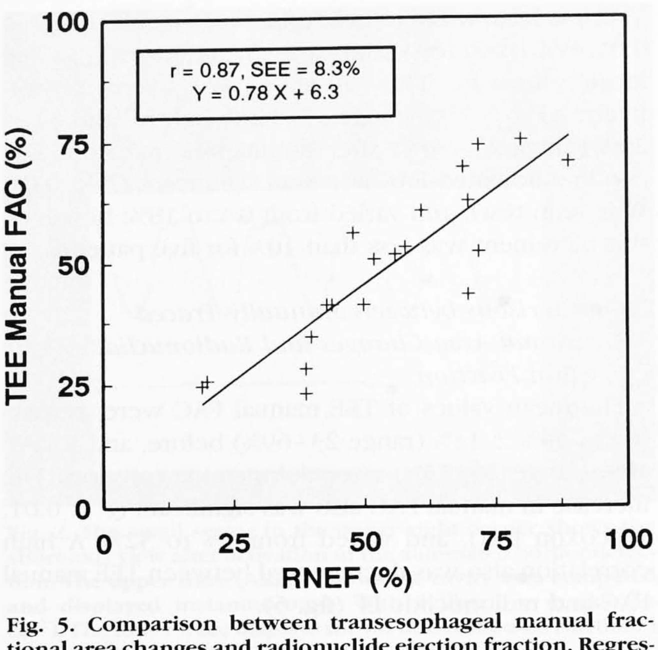

Fig. 5. Comparison between transesophageal manual fractional area changes and radionuclide ejection fraction. Regression line was not statistically different from the identity line ($P = 0.64$).

areas and FAC derived from the automated border detection system (fig. 6). There was no statistical difference between the regression line and the identity line ($P = 0.89$). Bias analysis showed a mean bias of 2.6% that was not statistically different from 0 ($P = 0.21$), with 2 standard deviations of 17.9% (fig. 6). Fractional area change variations before and after dobutamine as obtained from manual tracing and automated analysis were also correlated ($r = 0.75$, SEE = 4.6%, $P < 0.02$).

Discussion

This study assessed the ability of TEE to evaluate left ventricular EF by means of automated FAC, in critically ill and mechanically ventilated patients. The automated border detection system allowed, in real time, a good estimation of left ventricular function and correlated well with EF derived from radionuclide angiography ($r = 0.85$). In addition, EF variations were significantly identified by automated TEE, with no discrepancy between the two methods regarding the direction of variation. However, the correlation between radionuclide EF and FAC variations was only fair ($r = 0.70$), with changes in EF being overestimated by automated FAC. Previous studies using either transthoracic[8-10] or transesophageal[11] echocardiography have compared automated measurements of left ventricular mid-papillary cross-sectional area, with off-line manual analysis of identical or sequentially acquired echocardiographic images. They documented a significant correlation between automated and manually drawn FAC, similar to our results, with R-values ranging from 0.49 to 0.95.[8-10] In a recent editorial,[23] Martin pointed out that a comparison between the acoustic quantification and independent methods was needed to evaluate the accuracy of the automated border detection technique in

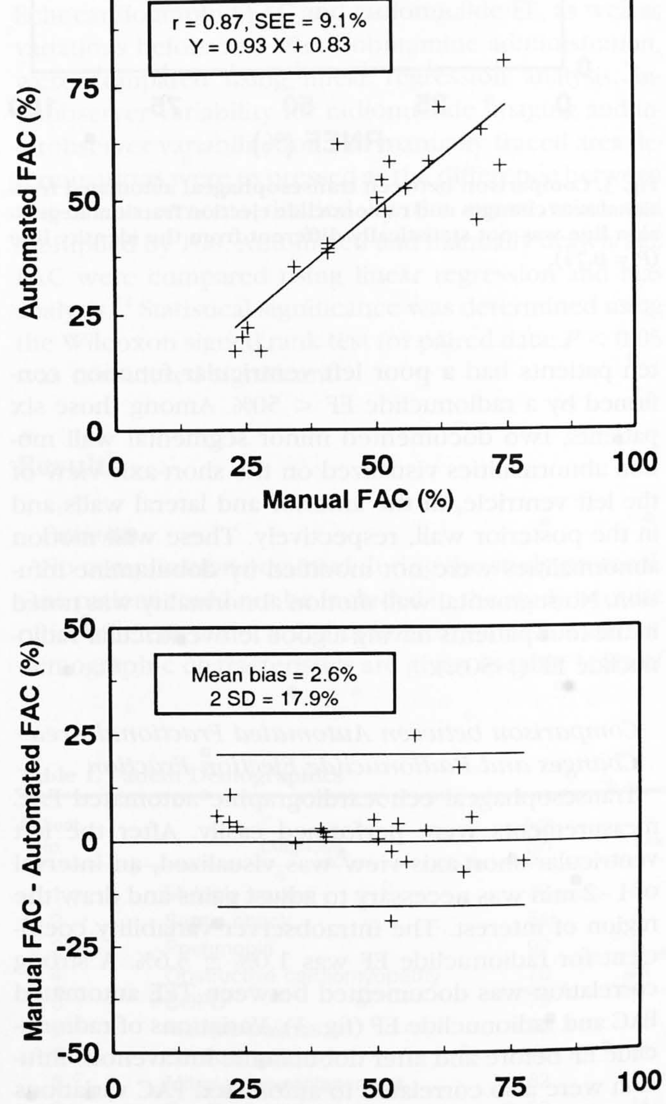

Fig. 6. Linear regression and bias analyses comparing transesophageal manual and automated fractional area changes.

assessing global left ventricular systolic function. Three recent studies, using transthoracic echocardiography, found a good correlation between automated FAC and either FAC determined by ultrafast computed tomography[12] or EF measured by radionuclide angiography,[13,14] with R-values ranging from 0.84 to 0.92. The main contribution of the current study is that TEE automated FAC was demonstrated to be strongly correlated to radionuclide EF in mechanically ventilated patients, and that dobutamine-induced variations of EF were also albeit less correlated to TEE automated FAC variations. However, for five of ten patients, these variations were less than 10%, which is close to the reproducibility range of both methods. This might explain why TEE automated FAC and radionuclide EF variations were less correlated than the measurements themselves.

Limitations of the Method

Results of this study apply to anesthetized patients during suspended mechanical ventilation, when adequate short-axis view is obtained. In 10% of all patients, this short-axis view cannot be obtained[4,7,11] and FAC measurements (either manual or automated) are not available. Border detection accuracy relies on the quality of echocardiographic images, and requires adequate endocardial definition. In previously reported studies, satisfactory results were obtained from automated border detection in only 72–81% of patients.[8,11] In addition, automated border detection is a highly gain-dependent method: any alteration in gain settings alters detection of the endocardial border: a gain variation of only 5 dB, modifies significantly the FAC obtained by automated border detection.[24] A low level of gain decreases the ultrasound signal reflected from the septal and lateral myocardium leading to overestimation of the cross-sectional area. Conversely, excessive high levels of gain generate an increase in cavity noise with underestimation of left ventricular area as a result.[8–11,24] The operator must therefore adjust the gain settings as a compromise between these two extremes. We did not change gain settings during the protocol to decrease gain variation effects on automated FAC measurements.

Lateral gain compensation has been recently developed, allowing a higher endocardial definition from the myocardial walls oriented parallel to the ultrasound scanning.[18,25] Gorcsan *et al.* have demonstrated that transthoracic automated border detection studies were inadequate in 19 of the 66 patients before using lateral gain compensation.[13] Overestimation of end-systolic area owing to septal and lateral wall dropout can be reduced by increasing lateral gain controls. Lateral gain compensation was not available in our study design, but our results are still comparable to those previously reported, using this software improvement. This is probably explained by the resolution image of TEE: the proximity of the heart to the echocardiographic probe allows the use of a higher frequency, near-focus transducer that produces higher resolution and improves signal-to-noise ratio.[16] Using TEE, the endocardial definition was thus sufficient enough to allow a good endocardial tracking by the automated border detection software leading to a good estimation of global left ventricular systolic function by automated FAC.

Lastly, radionuclide ventriculography also may be associated with variability[26] that could explain the merely fair correlation between variation measurements obtained in our patients.

In conclusion, FAC determined by automated border detection using TEE correlates well with EF measured by radionuclide angiography and allows on-line estimation of global left ventricular systolic function in selected intensive care unit patients. The accuracy of the automated method is comparable to that of manual planimetry provided that adequate endocardial definition is obtained.

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