Anesthesiology
70:470–476, 1989

Measurement of Stroke Volume with Three-dimensional Transesophageal Ultrasonic Scanning:

Comparison with Thermodilution Measurement

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The accuracy of measuring cardiac stroke volume with a new transesophageal phased array ultrasonic probe was investigated in 10 dogs. The method involved scanning the heart to obtain serial images covering the entire left ventricular cavity at end-expiration. An off-line computer analysis of the images was used to form three-dimensional reconstructions of the left ventricular cavity at end-diastole and end-systole, from which stroke volume was determined. Comparison with stroke volume determined by thermodilution during a wide range of hemodynamic conditions gave the following results for least-squares regression on 57 determinations (with the 95% confidence limits in parentheses): slope 0.95 (0.842–1.06), ordinate intercept 2.1 (2.0–2.2) ml, standard error of the estimate 4.1 ml, and correlation coefficient of 0.92 (0.87–0.95). Histologic examination of sections of esophagus surrounding the tip of the probe in nine dogs demonstrated minimal trauma to the esophageal wall, with eight specimens described as normal and one showing mild inflammation. The authors conclude that three-dimensional reconstruction of the left ventricular cavity from multiple transesophageal images offers a safe and accurate, although presently tedious, method for determining stroke volume. (Key words: Heart: cardiac output. Measurement techniques: transesophageal echocardiography; ventricular volume. Ultrasonic imaging.)

TRANSESOPHAGEAL ECHOCARDIOGRAPHY is a relatively new, semi-invasive method of monitoring the heart during surgery. In humans, two-dimensional imaging from the esophagus provides views of the heart that are unobstructed by the lungs or ribs. During anesthesia, the transducer is easily introduced, its position remains stable over time, and it does not interfere with most surgical procedures. Three recent reviews[1–3] and one book[4] illustrate the range of applications of transesophageal echocardiography in anesthesia.

Most of the reported studies of transesophageal echocardiography have involved either qualitative observations or simple diameter or planimetric measurements made from a single imaging plane. Although quantitative measurements of the heart have been made from multiple transcutaneous echocardiograms, the commercially available esophageal probes do not lend themselves to multiple-view reconstruction because their steering apparatus (based on the mechanical shell of a fiberoptic gastroscope) is not precise and provides no means to relate quantitatively the orientation of different images of the heart.

In order to measure left-ventricular volume, we have developed a modified transesophageal probe[5] with a precision micromanipulator and a mechanical–electrical transducer to measure the relative orientation of a series of imaging planes, enabling scanning of the heart to acquire multiple images for three-dimensional reconstruction of the left ventricular cavity by computer (fig. 1). The main purpose of this study was to compare the difference between the volume of the reconstructed cavity at end-diastole and end-systole with the stroke volume determined from thermodilution measurements. A second purpose was to investigate the possibility of injury to the esophagus by the presence of the probe over the course of the experiments.

Methods and Materials

TECHNICAL ASPECTS

Details of the probe design and its performance have been reported elsewhere.[5] Briefly, it is a 32-element 3.5-MHz phased-array probe (Diasonics, Inc., Milpitas, California) that has been modified by addition of a precision micromanipulator at the tip, while preserving the conventional gastroscope controls. A rotation transducer was added to the handle to allow the angle of the imaging plane to be measured as the micromanipulator is adjusted. The imaging plane can be scanned with the micromanipulator over a range of ±30 degrees from the neutral position, with an accuracy of 0.5 degrees (standard error of the estimate). The probe allows recording of a series of cardiac images having a known angular relationship with a Diasonics Cardiovue™ Model 6400 echocardiograph machine.

The image processing system consists of a videotape recorder, circuitry to digitize the selected images and read them into the memory of an IBM AT™–compatible computer, a display for the digitized images, and a "mouse"

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Received from the Departments of Anesthesiology and Bioengineering, University of Washington, Seattle, Washington. Accepted for publication October 7, 1988. Supported by National Institutes of Health grants HL 31413 and HL 41464. Presented in part at the Society of Cardiovascular Anesthesiologists Tenth Annual Meeting, New Orleans, Louisiana, April 1988, and at the American Society of Anesthesiologists 1988 Annual Meeting, San Francisco, California, October 1988.

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pointing device to use in outlining the endocardial borders. After outlining, the computer transforms the endocardial borders into a common three-dimensional coordinate system, and a reconstruction algorithm is then used to compute the volume of the left ventricle at end-diastole and end-systole. Stroke volume is then calculated as the difference between the two volumes. A commercially available three-dimensional modeling software package (ModelMate™, Control Automation Inc., Altamonte Springs, Florida) was also used for three-dimensional display of the endocardial borders or surfaces. The visual display reconstruction algorithm was different than the reconstruction algorithm used for computing volumes.

The algorithm for computing volumes has been described in detail elsewhere.[6] It has the advantage of requiring no assumptions about the basic shape of the ventricular cavity, nor does it require that the endocardial outlines be complete, closed curves. Briefly, it consists of four steps. First, the centroid of all of the endocardial outlines is calculated. A line defining the "major axis" of the ventricle is fit to pass through this centroid, and a new coordinate system is constructed, oriented along the major axis so defined. Next, a series of equally angularly spaced cutting planes are passed through the major axis, in a manner similar to the planes that separate an ordinary orange into its segments. Third, a linear interpolation scheme is used to fit an outer surface to each segment of the "orange," with the use of the relevant points from all of the endocardial outlines. Finally, the volume of each segment of the "orange" is calculated, and the sum of the segmental volumes gives the ventricular volume.

The frames for computer processing are selected from videotape previously recorded in the animal laboratory. For each imaging plane to be processed, a cardiac cycle occurring at end-expiration is first located on the tape. The end-diastolic frame is then identified by synchronization with the R-wave of the electrocardiogram (which is also recorded on the videotape). Similarly, the end-systolic frame is located by visually searching for the frame having the smallest ventricular outline within that cardiac cycle.

In outlining, the following procedure is used to compensate for the distortion of the ultrasound image caused by the finite duration of the ultrasonic pulses transmitted by the echo machine. Ideally, the indicated position of the endocardial border will be at the leading edge of the propagating wave when it makes the transition either from the endocardial wall to the cavity or from the cavity to the wall. However, with finite duration pulses, the leading edge echo for wall-to-cavity transitions is hidden by echoes that continue to occur at the border until the remainder of the propagating pulse passes it. Consequently, it is the trailing edge of the propagating wave that appears as the innermost echo when the beam makes a wall-to-cavity transition, whereas the innermost echo is the leading edge of the propagating wave for a cavity-to-wall transition. Therefore, the most accurate method of outlining takes these considerations into account and has come to be known as the "leading-leading" method.[7] The method is applied by manually tracing the border for wall-to-cavity

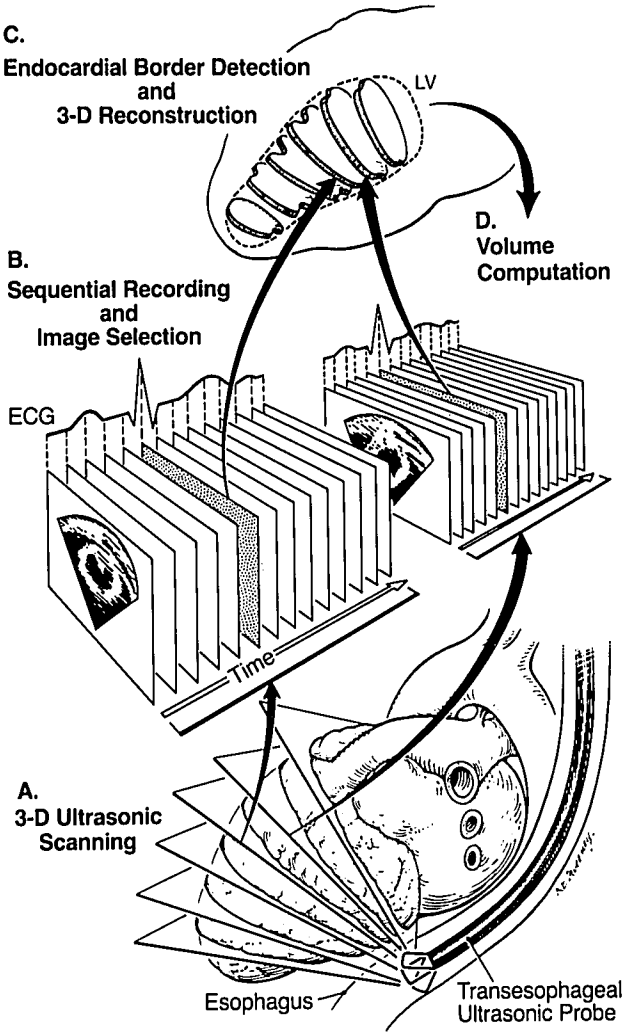

FIG. 1. The method of three-dimensional scanning of the heart and image selection for volume computation. *A.* The probe is located in the esophagus adjacent to the heart and is adjusted to give a series of imaging planes for the three-dimensional reconstruction. *B.* The ultrasonic phased array scans a sector of each imaging plane, generating a sequence of 30 cross-sectional images per second, which are recorded on videotape. At least one full cardiac cycle is recorded for each plane. Afterward, the end-diastolic frame of each imaging plane is selected for reconstruction by using the recorded electrocardiogram for time synchronization. (The end-systolic frame is selected by visually searching for the one with the minimum cross-sectional area.) *C.* The endocardial border is outlined on each selected image and it is positioned in space by the computer, using the imaging plane angle read from the controls of the ultrasonic probe. *D.* The volume of the left ventricle is then calculated with the use of the reconstruction algorithm.

transitions as occurring slightly towards the transducer location, whereas for cavity-to-wall transitions the border is identified as being precisely at the edge in the image. Where the ultrasonic beam passes tangentially to the endocardial border, there is a tendency for "drop-out" of the image to occur. In that case, we manually interpolated the missing border segment, although our volume computation algorithm does not require that each border outline be a closed contour.[6] Finally, the papillary muscles were excluded from the cavity in our outlining procedure and considered to be part of the ventricular wall.

Animal Study

With institutional review board approval, 10 dogs of 27 kg average weight were studied. After induction of anesthesia with intravenous sodium thiopental, the dogs were paralyzed with pancuronium, their tracheas intubated, and their lungs mechanically ventilated. Anesthesia was maintained with 1–2% halothane in oxygen.

A surgical preparation was necessary to eliminate acoustic interference from the accessory lobe of the right lung, which ordinarily makes it impossible to obtain short-axis transesophageal echocardiograms in the dog. This lobe is interposed between the posterior wall of the left ventricle and the esophagus in all common laboratory animals[5,8] but is not present in humans or the great apes.[9,10] Through a right thoracotomy, the accessory lobe was retracted with umbilical tape, the septum posterior to the heart between the dog's pleural cavities excised, and the resulting space filled with saline solution. With the use of this technique, no difficulties were encountered in obtaining short-axis views in any of the animals studied.

Acoustic gel was spread over the probe before it was passed into the esophagus. Occasionally resistance was met at the thoracic inlet, but by application of pressure to the animal's sternum, the probe could then be passed into the chest. When the transducer array reached the vicinity of the left atrium, the heart came into view, and by tilting the array slightly in the caudad direction, an excellent long-axis view was obtained. After the micromanipulator was readjusted to the neutral position, the probe was further advanced until a short-axis view of the heart was obtained at the level of the middle of the papillary muscles. Tilting the tip of the probe anteriorly with the main gastroscope controls usually improved the image quality, presumably because it applied the ultrasonic array more tightly to the esophageal wall. The heart was then scanned with the micromanipulator (see fig. 1) to determine whether the field of view from that probe position would encompass the entire left ventricle. If not, the micromanipulator was returned to neutral and the probe was repositioned. This process was repeated until the complete ventricle could be imaged, from the mitral valve to the apex, by sweeping the micromanipulator control. Positioning was usually accomplished within 3 min.

Images of oblique sections of the heart were taken at approximately every 3-degree increment of angulation, resulting in 12–15 images for each stroke volume determination. Recordings were made only under stable hemodynamic conditions during the expiratory phase of respiration, with the lungs at their functional residual capacity. Adjusting the micromanipulator to obtain a new imaging plane required only 1 or 2 s to perform, so it was possible to record one imaging plane for each cycle of the ventilator.

Cardiac output was manipulated by administration of intravenous fluids, by inflation of a balloon catheter positioned in the inferior vena cava, and in some cases, by drug administration. Initially each animal was given 500 ml of 6% dextran 70 solution intravenously to increase the cardiac output. The balloon catheter (Meditech® U OBW-40-8-2-100) was then incrementally inflated with saline to decrease venous return to the heart and diminish the cardiac output in a graded fashion. In some animals, xylazine (1 ml/kg) and propranolol (titrated in 1-mg increments) were administered to further alter the hemodynamics.

Thermodilution cardiac output determinations were made immediately before and after each ultrasonic scan, with the use of a standard Swan-Ganz™ catheter, 10 ml of iced 5% dextrose solution, and an American Edwards Laboratory Model 9502A® cardiac output computer. For each thermodilution determination, at least four measurements were made. The first was discarded (because of the loss of indicator in cooling the catheter). The succeeding measurements were all made with the lungs at end-expiration. Three sequential measurements were averaged, and if there was a more than 5% deviation between the measurements, additional injections were made. If the thermodilution cardiac output determinations made before and after ultrasonic scanning differed by more than 15%, the animal was considered not to be hemodynamically stable, and that trial was discarded. A trial was also discarded if the heart rate varied by more than 10% during the course of data collection or there was a prevalence of premature beats. Stroke volume was then calculated by dividing the cardiac output by the heart rate averaged over the duration of the scan. Statistical comparison between the two methods was made by linear least-squares regression.

Evaluation of the Effect of the Probe on the Esophageal Wall

The exposed tip of the micromanipulator moves against the esophageal wall during adjustment of the imaging plane, raising the question of whether it may cause injury

to the wall. To address this concern, postmortem examination was performed in nine of the dogs after they were killed with a barbiturate overdose upon completion of the experiments, when the probe had been in place for 4.3 ± 1.8 h (mean ± SD).

The location of the tip of the probe in the esophagus was palpated through the open chest, its position was marked, and the probe was then removed. A 4-cm section of the esophagus on either side of the mark was excised. It was opened longitudinally along the dorsal midline, pinned to paraffin at its original length, and fixed for 24 h in a sodium acetate buffered 30% formaldehyde solution. Histologic sectioning, staining, and light microscopic examination were performed by the Comparative Pathology Laboratory, Division of Animal Medicine, at the University of Washington. Random sections were taken from each specimen over the region where the probe had been located. These were examined by a veterinary pathologist and also reviewed by a human pathologist experienced in gastrointestinal histology.

Results

The probe position remained stable throughout the studies (2–7 h), and full scans of the left ventricle were obtained in all of the animals. In one, the probe position was observed with fluoroscopy and the body of the probe was found to remain stationary as the micromanipulator was adjusted. There was some longitudinal cyclic movement with respiration, but it appeared as though the heart moved with the probe during diaphragmatic excursion. By analysis of only the images taken at end-expiration, any effect of respiratory movement was minimized.

A representative pair of end-diastolic and end-systolic endocardial surfaces reconstructed from the ultrasonic outlines by the three-dimensional solid modeling software is shown in figure 2. The scattergram comparing 57 ultrasonic determinations of stroke volume with those determined by thermodilution is shown in figure 3. The least-squares regression results are as follows (with the 95% confidence intervals shown in parentheses): ordinate intercept, 2.1 (2.02–2.24) ml; slope, 0.95 (0.84–1.06); and correlation coefficient, 0.92 (0.87–0.95). The standard error of the estimate was 4.1 ml.

The findings of histologic examinations were reported as entirely normal in seven animals. In an eighth animal, the first examiner suspected mild submucosal edema but also thought it could have been an artifact of preparation. The second examiner interpreted the slides from that animal as normal. In the ninth animal, the diagnosis was moderate esophagitis. The accompanying comment by the first examiner was that "the damage seen in the esophagus is consistent with what we have associated previously with intubation procedures of luminal surfaces

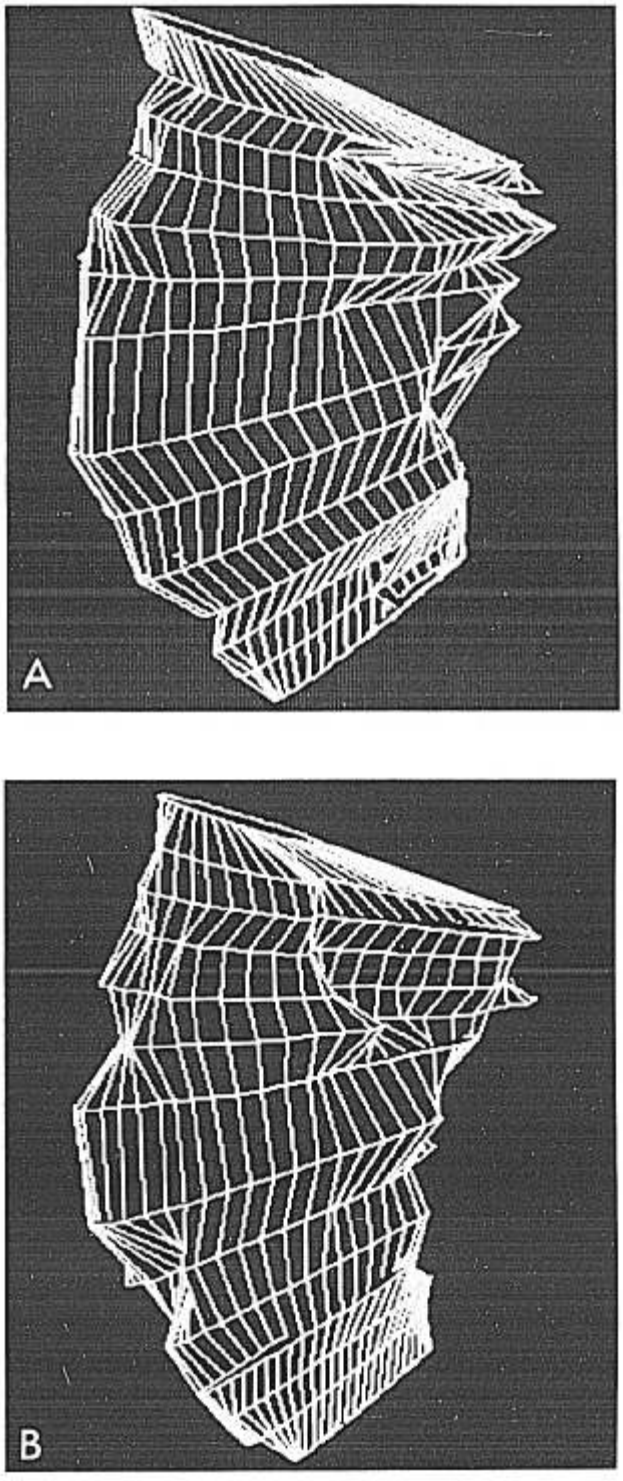

FIG. 2. A computer-generated reconstruction of the endocardial surfaces of the left ventricle of one dog. The upper image (*A*) is taken at end-diastole and lower (*B*) at end-systole of the same cardiac cycle from approximately a left posterior oblique viewpoint. The aortic valve annulus is located in the upper left portion of the images. The stroke volume determined from these two volumes was 22.8 ml, compared with a value of 17.2 ml determined by the thermal dilution method.

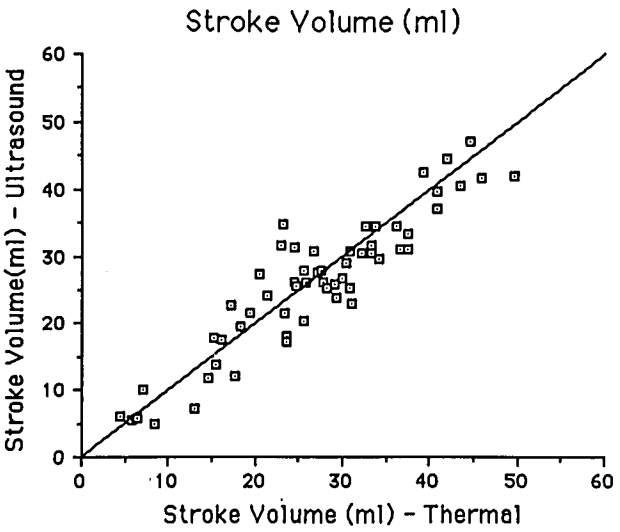

FIG. 3. Scattergram of the ultrasonic stroke volume determinations *versus* those made by thermodilution. Each ultrasonic stroke volume was calculated as the difference between the corresponding end-systolic and end-diastolic volumes. Each thermodilution stroke volume was calculated by taking the average of three thermodilution cardiac output measurements divided by the average heart rate during each measurement. The line shown is the line of identity.

such as the esophagus and trachea." The second examiner concurred with this report. Finally, the second examiner reviewed the histologic sections to determine whether the muscularis propria at the level of the tip of the probe consisted of skeletal or smooth muscle. The muscle was found to be skeletal muscle in all specimens.

Discussion

Our results demonstrate the feasibility of measuring stroke volume by three-dimensional reconstruction from multiple transesophageal images. In assessing the accuracy of our measurements, one must consider the errors of the comparative thermodilution measurements. Levett and Replogle[11] reviewed the accuracy of thermodilution reported in 20 *in vivo* studies and concluded that the typical error of the method is in the range of 15–20%. Stetz *et al.*[12] recently reviewed 14 clinical studies of the accuracy and reproducibility of thermodilution. They concluded that if three measurements are averaged for each cardiac output determination, a change in cardiac output between two determinations must differ by 12–15% to be considered of clinical significance. Our measurement accuracy is similar to that of these reports, and improvement could be anticipated from using one of the newer, high-resolution imaging systems working at 5 MHz.

The analysis of the recorded images is very time consuming. It involves first searching the videotape to locate the frame of interest and keying into the computer information about the scan angle and whether the image is diastolic or systolic. Then the endocardial border is outlined with the use of a "mouse" pointing device. Finally, the computer combines the appropriate outlines into three-dimensional reconstructions and calculates their volumes. The whole process takes approximately 30 min to determine one stroke volume, so our method is presently suitable only for research studies.

If ultrasonic measurements of stroke volume are ultimately to be used for acute patient management, the process of acquiring multiple images and reducing the data will need to be automated. As a first step toward this goal, the process of selecting the frames for processing can be automated by encoding directly on the videotape the occurrence of the R-wave of the electrocardiogram, the second heart sound, the airway pressure, and the angle of the micromanipulator. Commercially made encoding equipment for broadcast television use can be adapted for this purpose, and it would reduce the analysis time by at least a half.

The problem of automatic endocardial border detection must also be solved. Encouraging results have been obtained by several investigators in analyzing diagnostic echocardiograms.[13,14] With the increasing speed and decreasing cost of microcomputers and the continuing improvements in ultrasonic image quality, it is reasonable to expect that within a few years it will be possible to process multiple images rapidly enough to make the information available for acute clinical decision making.

Others have suggested using a single short-axis view of the heart at the level of the midpapillary muscles for the purpose of monitoring the filling volume, ejection fraction, and abnormalities of wall motion.[1–3] However, the shortcomings of single plane measurement are well-recognized when the heart is dilated or has wall motion abnormalities.[15] In addition, it may not be possible to obtain a true short-axis view from the esophagus in patients with a large or horizontally situated heart.[16] Finally, calculations based upon one imaging plane are subject to error because the orientation of the plane with respect to the heart changes as the heart rotates and translates in the chest during cardiac cycle.[17]

The three-dimensional reconstruction technique has the important advantage that it does not require direct comparison between the endocardial outlines obtained at end-systole and end-diastole in any of the individual imaging planes. Instead, one set of images is used to calculate the diastolic volume, whereas another set of images (which have somewhat different orientation because of cardiac motion) is used to calculate the systolic volume (*e.g.*, fig. 2). Furthermore, because the reconstruction method used is not based upon any assumptions about the shape of the ventricular cavity,[6] it should perform well in the presence of cardiac dilatation or segmental wall motion abnormalities.

Our observation of the probe by fluoroscopic examination supports the one inherent assumption in the method: that the position and orientation of the body of the probe remain fixed when acquiring all images used in a given three-dimensional reconstruction. The reconstructed endocardial surfaces shown in figure 2 further support this assumption, as have other endocardial surfaces we have reconstructed. For example, a shift in the position of the probe during the acquisition of the data for a volume determination would appear as a slippage or disruption in the orientation of the "slices" making up the reconstructed visual image. Little of this is apparent in figure 2. On the other hand, any movement of the transducer between end-diastolic and end-systolic volume determinations would only cause the heart to be viewed from a slightly different perspective and should not have any major effect on the accuracy of the individual volume determinations.

Another feature of ultrasonic scanning is that the end-diastolic and end-systolic left ventricular volumes are individually determined, allowing use of these quantities themselves‡ and allowing calculation of the ejection fraction. The end-diastolic volume can be used as a direct measure of myocardial preload.[18] Pulmonary artery-occluded pressure is presently used to assess preload in the clinical setting, but it is subject to error because the compliance of the left ventricle is nonlinear[19] and varies between subjects.[20] Several reports show poor correlation between pulmonary artery–occluded pressure and end-diastolic volume,[20–22] and having a direct measurement of myocardial preload may improve patient management. The end-systolic volume, in conjunction with the end-systolic ventricular pressure, may provide a useful measure of contractility that is independent of preload.[23] Although still investigational, this approach has been reported to be sensitive to inotropic agents, global depression of contractility, and ischemia.[23–26] Although left-ventricular ejection fraction has not been available previously for monitoring purposes, it has been shown to be of significant prognostic value in the critical care setting[27,28] and in patients with severe left-ventricular dysfunction.[29] Finally, we are investigating the possibility that numeric reconstructions of the left-ventricular cavity through the cardiac cycle can be used to assess regional wall motion abnormalities. The use of three-dimensional reconstruction may overcome some of the difficulties in assessing wall motion from a single imaging plane.[17]

The safety of one commercially made transesophageal probe has been demonstrated in more than 800 patients at one center.[1] Persistent hoarseness has been the only adverse effect reported (in two patients having craniotomies while in the sitting position with their necks in nearly full flexion).[30] A mild degree of esophageal mucosal injury was seen in one, or possibly two, of our nine specimens. Although no comparative specimens were collected from animals in which the standard commercially made transesophageal probe was used, the degree of injury found was reported as consistent with that of other esophageal intubation procedures. Because these did not extend into the muscular layers, they would probably be of no clinical significance.

Furthermore, we believe that our use of the new probe in dogs constitutes a more strenuous test than it would in humans. The dog's heart is angulated away from the esophagus, making it necessary to use the standard gastroscope controls to accomodate for the divergence. This maneuver applied more force to the esophageal wall than would probably be necessary in humans. Of further interest is the finding that the muscularis propria in the dog is entirely composed of skeletal muscle at this level, whereas in humans it is mostly smooth muscle. Thus, the esophagus of the dog will lose most of its tone under the influence of muscle relaxants and anesthetics, whereas in humans we expect that more esophageal tone will remain, making for better contact between the esophageal wall and the probe without applying so much force *via* the gastroscope controls. Considering all these factors, we believe that this probe design will be safe for human investigation.

The authors thank Michael Nessly for his diligent help in the animal laboratory; Robert G. Russell, B.V.Sc., Ph.D., and his staff at the Comparative Pathology Laboratory, Division of Animal Medicine, for performing the histologic analysis; and Rodger C. Haggitt, M.D., Department of Pathology, for a second review of the histologic findings and analysis of the mucularis propria. They also thank Kate Sweeney for her fine work in illustrating figure 1.

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‡ The accuracy of measuring these volumes individually has not as yet been evaluated. Indeed, any systematic error present in the calculation of end-diastolic and end-systolic volumes would disappear upon taking their difference to calculate the stroke volume.

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