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Assessment of Left Ventricular Ejection Fraction and Volumes by Real-time, Two-dimensional Echocardiography

A Comparison of Cineangiographic and Radionuclide Techniques

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SUMMARY Five different algorithms for determining left ventricular (LV) ejection fraction (EF) and volumes from two-dimensional echocardiographic examination (TDE) were compared with standard methods for obtaining EF and volume from x-ray cineangiography (cine) and EF from radionuclide ventriculography (RVG) in 35 patients. Although all methods correlated positively, the degree of correlation varied with the algorithm used. For EF determination, TDE algorithms (especially those using multiple planes of section) were superior to unidimensional algorithms commonly used with M-mode echocardiography. The best algorithm (modified Simpson's rule) correlated well enough with cine EF ($r = 0.78$; SEE 0.097) and RVG EF ($r = 0.75$; SEE 0.087) to make clinically useful estimates. TDE volumes also correlated meaningfully with cine end-diastolic and end-systolic volumes ($r = 0.84$; $n = 70$) but were associated with a large standard error of the estimate (43 ml) and offered less advantage over unidimensional volume estimations. Quantitative application of TDE appears to be a useful noninvasive method of evaluating LVEF, but is not as useful for estimating LV volumes.

LEFT VENTRICULAR PERFORMANCE is one of the most important factors for the prognosis of acquired heart disease, whether treated medically or surgically.[1-4] Measures of left ventricular performance such as chamber volume and ejection fraction (EF) are usually deemed most reliable when derived from cardiac catheterization data. Recently, several investigators have shown that EFs derived from radionuclide ventriculograms (RVG) correlate well with EFs derived from x-ray cineangiograms. Two-dimensional echocardiography (TDE) has been used qualitatively to identify regional abnormalities of left

ventricular function,[9, 10] and there is preliminary data suggesting that it has promise in assessing global left ventricular performance.[11-16] We compared EF and ventricular volumes obtained from TDE images with corresponding determinations derived from RVGs and from x-ray cineangiograms made at cardiac catheterization in the same series of patients.

Methods

Patient Selection

Fifty patients scheduled for diagnostic cardiac catheterization underwent examination by TDE and RVG during the same hospitalization. Thirty-five of these patients were selected because they had studies of adequate quality for quantitative interpretation. Specific reasons for exclusion were technically inadequate echo (13 patients) and cineangiograms with excessive premature complexes (two patients). The clinical status of all patients was unchanged between studies. Twenty-six patients had coronary artery disease, four had valvular heart disease, four had com-

bined valvular and coronary disease, and one had constrictive pericarditis. Twenty of 35 patients had cineangiographic segmental contraction abnormalities. All were in normal sinus rhythm.

Imaging Methods and Processing

Images from the three methods were processed by independent observers who were unfamiliar with each other's results. In all instances, echocardiographic images were traced before cineangiography. Beats immediately succeeding premature ventricular depolarizations were excluded from consideration.

Echocardiographic Images

TDEs were recorded using a commercially available, phased-array sector scanner (Varian V-3000) within 24–48 hours of cardiac catheterization. On each patient, two parasternal cross-sectional images — the first at the level of the mitral valve leaflet tips, and the second at the base of the papillary muscles — and one apical view were obtained (fig. 1). The mitral valve view was usually obtained from the third left interspace and the papillary muscle view 1–3 cm inferior and lateral from the mitral valve view. The apical view included all four cardiac chambers in the plane of both mitral and tricuspid valves. All studies were performed with the patient in a semirecumbent position with various degrees of left lateral rotation to optimize image quality. Two-dimensional images were stored on ½-inch tape on a reel-to-reel magnetic videotape recorder (Panasonic NV-3160) and played back on a high-resolution monitor (Conrac SNA-14/c).

Diastolic images were identified from the QRS complex of the simultaneously recorded ECG; systolic images of the same beat were identified from the first high-frequency component of S_2 in the concomitantly recorded phonocardiogram. With stop-frame techniques, outlines of diastolic and systolic images were traced with a light pen digitizer (fig. 2) and analyzed using a computerized system adapted for echocardiographic analysis (Electronics for Medicine VVF). When portions of endocardium could not be recognized from the stopped frame of a single beat, slow and fast playback of the contraction pattern of preceding and succeeding beats provided a further guide to endocardial targets. All images were traced along the innermost edge of endocardial echoes as they abutted the left ventricular cavity.

The parasternal images at mitral and papillary levels were divided by an axis constructed from the midpoint of the septum to the posterolateral wall so as to divide the diastolic image into halves. This was maintained as a fixed reference for systolic images. The diastolic and systolic lengths of this axis and the diastolic and systolic areas at both mitral valve and papillary muscle levels were determined using the computer system.

The long axis of the apical view was constructed separately for diastolic and systolic images as a line from the midpoint of the mitral valve to the apex. The
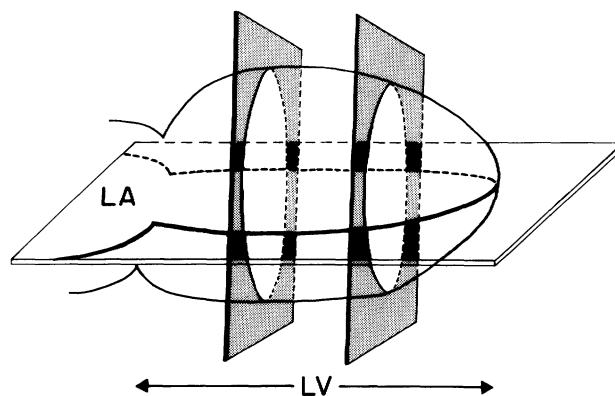

FIGURE 1. *Schematic diagram of the left atrium (LA) and left ventricle (LV), with stippled planes indicating the projection of two-dimensional images. The two vertical planes correspond to transverse sections at the level of the mitral valve and papillary muscles, while the fine-stippled horizontal plane corresponds to an image obtained from the left ventricular apex.*

area and long-axis length of diastolic and systolic apical images were then measured.

The following assessments of the left ventricular function were made (fig. 3).

1) The total EF, end-diastolic volume (EDV) and end-systolic volume (ESV) were calculated from five different algorithms:

Modified Simpson's rule. The left ventricle was considered the sum of a cylinder (from the base of the heart to the mitral valve), a truncated cone (from the level of the mitral valve to the level of the papillary muscles), and below this another cone to the cardiac apex. These three sections were arbitrarily assumed to be of equal height (L/3). The paucity of reproducible landmarks precluded the use of more than three sections (as would ideally be the case in a true Simpson's rule application).

An ellipsoid model using biplane data (after Sandler and Dodge[17]). Two perpendicular echo planes (the mitral valve and apical view) were substituted for two angiographic projections. The apical (horizontal in fig. 1) plane minor (septal-posterolateral) axis is derived from the image area (A_l) and its longest length (L). For this model the mitral plane is arbitrarily assumed to be midway between the base and apex. The mitral (vertical in fig. 1) plane minor axis is derived from the area (A_m) and the septal-posterolateral dimension (D) of the mitral level image.

An ellipsoid model using single-plane data. Area (A_l) and length (L) from the apical echocardiographic image were substituted into the standard single-plane area-length equation.[18]

A hemisphere-cylinder model using biplane data. The cross-sectional area (A_m) at the mitral valve level and long axis (L) from the apical view were used to solve for volume of a cylinder capped on one end by a hemisphere with a base area (A_m) and height (L/2) equal to that of the cylinder.

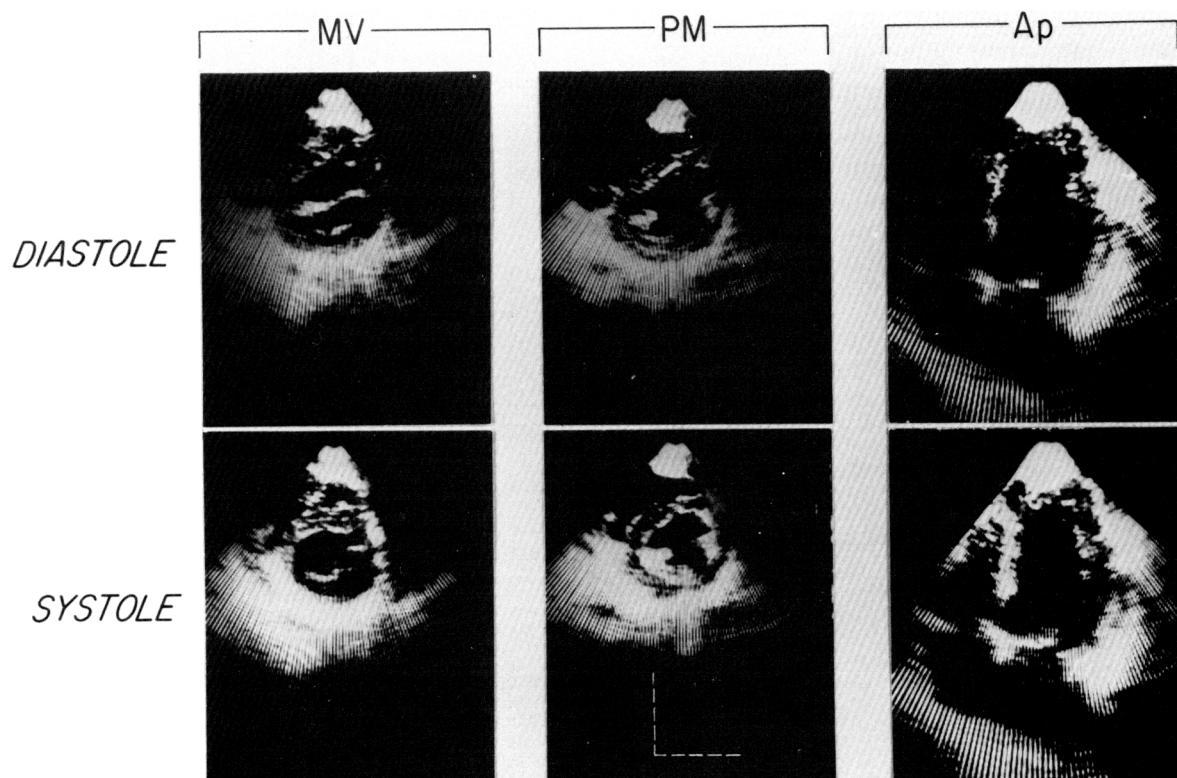*A modified ellipsoid model using unidimensional*

FIGURE 2. *Examples of normal two-dimensional echo images in end-diastole (above) and end-systole (below). The cross-sectional plane is shown at the level of the mitral valve (MV) and the papillary muscles (PM). The apical four-chamber plane (Ap) is oriented so that the left ventricle is to the right. The cardiac apex is at the top and the atria are at the bottom of each apical photo. The calibration lines in the lower middle panel mark 5 cm on each axis.*

data. The septal-posterior wall dimension (D) was substituted into a formula described by Teichholz based upon an ellipsoid model where the major axis

$$2(\frac{7.0}{2.4 + D})D$$

is a variable function derived from the measured minor axis, D. This formula is intended to compensate for the deviation from the ellipsoid model seen in both unusually large and small ventricles.[19]

2) Fractional shortening was calculated from the diastolic and systolic septal-posterolateral axes (D) measured at the mitral level.

Radionuclide Ventriculograms

Cardiac imaging was accomplished during the first transit of a 15-mCi bolus of technetium-99m rapidly injected into an antecubital vein. With a multicrystal scintillation camera (Baird Atomic System 77) in the 45° left anterior oblique position with a 20° caudal tilt, a left ventricular region of interest was defined and a time-radioactivity histogram was constructed during the passage of the bolus through the left ventricle. The beats with maximum activity (usually four or five) were selected and corrected for background activity by subtracting the activity measured over the left ventricular region of interest immediately before radionuclide entry.

The sums of background-corrected activities during diastole (DA) and systole (SA) were used to calculate the EF as follows

$$EF = \frac{DA - SA}{DA}$$

X-ray Cineangiograms

Patients were premedicated orally with 10 mg diazepam before catheterization. Left ventricular cineangiograms, the first part of the procedure to use contrast material, were filmed at 60 frames/sec using a 9-inch image intensifier in the 30° right anterior oblique projection during held inspiration. Forty to 60 milliliters of contrast material (Renografin-76) were injected over 2–3 seconds. Magnification correction was accomplished by filming a metallic grid of centimeter squares at the same level with respect to x-ray tube and image intensifier position as the palpable cardiac apex. A single cardiac cycle showing good opacification and at least one cycle removed from the last premature complex were chosen for analysis. End-diastolic and end-systolic outlines of the projected 35-mm image were traced directly on celluloid from a viewing screen (Vanguard XR-35), including trabeculae and papillary muscles within the outline. The correcting grid was similarly traced. These outlines on celluloid were then televised. Using the same light pen computerized system described earlier, EDV,
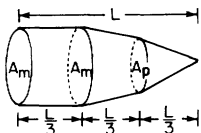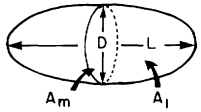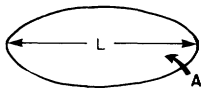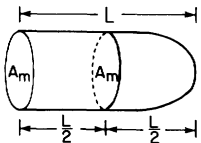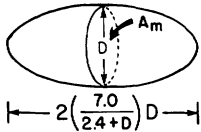
Algorithm | Formulation | Geometric Model

Simpson's Rule

$$V = (A_m)\frac{L}{3} + (\frac{A_m + A_p}{2})\frac{L}{3} + \frac{1}{3}(A_p)\frac{L}{3}$$

Ellipsoid – Biplane

$$V = \frac{\pi}{6} L (\frac{4A_m}{\pi D})(\frac{4A_l}{\pi L})$$

Ellipsoid – Single Plane

$$V = \frac{8(A_l)^2}{3\pi L}$$

Hemisphere – Cylinder

$$V = (A_m)\frac{L}{2} + \frac{2}{3}(A_m)\frac{L}{2}$$

Modified Ellipsoid

$$V = (\frac{7.0}{2.4 + D})D^3$$

FIGURE 3. *Summary of the geometric models and algorithms used to generate left ventricular volume and ejection fraction from two-dimensional echo data. A = area measurements; L = the longest length of the ventricle from the long-axis section; D = the septal-lateral diameter from the high cross section of the ventricle. The subscripts m, p, and 1 refer to the mitral valve, papillary muscle, and long-axis sections, respectively.*

ESV and EF were calculated using the single-plane area-length method and regression equations described by Kennedy et al.[18]

Statistics

Data obtained from each of the above methods were compared by linear and nonlinear regression analysis using standard statistical formulas and a Monroe 325 programmable calculator.

Results

Ejection Fraction

The relationship of TDE EF to radionuclide and cineangiographic EF was highly dependent on the algorithm chosen for analysis (table 1). Formulations involving one or more image areas had clearly superior correlations compared with the Teichholz formula, which depends solely on a linear-axis dimension. Fractional shortening of the left ventricular septal-posterolateral dimension (similar to that commonly measured by M-mode display) correlated even more poorly with cineangiographic EF ($r = 0.34$). The best correlation with RVG and cineangiographic EFs was obtained using the modified Simpson's rule model. The regression relationship of TDE EF predicted by modified Simpson's rule to cineangiographic EF is shown in figure 4 along with a plot of the estimating equation. The correlation coefficient was

0.78 and the standard error of the estimate was 0.097. A similar plot relating the same TDE EF to RVG EF ($r = 0.75$; SEE 0.087) is shown in figure 5. Of the three methods, RVG EF and cineangiographic EF correlated best ($r = 0.88$; SEE 0.073).

Volume Estimations

TDE ventricular volumes computed by the models described had a predictable relationship to cineangiographic volume, with r values of 0.61–0.76 (SEE 52–43 ml) for EDV and 0.64–0.86 (SEE 48–32 ml) for

TABLE 1. *Relationship of Ejection Fractions Determined by Two-dimensional Echocardiography, Cineangiography, and Radionuclide Ventriculography*

Echo algorithm	Cine*		RVG	
	r	(SEE)	r	(SEE)
Modified Simpson's rule	0.78	(0.097)	0.75	(0.087)
Ellipsoid biplane	0.78	(0.098)	0.73	(0.089)
Ellipsoid single plane	0.76	(0.101)	0.71	(0.092)
Hemisphere-cylinder	0.66	(0.116)	0.58	(0.107)
Modified ellipsoid (Teichholz)	0.55	(0.130)	0.46	(0.117)

*X-ray cineangiographic vs RVG ejection fractions (linear regression): $r = 0.88$; SEE = 0.073.

Abbreviations: Cine = x-ray contrast cineangiography; RVG = radionuclide ventriculography.
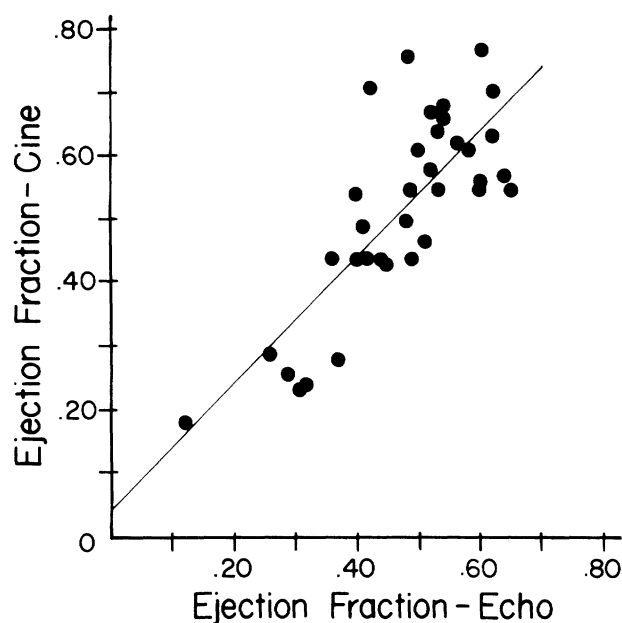
FIGURE 4. Relationship of left ventricular ejection fraction determined by two-dimensional echocardiography, modified Simpson's rule method (horizontal axis), compared with ejection fraction determined by x-ray cineangiography (vertical axis). A regression line corresponding to the equation $y = 1.01x + 0.04$ is shown $(r = 0.78; \text{SEE} = 0.097)$.
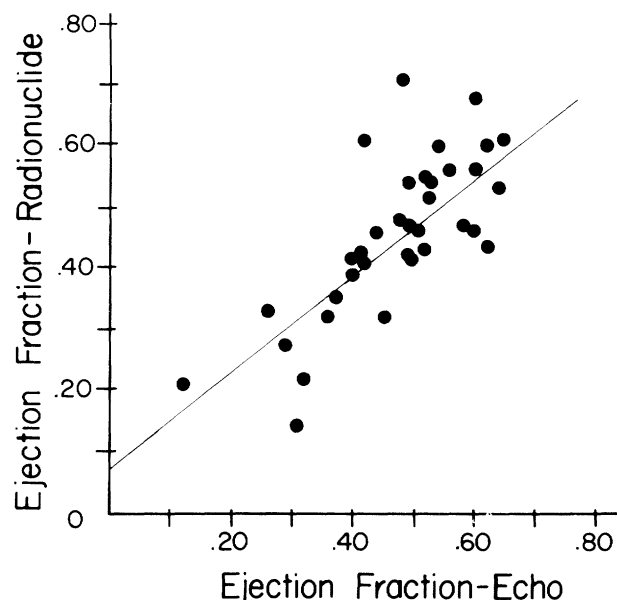

FIGURE 5. Left ventricular ejection fraction determined by two-dimensional echocardiography, modified Simpson's rule method (horizontal axis), and ejection fraction determined by radionuclide angiography (vertical axis) in the same patients. The regression equation is $y = 0.75x + 0.07$ $(r = 0.75; \text{SEE} = 0.087)$.

ESV (table 2). The modified Simpson's rule model produced the best correlation (fig. 6). This approximation systematically underestimated ventricular volumes, as did the other algorithms.

Discussion

TDE, radionuclide and x-ray cineangiographic techniques are fundamentally different approaches to measuring left ventricular function. X-ray cineangiography derives volume and EF from a two-dimensional silhouette of the left ventricle. Volume can be similarly derived from a radionuclide image; however, radionuclide EF is most accurately measured by the time-activity method described earlier and used in this study.[5] TDE is a tomographic method, producing slice-like images of the ventricle along the plane of orientation of the ultrasonic beam. Theoretically, integration of an appropriate selection of "slices" would produce a composite, three-dimensional reconstruction of left ventricular geometry. The approach chosen here is a compromise between limitations of ultrasonic methods and practicality. The 1-cm-wide beam generated by the phased-array scanner allows only a finite number of slices to be taken in transverse or apical orientations. Ventricular landmarks are few, allowing reproducible sampling at a limited number of sites. Imperfect lateral resolution distorts endocardial targets as a function of both depth of field and beam orientation. Accordingly, our approach is the simplest and most pragmatic we could find for this problem. Further refinement of ultrasonic imaging, different

"slice" orientations and different algorithms may be more satisfactory in the future.

The models used rest upon arbitrary and sometimes different assumptions about ventricular anatomy. For instance, two of three models using biplane data assume that the mitral level echo plane is midway between the apex and base of the ventricle. The third model, modified Simpson's rule, assumes that the mitral and papillary muscle echo levels trisect the ventricle equally. The models also assume that the relative position and/or geometry of the involved planes is constant in systole and diastole. Therefore, the value of these models is best judged by the extent of agreement between information derived from each model and analogous information derived from independent standards such as x-ray contrast and RVG.

Accurate assessment of left ventricular function by

TABLE 2. Relationship of Two-dimensional Echocardiographic Volumes to Cineangiographic Volumes

Echo algorithm	Cine EDV*		Cine ESV	
	r	(SEE)	r	(SEE)
Modified Simpson's rule	0.76	(43 ml)	0.86	(32 ml)
Ellipsoid biplane	0.67	(49 ml)	0.72	(44 ml)
Ellipsoid single plane	0.61	(52 ml)	0.64	(48 ml)
Hemisphere-cylinder	0.68	(49 ml)	0.75	(42 ml)
Modified ellipsoid (Teichholz)	0.72	(46 ml)	0.81	(37 ml)

*Cine vs modified Simpson's rule echo (all volumes): $r = 0.84$; SEE $= 43$ ml.

Abbreviations: EDV = end-diastolic volume; ESV = end-systolic volume; cine = x-ray contrast cineangiography.
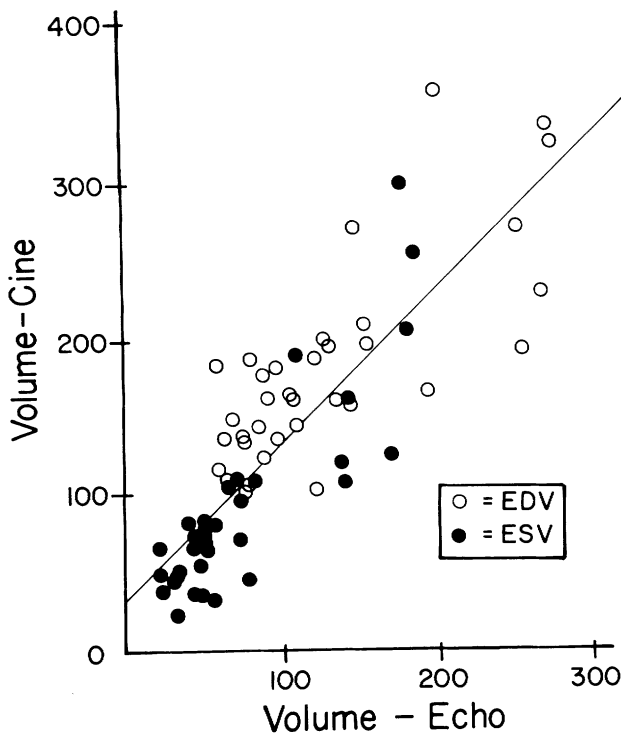
FIGURE 6. *End-diastolic (EDV) and end-systolic (ESV) volumes determined by two-dimensional echocardiography (horizontal axis) compared with left ventricular cineangiography (vertical axis). The regression equation for all volumes is y = 1.02x + 34 (r = 0.84; SEE = 43 ml. See table 2 for further details.)*

ultrasound is an important advance, because the method is totally noninvasive, painless and the risk to patients is theoretical and remote. Moreover, it can be repeated with greater ease than RVG. Correlations between functional indices derived from M-mode ultrasound and x-ray contrast cineangiography have been variable and often disappointing.[19-23] The explanation most commonly given for lack of correlation is nonrepresentative sampling of the left ventricle by the unidimensional M-mode echo beam. This error is especially troublesome in evaluating patients with regional ventricular dysfunction.[19] Global ventricular EF may be either overestimated or underestimated, depending upon whether normal or abnormal ventricular regions are sampled by the echo beam. Another source of error in M-mode methods is the atypical geometry of dilated hearts. Both kinds of error should be considerably reduced by two-dimensional representation of the ventricle with ultrasound sector scanning, particularly if images from multiple section planes are integrated. Our data support this viewpoint, because 20 of our 35 patients had regional contraction abnormalities and eight of 35 patients had ventricular volumes > 200 ml. Although the correlation coefficients of the best methods (modified Simpson's rule and biplane) are only fair (r = 0.78 for both), the standard errors of the estimate (0.097 and 0.098, respectively) compare favorably with the standard error of the estimate between RVG

and cineangiographic EF reported both in this study (0.073) and by other investigators.[5-8]

Our EF correlations are not improved by separate analysis of the subgroup of 15 patients without segmental contraction abnormalities. All of these patients have EFs clustering between 0.48–0.77; hence, there is not enough spread of data points for meaningful correlation in this sample. The volumes in this subgroup are more variable and the modified Simpson's rule algorithm produced slightly improved correlation with cineangiographic volume compared with the total group (0.87 vs 0.84). Considering only the subgroup of 20 patients with contraction abnormalities, the modified Simpson's rule EFs correlate better with cineangiographic EF than does the study population as a whole (0.83 vs 0.78). Modified Simpson's rule volume correlations for this subgroup are slightly less than for the total group (0.80 vs 0.84).

Our correlations might have been improved if it had been possible to compare our TDE data with data from biplane rather than single-plane cineangiography. Some preliminary clinical studies using biplane cineangiographic data have reported closer correlations,[12, 14, 15] but not consistently.[16]

The advantage of TDE over unidimensional echocardiography for approximating cineangiographic EF is seen in the contrast between correlation coefficients derived from two-dimensional representations (r = 0.66–0.78) and those derived from single-dimensional data (r = 0.55 Teichholz formula; r = 0.34 fractional shortening).

Although the standard error of the estimate of our TDE methods is approximately twice that obtained by comparison of single-plane cineangiographic EF with direct biplane radiographic EF (0.04),[20] it was, nevertheless, useful enough to separate normal from severely impaired ventricles (EF < 35%) in 34 of 35 patients when cineangiographic EF was used as a standard and 33 of 35 when RVG EF was the standard.

The correlations between EF determined by various formulations of ultrasound data and EF derived from RVG are remarkably similar to the analogous correlations between ultrasonic and cineangiographic data. Comparison between cineangiographic and RVG EF produced the highest correlation (r = 0.88) and lowest standard error of the estimate (0.073) in this series. Ultrasound examination yields additional information concerning fine anatomic detail and chamber size that is not so readily available from current radionuclide techniques.

The scatter of points was greatest among patients with normal left ventricular function. Among our subjects, TDE appears to underestimate EF relative to cineangiography in the normal range. Several factors may be responsible for this, including inherent systematic errors in both TDE and cineangiographic techniques, as well as unavoidable changes in physiologic state between examinations. Errors from the latter source might be minimized by performing TDE examinations in the catheterization laboratory immediately before angiography, but practical limitations precluded this. Similar wide scatter in the

normal range has been noted in other studies where EFs obtained invasively and noninvasively were compared.[5]

Volumes derived from TDE and cineangiographic methods correlate well, especially when modified Simpson's rule is used to derive TDE volume ($r = 0.76$ EDV and $r = 0.86$ ESV). The scatter of measurements about the regression line is wide, however, and produces a rather large standard error of the estimate (at best 43 ml for EDV and 32 ml for ESV), which is considerably greater than the standard error of the estimate noted when volumes derived from single-plane cineangiography are compared with those derived from direct biplane radiography (21 ml for EDV and 13 ml for ESV).[20] A 95% confidence limit for EDV of ± 86 ml limits the value of TDE volume determinations for patients with normal to moderately increased ventricular size. However, the reproducibility of these measurements in the same subject has not been tested. Should they prove highly reproducible, these measurements could be useful in the longitudinal follow-up of patients in spite of their variability compared with x-ray cineangiography.

A consistent advantage of TDE data over unidimensional data in approximating cineangiographic volumes was not demonstrated. Cineangiographic correlations of volumes derived from the Teichholz model were exceeded only by the modified Simpson's rule correlations, perhaps indicating a need for further refinement of the formulations.

In conclusion, the data presented indicate that TDE can be used as a reasonable predictor of left ventricular EF, particularly when patients with moderate or severe dysfunction are being separated from those with normal or less severely depressed EFs. Volume determinations are more problematic. Though there is a statistically significant correlation between invasive and noninvasive data, the scatter of our results indicates that the current approach is not likely to be highly accurate in estimating ventricular volumes when single-plane x-ray contrast cineangiograms are used as the standard.

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