Cross-sectional Echocardiography

II. Analysis of Mathematic Models for Quantifying Volume of the Formalin-fixed Left Ventricle

H. L. Wyatt, Ph.D., Ming K. Heng, M.D., Samuel Meeraum, Ph.D., Pascal Gueret, M.D., John Hestenes, Ph.D., Eugene Dula, B.S., and Eliot Corday, M.D.

SUMMARY  Cross-sectional echocardiography was used to quantify volume in 21 canine left ventricles that were fixed in formalin and immersed in mineral oil. Area, length and diameter measurements were obtained from short- and long-axis cross-sectional images of the left ventricle and volume was calculated by seven mathematic models. Calculated volume was then compared, by linear regression and percent error analyses, with fluid volume of the left ventricle, obtained by filling the chamber with a known amount of fluid. Volumes ranged from 13–146 ml. Mathematic models using short-axis area and long-axis length gave higher correlation coefficients (r = 0.982 and r = 0.969) and lower mean errors (10–20%) than standard formulas previously used with M-mode echo and angiography. Thus, short-axis area analysis with cross-sectional echocardiography is well-suited for quantifying left ventricular volumes in dogs.

Although several studies have indicated that left ventricular (LV) volume determined by cross-sectional echocardiography in patients correlates with angiography, true echocardiographic quantification requires validation against an absolute standard and study of specifically applicable models. Investigation in this laboratory has shown that cross-sectional echocardiographic measurements of left ventricular mass in the closed-chest dog correlated well with anatomic LV mass. Particularly good correlations were observed with new mathematic models using short-axis cross-sectional areas of the left ventricle. The application of these echocardiographic models to LV volume quantification was therefore tested in the present study.

The plastic casts of ventricular chambers frequently used in angiographic validation studies are not suitable for ultrasonic visualization. In the present study, formalin-fixed canine left ventricles served as a known standard for comparing echocardiographic volume determinations using mathematic models described previously. The echocardiographic cross-sectional images of the formalin-fixed left ventricle were similar to those available in the left ventricle of the closed-chest dog. Several mathematic models were tested, including those requiring multiple short-axis sections and simplified reconstructions based on double- or single-section images. These new models were compared with standard formulas for angiography and M-mode echocardiography.

Methods

Cross-sectional echocardiographic studies were performed with an electronic, phased-array sector scanner (Varian Associates, Palo Alto, California) with a real-time, high-resolution, 32-element transducer, an 84° sector angle and a videotape recording rate of 30 frames/sec. The 84° sector angle enables the recording of entire cross sections of the left ventricle, using either short- or long-axis orientations. Twenty-one dogs were killed with an overdose of anesthetic, their hearts removed, and the atria dissected at the atroventricular grooves. The left ventricles were stuffed with gauze to avoid shrinkage of the chambers and subsequently fixed in formalin for at least 3 days. Formalin-fixed left ventricles were immersed in mineral oil and viewed with the phased-array sector scanner to obtain left ventricular cross-sectional images similar to those described for closed-chest dogs. Mineral oil was chosen as a medium for this study because of its ready availability and its similarity to castor oil, the standard medium used for calibration procedures. The velocity of ultrasound transmission in mineral oil is about 1.4% higher than in aqueous solutions such as water or blood; however, differences in ultrasound transmission velocity should not affect myocardial boundary delineation measurements with cross-sectional echocardiography. Six to 10 short-axis cross sections were obtained from base to apex by moving the transducer in the mineral oil over the left ventricle. Long-axis cross sections were obtained by rotating the transducer 90°. All views were recorded on videotape and played back later for analysis. After the echocardiographic procedures, the left ventricle was removed from the mineral oil, rinsed thoroughly with water, blotted dry with paper towels, and filled to the mitral and aortic valve rings with a known amount of mineral oil from a graduated cylinder. This procedure was performed three times...
and an average was obtained for fluid volume of the LV chamber. This fluid volume then provided the known standard for comparison with echocardiographic volume measurement. Anatomic length was measured in all ventricles by inserting a rod through the mitral opening and measuring the distance from the LV apex to the mitral-aortic valve junction.

**Determination of LV Volume**

Using cross-sectional echocardiographic images, seven mathematic models were tested by comparing calculated LV volume with true volume. Endocardial outlines were traced from projections of short-axis and long-axis cross sections during videotape stop-motion replay. Linear measurements were obtained from the cross-sectional outlines and areas enclosed within the outlines were derived by planimetry. Two-dimensional echocardiographic short-axis images in formalin-fixed canine ventricles are characterized by strong circumferential echoes at the endocardial interfaces (fig. 1). By tracing at the inner border of circumferential echoes, the thickness of the endocardial echo is excluded from endocardial area. This procedure was used to reduce potential errors. LV diameter and long-axis cross-sectional area were also measured from the inner borders of endocardial echoes, taken at appropriate locations. The length of the ventricle was measured in the long-axis section (fig. 2) as the distance from apex to the mitral ring at the base. Seven mathematic models for quantifying LV volume from cross-sectional echocardiographic measurements were described in detail in the previous quantitative study in dogs. The same models are used in the present study. Volume formulas and geometric models from which they were derived are illustrated in figures 3A–G, along with the results.

In this study, model 1 (Simpson's rule, fig. 3A) used the LV endocardial area (A) of six to 10 short-axis sections from base to apex and LV length (L) from a long-axis section. The height (h) of each short-axis section was determined arbitrarily by dividing length by the number of sections available. Volume was calculated generally by summing the product A·h for all sections. In the previous study in dogs, single measurements of left ventricular short-axis diameter and area were obtained from a section at the high papillary muscle level for use in models 2–6 (figs. 3B–F). As a result of formalin-fixation methods in the present study, LV geometry deviated from normal because the LV chamber was constricted toward its base. To avoid this constriction, a short-axis section at the low papillary muscle region, two-thirds of the distance from base to apex, was used for diameter and area measurements (models 2–6). Models 2–4 are represented in figures 3B–D by the formula \( LVV = K \cdot AL \), where \( K = 1 \) for the cylindrical geometry of model 2, \( K = 2/3 \) for the ellipsoidal geometry of model 3 and \( K = 5/6 \) for the half-cylinder, half-ellipsoid geometry of model 4. Model 5 is represented in figure 3E by the formula \( LVV = \pi/6 (D_1 D_2 L) \); model 6 (fig. 3F) is the standard cube method, \( LVV = D^3 \), and model 7 (fig. 3G) is the long-axis area-length method, \( LVV = 0.85 A^2/L \). Models 5–7 are derived from ellipsoid geometry.

Calibration of cross-sectional echocardiographic measurements was performed from scales along the
horizontal and vertical axes of the images. These calibration scales were predetermined in the system used (Varian, Inc.) from precise fixed-distance objects immersed in castor oil and imaged with the echocardiographic system. The calibration, subsequently determined in our laboratory with objects immersed in water, was found to be accurate.

The calibration scale was remeasured for each echocardiographic measurement because some variation may occur with changes in gain settings and variation in calibration may also occur over the range of the screen. Calibrations were measured during videotape motion replay to allow better visualization of the scale and then applied to each volume calculation.

**Data Analysis**

In 21 formalin-fixed left ventricles, the chamber volume, calculated from seven mathematic models, was compared with the fluid volume of the left ventricle. Linear regression analysis was performed and the standard error of estimate was calculated. For seven models, calculated LV volume on the y-axis was plotted against true LV volume on the x-axis (figs. 3A–G). Percent errors were determined for echocardiographic LV volume vs true LV volume according to the following formula:

\[
\frac{\text{calculated LV volume} - \text{fluid LV volume}}{\text{fluid volume}} \times 100
\]

Mean percent errors were calculated as an average of absolute percent errors for the 21 left ventricles and served to indicate the variability of data about the identity line. Reproducibility of left ventricular short-axis area and left ventricular long-axis length measurements was assessed by determining percent error from the average of duplicate measurements by two observers (interobserver reproducibility); the mean percent error was then calculated. Echocardiographic length was compared with directly measured anatomic length for the 21 ventricles, using both linear regression and percent error analyses.

**Results**

The results of testing seven mathematic models are illustrated in figures 3A–G. Points are plotted for calculated volume vs fluid volume in 21 left ventricles. From a linear regression analysis of these data, a regression equation, correlation coefficient, standard error of estimate and mean percent error are illustrated for each model. LV volume was 13–146 ml. Excellent correlations were observed for models using short-axis area measurement. The multisec- tion Simpson’s rule reconstruction procedure (model 1, fig. 3A) gave the highest correlation coefficient (0.982), the lowest mean percent error (9.6%) and a generally even distribution of points about the identity line, with a regression intercept (0.7) near zero and a slope of one. Models 2, 3 and 4 (figs. 3B–D) are based on one short-axis section and are derived from the same basic formula: \( V = kAL \), where \( k \) = constant, \( A \) = short-axis area and \( L = LV \) length. These model formulas, differing only in a constant, exhibit equally high correlation coefficients (0.969), but different mean percent errors. Of the three, model 4 has the lowest mean percent error (17.9 ± 4.6% [± SEM]), model 3 has the intermediate value (22.4 ± 4.7%) and model 2 has the highest value (31.9 ± 4.3%); however, the difference between mean percent errors for models 3 and 4 was...
not statistically significant. Model 2 generally overestimates LV volume, model 3 generally underestimates, and model 4 results in a relatively even distribution of points close about the identity line (figs. 3B-D). An excellent correlation coefficient (0.956) was also obtained with model 5 ($V = \pi/6 [D_1 D_2 L]$), which uses two short-axis diameters in lieu of short-axis area (fig. 3E). However, if only one short-axis diameter is used and length is assumed to be twice the diameter, as with the M-mode LV volume model 6 ($V = D^3$, fig. 3F), the correlation coefficient is substantially poorer (0.828). When the angiographic formula of model 7 ($V = 0.85 A_L'/L$, fig. 3G) was tested using long-axis area ($A_L$) and length ($L$), a good correlation coefficient resulted ($r = 0.903$). Only model 1 (Simpson's rule) and model 4 (half-cylinder, half-ellipsoid geometry) showed a generally even distribution of points close about the identity line; models 3, 5 and 7 (ellipsoid geometry) showed a generally underestimated LV volume and model 2 (cylindrical geometry) generally overestimated LV volume.

By multiplying the formula of model 3 by 1.25, the ellipsoid figure of model 3 was converted to the half-ellipsoid, half-cylinder figure of model 4. Similarly, by multiplying the formulas of models 5, 6 and 7 by 1.25, the ellipsoid figures may be converted to the half-
cylinder, half-ellipsoid figure of model 4. Correlation coefficients are not changed by this procedure, but mean percent errors are reduced and the distribution of points about the identity line is improved for models 3, 5 and 7.

Interobserver reproducibility was determined for short-axis area, long-axis area and LV length using linear regression and percent error analyses. For short-axis area from 33 sections, the correlation coefficient is 0.993 and the mean percent error is 5.5%. For long-axis area from 15 sections, the correlation coefficient is 0.986 and the mean percent error is 6.6%. For LV length from 15 long-axis sections, the correlation coefficient is 0.979 and the mean percent error is 3.0%. A comparison of LV echocardiographic length vs anatomic length in 21 left ventricles shows a 0.912 correlation coefficient and a 7.2% mean error.

**Discussion**

With fluid volume of formalin-fixed left ventricles as a standard, LV volume was accurately quantified with cross-sectional echocardiography utilizing mathematic models developed for closed-chest dogs. Although previous clinical studies1-4 of LV volume quantification indicate good correlations for cross-sectional echocardiography vs cineangiography, both
techniques involve calculations based on long-axis models of the left ventricle. Preliminary reports of more recent in vitro studies from this and other laboratories, have suggested reliable quantification of LV volume with cross-sectional echocardiography by comparison with directly measured LV fluid volume.

The findings of this in vitro study on LV volume were similar to the findings of a recent in vivo study on LV mass by two-dimensional echocardiography in closed-chest dogs. Although the strongest correlation was obtained with model I, excellent correlations were also obtained with models 2-4. Models 1-4 use short-axis areas of the left ventricle; thus models 1-4, unlike models 5-7, do not require any assumption of short-axis geometric symmetry because the short-axis area incorporates endocardial irregularities due to trabeculae carnæ and papillary muscle invaginations. A very good correlation was also obtained with model 5, but less reliable results were obtained with model 6 (cube method) and model 7 (long-axis area-length method), probably because they require the assumption of geometric symmetry about the short axis. Despite the generally strong correlations of all models, only model I (Simpson’s rule reconstruction procedure) and model 4 (half-cylinder, half-ellipsoid geometry) resulted in low mean percent errors and a generally even distribution of points about the identity line. Models 3, 5 and 7 (ellipsoid geometry) generally underestimated the LV volume, whereas model 2 (cylindrical geometry) generally overestimated LV volume. The fact that these findings are consistent for studies of both volumes and mass of the left ventricle lends credence to the observation that the geometry of the left ventricle is best represented by a half-cylinder, half-ellipsoid model or by a truncated ellipsoid. Thus, experimental quantification of LV volumes in dogs might best be performed by either model 1 or model 4, depending upon the nature of the contemplated study. However, the feasibility of applying these models clinically cannot be determined from this study.

Correlation coefficients for linear regression analysis were slightly higher for each mathematic model in the present study of LV volume than in the former study of LV mass, probably due to the simpler calculation of chamber volume. The only critical discrepancy between in vitro volume and in vivo mass results was the substantial difference between correlation coefficients for model 7, the area-length method (r = 0.903 and 0.744, respectively). The poor correlation for LV mass by this method was probably due to the sometimes incomplete area and length information of in vivo long-axis sections.

Although the cross-sectional echocardiographic techniques and models of the present in vitro study were patterned after previous in vivo work, obvious differences exist between the two applications. The foremost of these relates to orientation of the transducer with respect to the heart. To obtain short-axis sections of the in vitro left ventricle, the transducer is moved from base to apex in a plane parallel to the long-axis so that the ultrasonic beams intersect the left ventricle in a plane perpendicular to the long-axis and the myocardial wall of the left ventricle. In contrast, for the closed-chest dog or the human being, the exact orientation of the left ventricle with respect to the transducer is not known; short-axis sections are obtained from base to apex both by moving the transducer along the chest wall and by changing the angle of the transducer direction. Perpendicular intersection of the ultrasonic beam with the LV long axis is judged by the circularity of the short-axis section during late diastole. The exact location or exact height for each short-axis section is not known for in vitro or in vivo studies.

Cross-sectional images of the formalin-fixed left ventricle are qualitatively different from those of the beating left ventricle, but endocardial definition is sharp for both preparations; this subjective judgment is confirmed by the comparable interobserver reproducibility for short-axis area from both studies (mean percent error less than 6%). Qualitative differences in endocardial outlines may result from several factors: 1) in vitro left ventricles are not moving; 2) in vitro endocardial surfaces are smooth after formalin fixation; and 3) the in vitro left ventricle differs further from the beating ventricle in that the shape of the chamber is formed by the gauze sponges instead of by normal blood flow. Thus, the method of filling the chamber with gauze is important in determining its shape. Because of the method used, in vitro ventricular chambers tend to be constricted toward the mitral and aortic valve rings, and the short-axis section at the high papillary level is not representative of the remaining left ventricle. To avoid any constriction toward the base of the left ventricle, a section was chosen arbitrarily at the low papillary muscle level, two-thirds of the distance from base to apex; measurements from this section were then used to compute LV volume with models 2-6. Results of this study should be considered in light of the minor differences in shape and texture of the in vitro vs the in vivo left ventricle. Because of these factors, specific regression equations for LV volume determined from this study should not be applied to the beating heart. Nevertheless, reliability of the mathematic models alone for quantifying LV volume in vitro should also be representative of the canine beating heart. Support for this hypothesis has been demonstrated in a recent preliminary study in this laboratory, some of the results of which were published previously; quantification of LV volumes in closed-chest dogs demonstrated very good correlations between cross-sectional echocardiography and cineangiography.

In summary, results of the present study show that LV volume may be accurately quantified in vitro by cross-sectional echocardiography using seven mathematic models, the best of which use short-axis area analysis. These results support and confirm similar findings of a previous study on LV mass by cross-sectional echocardiography in dogs.
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Evaluation of Pulmonary Hypertension by M-mode Echocardiography in Children with Ventricular Septal Defect

NORMAN H. SILVERMAN, M.D., A. REBECCA SNIDER, M.D., AND ABRAHAM M. RUDOLPH, M.D.

SUMMARY We evaluated the ratio of the right ventricular pre-ejection period to the right ventricular ejection time (RVPEP/RVET) as a predictor of pulmonary hypertension in 16 children with ventricular septal defects (VSD) (group 1). The children ranged in age from 5 months to 18 years. The RVPEP/RVET was measured at the time of cardiac catheterization by M-mode echocardiography from the pulmonary valve echogram and from a simultaneously displayed pulmonary arterial pressure signal obtained with a microtip, manometric catheter. The RVPEP/RVET measured by both methods was comparable ($r = 0.91$). The RVPEP/RVET was compared with the pulmonary artery diastolic pressure (PADP) ($r = 0.54$). The RVPEP/RVET ratio correlated less well with the pulmonary arterial mean pressure and pulmonary vascular resistance. In a second group of 51 children with VSD, echocardiographic measurement of the right ventricular systolic time intervals was performed within 24 hours before cardiac catheterization. The same variables of pulmonary arterial pressure as for group 1 were compared with the RVPEP/RVET ratio, and the results were similar. These data indicate that, although there is a relationship between the RVPEP/RVET and pulmonary hypertension, the ratio alone is not accurate enough to avoid cardiac catheterization in patients considered at risk for pulmonary vascular disease.

PERSISTENT ELEVATION of the pulmonary arterial pressure in children with ventricular septal defects may lead to irreversible pulmonary vascular disease. Currently, the only reliable method for detecting alterations in the pulmonary arterial pressure in the course of the disease is through repeated cardiac catheterization. Recently, M-mode echocardiographic measurement of the ratio of the right ventricular pre-ejection period (RVPEP) to the right ventricular ejection time (RVET) has been used to detect pulmonary hypertension. The RVPEP/RVET ratio has been reported to predict pulmonary arterial hypertension in children with left-to-right shunts and in infants with pulmonary hypertension complicating noncardiac neonatal problems. If the ratio of RVPEP/RVET accurately predicted pulmonary arterial hypertension in children with ventricular septal defects, the need for repeated cardiac
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