Accuracy of Left Ventricular End-Diastolic Dimension Determinations Obtained by Radionuclide Angiocardiography

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This study tested the ability of first-pass radionuclide angiocardiography to detect accurately the left ventricular endocardial surface of the intact, conscious, chronically instrumented dog. A spherical phantom was used to define the influence of collimation: with a 1.0-in. collimator, the optimal count threshold was a border at 31% of the image's maximum counts; and with a 1.5-in. collimator, the optimal count threshold was at 21%. These were used to analyze cardioscintigrams obtained in 19 studies of six dogs. The dogs were provided with pulse transit sonomicrometer dimension transducers on the endocardium, right-atrial pacing electrodes, electrocardiographic leads, and catheters in the superior vena cava and right or left atria. The minor-axis dimension of the left ventricle was measured ultrasonically while the cardioscintigram was being stored. The minor-axis dimension and end-diastolic volume obtained by the two techniques had linear correlation coefficients of 0.95 and 0.98. This correlation indicates the inherent accuracy of radionuclide techniques by defining left-ventricular endocardial edges for a large range of volumes in the dog (18–44 ml).

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Measurements of cardiac chamber volumes have been made using first-pass radionuclide angiocardiography. These measurements of left-ventricular end-diastolic volume have been reproducible and have correlated well to those derived from contrast ventriculograms (*1*,*2*). Another technqiue for measuring ventricular dimensions uses dimension transducers, i.e., sonomicrometer crystals implanted on the endocardial surface of the left ventricle. These transducers have been shown in animals to reflect accurately dimension and volume changes in a variety of physiologic states (*3–5*). The purpose of this investigation was to compare measurements made by this highly accurate in vivo method with dimensions derived from scintigraphic images of the left ventricle. Initial observations were made on a spherical phantom to define parameters of data acquisition and to display those that were most likely to define the endocardial edge on a scintigram. The method confirmed by phantom studies was then applied to in vivo radionuclide measurements in animals with chronically implanted sonomicrometer dimension transducers.

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METHODS

Phantom studies. A spherical rubber ball (phantom) with a 2-mm wall thickness and a 5-cm internal radius was filled with 350 ml of water containing 5 mCi of pertechnetate (Tc-99m). A sheet of Plexiglas 1/4-in. thick was placed on the detecting surface of a multicrystal gamma camera.* A series of images were obtained with the phantom placed on the Plexiglas, then one-fourth of an inch from the collimator surface, then with the phantom suspended in air at 1, 2, and 3 in. from the collimator. Using the 1.0 and the 1.5-in. multihole collimators, the phantom was imaged with counting times ranging from 10–250 msec in 10-msec steps, to provide a series of measurements with a range of total counts.

Data processing was begun on the images with the

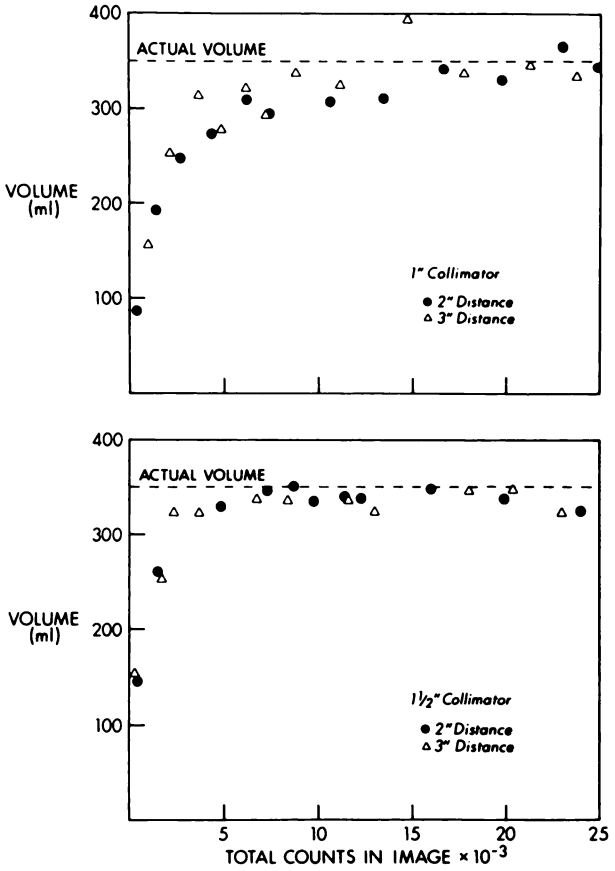

FIG. 1. Plot of estimated volume of spherical phantom as a function of total counts in image using either 1.0- or 1.5-in. collimator. Phantom's true volume was 350 ml.

highest total counts by isocount images for each 5% count level from 0–70%. The areas enclosed by the outer borders of these images were measured with a sonar digitizing GrafPen connected to a computer. The radius of the circular image was derived from the relationship $A = \pi r^2$, and this radius was used to calculate the volume of the spherical phantom, $V = 4/3\ \pi r^3$. This initial process showed that to measure the volume accurately the "best border" was that defined by a threshold at 31% of the maximum counts in the images obtained with a 1.0-in. collimator, or at 21% of the maximum in the images obtained with the 1.5-in. collimator (Fig. 1). Thereafter, all images of the spherical phantom were processed using these ranges to define the border. Volumes were calculated from images obtained at different total counting rates and at different distances from the two collimators (Fig. 2).

Animal studies. *Preparation of chronically instrumented animals.* Six mongrel dogs (20–26 kg) underwent sterile median sternotomies with implantation of pulse-transit sonomicrometer dimension transducers† (resonant frequency 5 MHz), bipolar right-atrial pacing electrodes, and a catheter‡ to the right or left atrium. The left-ventricular transducers, 3 mm diameter, were placed on the endocardium through ventricular puncture wounds (Fig. 3). When viewed in anterior projection, the crystals were in the minor-axis dimension (*3,4*). Using an anterior midline cervical incision, a catheter‡ was placed in the superior vena cava through the external jugular vein. Electrocardiographic electrodes were implanted subcutaneously in the right shoulder and left hip. The leads and catheters were tunneled through the skin and secured at the base of the neck. The catheters were filled with heparin (1000 IU/ml). The chest was closed, and air and blood drained through a chest tube. The dogs received procaine penicillin and dihydrostreptomycin intramuscularly for seven days following surgery.

Data acquisition. After a minimum recovery time of 14 days following surgery, the dogs were brought to the laboratory and trained to lie quietly on the collimator. Nineteen studies were obtained from the six dogs during the series of interventions that were performed to provide a wide range of end-diastolic volumes and heart rates. The heart rate was controlled by atrial pacing with a 5-msec pulse (10% above threshold) using a programmable digital stimulator with its output passed to an isolator. Pacing at a constant rate ensured that the diastolic filling time for each beat during the study would be the same. Consequently, left-ventricular end-diastolic dimensions and volumes for each beat during any intervention would be approximately constant, thereby minimizing problems related to averaging.

The dimension transducers were directly coupled to the sonomicrometer. The minimum resolution of the system was 0.05 mm, and electronic drift was less than 0.05 mm/hr (*5*). The sonomicrometer data were monitored on an oscilloscope while being recorded on an oscillographic recorder (frequency response 1000 Hz, paper speed 5 in/sec). The signals were calibrated with an internal time delay.

To produce changes in end-diastolic dimension and volume from the control values, the following interventions were performed: infusion of methoxamine (16 μg/kg-min, n = 4), isoproterenol (0.05 μg/kg-min, n = 3) and 0.9% NaCl 500–600 cc (n = 5).

During each intervention, left-ventricular end-diastolic dimension was monitored with the sonomicrometer to determine whether it was being progressively altered by the intervention. When no further change in dimension was observed, the scintigram was obtained in the anterior projection while the sonomicrometer dimension was recorded.

For each cardioscintigram, 10 mCi of pertechnetate (Tc-99m) were injected through the right or left atrial catheter, and counts were recorded at 100-msec intervals for a 30-sec period using a computerized, multicrystal gamma camera with a 1.0-in. collimator. A 30-sec measurement of background was obtained for correction of each serial image. After the completion of the series of experiments, each dog was killed and an autopsy performed. In all dogs the sonomicrometer crystals were

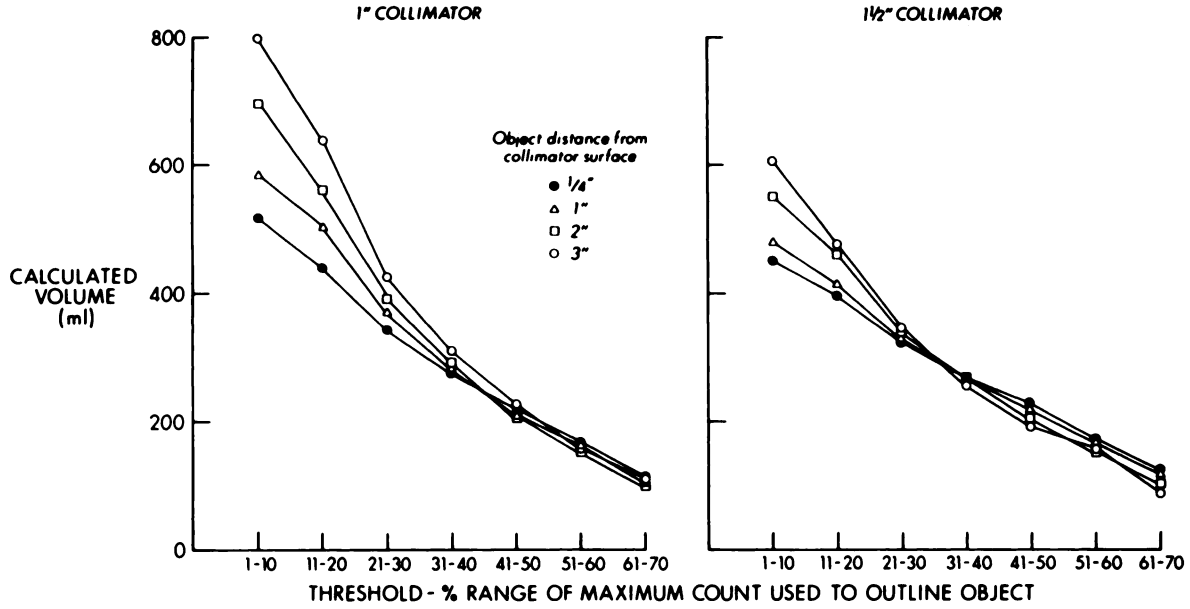

FIG. 2. Calculated volume of spherical phantom using different thresholds for the borders, expressed as a function of maximum counts in image, at different distances from collimator. 1.0-in. collimator (left); 1.5-in. collimator (right).

found to lie flat against the endocardial surface, facing each other across the minor axis of the left ventricle (Fig. 3).

Data analysis. The ultrasound signal obtained from the ventricular dimension transducer was converted to millimeters by using the calibration provided in each experiment by the interval time-delay calibration signal, together with the known velocity of sound through blood (1.5 mm/μ sec). The interval time delay provided lines on the oscillographic paper representing left-ventricular dimensions in steps of 1.5 mm. These data were analyzed by one of us (PAWA) without knowledge of the radionuclide angiocardiographic results. Following the analysis of the angiographic information by another investigator (SKR), the results were compared.

All radionuclide angiocardiogram data were processed using the software developed at this institution and subsequently incorporated into a commercial package.* Details of this processing have been published previously (*6*,*7*). The time-activity curve for the left ventricle was used to identify times of end diastole (ED) and end systole (ES) as the tracer bolus passed through the left ventricle. Data from three to six individual beats were superimposed while retaining their basic relationship to the cardiac cycle. This resulted in a single average or representative cardiac cycle. A computer program outlined the ED perimeter at the 21% isocount contour of the ED image. The plane of the aortic valve was identified from dynamic images and by isolation of the zone demarcating alternate count increases and decreases during diastole and systole. The area and length of the ED image were obtained using a sonic digitizing device (GrafPen) coupled to the computer.

The end-diastolic volume (EDV_{RNA}) was calculated from an ellipse of revolution (A) modified for the single anterior plane projection (*6*,*8*),

$$EDV_{RNA} = \frac{0.85\,A^2}{L_m}, \qquad (1)$$

where L_m is the longest length in the major axis of the left ventricle in the scintigram. The radionuclide minor axis (D_{RNA}) was derived by the formula for the (measured) area of the ellipse and the value of L_m,

$$D_{RNA} = \frac{4A}{\pi L_m}. \qquad (2)$$

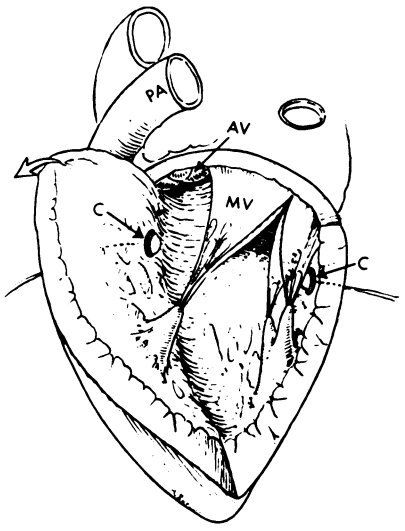

FIG. 3. Left ventricle of dog, viewed with anterior papillary muscle toward left and posterior to right. C, endocardially placed sonomicrometry dimension transducers; PA, pulmonary artery; AV, aortic valve; MV, anterior leaflet of mitral valve.

The radionuclide-derived, minor-axis end-diastolic dimensions (D_{RNA}) were correlated with those measured by sonomicrometry (D_s) (see Fig. 4).

The sonomicrometer-derived, end-diastolic minor-axis dimension (D_s) was combined with the radionuclide-derived, major-axis dimension (L_m) to determine end-diastolic volume, EDV_s, using sonomicrometer data, in the following manner:

$$A_s = \frac{\pi}{4} D_s L_m \quad (3)$$

$$EDV_s = 0.85\, A^2{}_s / L_m. \quad (4)$$

The end-diastolic volume obtained, in part, with sonomicrometry data (EDV_s) was compared with the end-diastolic volume obtained with the radionuclide angiocardiogram, EDV_{RNA} (Table 1), with the realization that the derived volumes are interdependent.

Statistical methods. Sonomicrometer and radionuclide measurements were compared by a linear least-squares regression analysis. The mean and standard deviation of the difference between the measurements were obtained as an index of agreement.

RESULTS

Phantom data. The calculated volume of the spherical phantom outlined by different activity ranges was compared with its actual volume (Fig. 1). Using a 1.0-in. collimator, the best correlation with the true volume of the sphere was obtained with an activity level range from 31–40%. The 1.5-in. collimator provided the best volume correlation with an activity level range of 21–30%.

Variation in calculated volume of the phantom as a function of distance was less in measurements using the 1.5-in. collimator than with those using the other. The effect of total image counts on the accuracy of calculated volumes of the sphere was assessed using the 1.0-in. and the 1.5-in. collimators with the phantom at distances simulating those encountered in cardiac studies in man (Fig. 2). Accurate volume estimation required at least 5000 counts using the 1.5-in. collimator and 10,000–15,000 counts for the 1.0-in.

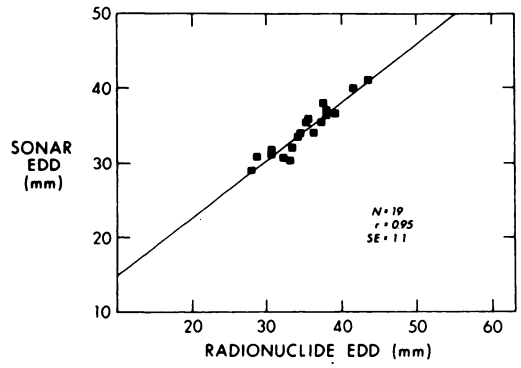

FIG. 4. Minor-axis dimension of left ventricle, as measured by sonomicrometer ($sonar_{EDD}$), plotted against same dimension derived from scintigram ($radionuclide_{EDD}$). r = coefficient of correlation from linear regression analysis.

Chronically instrumented animals. The endocardial minor-axis dimension determined from sonomicrometer measurements compared well with that derived from the radionuclide angiocardiogram (Fig. 4). The mean and standard deviation of the differences between the measurements was 1.8 ± 2.7 mm. In all of the animals the radionuclide and the sonomicrometer minor-axis dimensions (D_s and D_{RNA}) were within 8% of each other over the wide range of end-diastolic volumes and heart rates (Table 1).

The end-diastolic volume determined with the sonomicrometric minor-axis dimension (D_s) and the radionuclide long-axis dimension (L_m) correlated well with the radionuclide angiocardiographically derived volume (Table 1).

DISCUSSION

Radionuclide technology has been widely used to determine left-ventricular volume. Several laboratories have demonstrated that these volume estimates are quite similar to those determined from left-ventricular cineangiocardiograms obtained at cardiac catheterization (*1,2,6*). However, contrast ventriculograms themselves may not accurately reflect the endocardial surface because of incomplete mixing of dye with blood near the chamber wall (*9*). Moreover, comparison of the volumes obtained by the two techniques has been done only in resting subjects with a slow heart rate. A major advantage of the radionuclide technique is that the relatively noninvasive nature of the procedure permits determinations during drug or exercise interventions, which often result in a rapid heart rate and smaller ventricular volume. Moreover, the present use of the end-systolic pressure-volume relationship (*10,11*) as a descriptor of ventricular function may lead to the use of radionuclide techniques to provide good estimates of end-systolic volume. These facts emphasize the need to compare measurements derived from radionuclide images with those obtained simultaneously by a technique that accurately locates endocardial surface over a variety of physiologic conditions and ventricular volumes.

Our approach to testing the accuracy of detection of the edge of the left-ventricular blood pool by radionuclide techniques required definition of optimal techniques of data acquisition and processing. A spherical phantom was counted using ¼-in. Plexiglas to simulate scatter conditions in the normal dog's chest wall. The purpose of the phantom study was to define parameters of image acquisition and processing that were most likely to provide accurate in vivo measurements. The influence of total counts per image, collimator thickness, and distance of the phantom from the collimator were documented.

TABLE 1.

Dog	D_S*	D_{RNA}*	EDV_S*	EDV_{RNA}	Heart rate	Intervention
1	30.5	33.1	27	32	112	Control
	31.4	30.7	27	26	148	Isoproterenol
	33.6	34.3	40	42	88	Methoxamine
2	32.1	33.4	28	31	148	Control
	35.6	35.4	44	43	130	Methoxamine
	34.0	34.5	31	32	130	Control
	30.9	32.2	28	31	220	Isoproterenol
	37.1	38.0	38	40	60	Methoxamine
3	34.0	36.3	28	33	146	Control
	38.0	37.6	38	37	122	Saline
4	40.0	41.6	63	68	118	Control
	41.1	43.6	58	65	180	Saline
5	31.8	30.6	23	22	130	Control
	36.8	39.2	33	38	115	Saline
6	35.5	37.4	37	41	120	Control
	36.7	38.0	37	40	156	Saline
	30.9	28.7	23	20	120	Control
	29.0	27.9	18	17	200	Isoproterenol
	36.6	35.6	44	43	52	Methoxamine

* $D_s \geq$ end-diastolic minor axis by sonor crystal (mm); D_{RNA} = same dimension by scintigram (mm); EDV = end-diastolic volume (ml).

The 1.0- and 1.5-in. collimators were used, since they provided adequate sensitivity for use in dynamic cardiac studies by this instrument. The 2.5-in. collimator that has a high resolution does not provide enough counts to be of clinical relevance for cardiac studies. Border definition by isocount contours required definition of an optimal activity range that most accurately outlined the projected edge of the tracer pool. This optimal activity range is unique to the specific instrument used and would require definition for other counting situations. Phantom studies showed that accurate border definition requires a minimum of 5000 total image counts, and this requirement was easily met using five cardiac cycles in all the dogs. Image quality in patient studies using this instrument has been shown to deteriorate when total image counts fall below 5000 (*11*). The total number of image counts necessary to provide accurate endocardial definition might be less in studies using instruments with better intrinsic spatial resolution.

Left-ventricular dimension transducers accurately delineate the ventricular chamber and have been used previously to estimate left-ventricular volume (*3,4*). Therefore, comparisons of left ventricular dimensions obtained by this technique with those simultaneously acquired with the radionuclide angiocardigram would test the hypothesis that the phantom-derived criteria would be useful in allowing the angiocardiogram to define successfully the endocardial surface and thus ventricular volume. An excellent relationship was observed between the directly measured sonomicrometer minor axis dimension and the minor-axis dimension derived from the cardioscintigram. An actual L_m could not be measured using the sonar crystals implanted in this study, and volumes were compared using a value of L_m derived from the radionuclide image. This calculation provided a more severe test of the accuracy of edge detection, since squaring the minor-axis dimension should make differences between the two differently derived dimensions and volumes more apparent.

The accuracy of dimension measurements cannot be directly extrapolated to the evaluation and analysis of the left-ventricular radionuclide angiocardiograms obtained in patients, who have a different chest configuration and often have more soft tissue and a greater amount of scattered radiation. However, the range of ventricular volumes evaluated in the dogs extended from that of the child to that of the small adult (*13*). The excellent correlation observed in dogs indicates the inherent accuracy of radionuclide techniques for estimating left-ventricular volume and defining the edges of the left-ventricular chamber. This inherent accuracy documents the potential accuracy of the method in evalu-

ating regional wall motion in patients and is well within the range necessary for studies in patients with ischemic heart disease. This accuracy allows the radionuclide technique to be useful in obtaining end-systolic volume in the adult in different physiologic states that can be coupled to pressure measurements to derive end-systolic pressure-volume relationships.

In summary, we have tested the ability of our radionuclide procedure and the criteria experimentally derived to estimate the volume of the sphere and hence the left-ventricular volume. When a correlation was made between the directly measured left-ventricular dimensions and those derived from the radionuclide angiocardiograms analyzed with these criteria, an excellent correlation was found.

FOOTNOTES

* System 77, Baird Corp., Bedford, MA.
† Transducer Products, LTZ5.
‡ Tygon HL54.

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