Intracardiac Ultrasound Measurement of Volumes and Ejection Fraction in Normal, Infarcted, and Aneurysmal Left Ventricle Using a 10-MHz Ultrasound Catheter

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Background  Our objective was to examine the accuracy of intracardiac ultrasound (ICUS) measurement of left ventricular (LV) volumes and ejection fraction (EF) using a 10-MHz ultrasound catheter. ICUS can image the LV in cross sections at all levels along the long axis with a transducer mounted on the tip of a catheter. Sequential serial LV cross-sectional images can be obtained during cardiac catheterization and used to calculate LV volumes by Simpson's rule. This technique may be an alternative to contrast LV angiography.

Methods and Results  A beating-heart in vivo model was created to measure LV volume directly and continuously with an intracavity high-compliance latex balloon connected to a calibrated extracardiac reservoir in eight dogs in 35 experimental stages. A 10F ICUS catheter with a 10-MHz single-element transducer was introduced retrogradely via the aortic valve to the apex. Series of sequential LV cross-sectional images were recorded from the apex to the base during a calibrated pullback of the catheter. At each 5-mm interval, the LV cross section was traced at end diastole and end systole. LV volume was calculated by Simpson's rule by integrating all segmental areas multiplied by segmental height. The effect on accuracy of selecting 5-, 10-, or 15-mm heights or a single section at the midventricular level for measurement was assessed. The influence of distorted ventricular shape on the accuracy of ICUS measurements of LV volume was evaluated. This method was applied in 19 experimental stages in 10 intact dogs and pigs catheterized via the femoral artery. In the in vivo canine model, LV end-diastolic volume, end-systolic volume, and EF determined by ICUS using 5-, 10-, or 15-mm segments were not different from the actual measurements. But correlation and agreement between ICUS end-diastolic volume and direct measurements for 5- and 10-mm segments were significantly better than for 15-mm segments or a single section. Similar excellent correlations and agreement were observed for actual and ICUS-derived end-systolic volumes using 5-, 10-, or 15-mm segments. The ICUS-derived EF correlated very well with actual EF with a small measurement error of 3.91±2.59% for 5-mm or 4.13±2.79% for 10-mm segments but a significantly greater measurement error for 15-mm segments (5.35±3.76%) or single sections (14.8±12.2%). The presence of LV infarction or aneurysm did not significantly influence the accuracy of ICUS calculations for segmental heights ≤10 mm. Application in intact animals demonstrated a good correlation between stroke volume measured by ICUS and by thermodilution or flowmeter. ICUS-derived LV volumes correlated well with biplane angiographic volumes, with a tendency toward underestimation. There was no significant difference between ICUS-determined LV EF and EF determined by angiography.

Conclusions  Intracardiac echocardiography accurately measures LV volumes and global systolic function in both regularly shaped and distorted left ventricles. This technique directly and continuously visualizes circumferential LV endocardium and wall thickness without contrast agents or geometric assumptions for calculation of LV volume. Thus, it should be particularly useful in patients at high risk for contrast-related complications or distorted LV shapes in which geometric assumptions may not be valid. (Circulation. 1994;90:1481-1491.)

Key Words  • ultrasound • ventricle • echocardiography

Contrast left ventriculography is the standard method for assessing left ventricular (LV) volume, ejection fraction (EF), and regional wall motion in the cardiac catheterization laboratory.1-6 However, rapid injection of enough contrast agent to opacify the LV may impose a significant risk to patients with severe LV dysfunction or renal failure.7 Furthermore, because the toxicity of contrast agents is dose related, serial angiography often cannot be used for assessment of changes in LV function during interventional procedures.

Previous studies have demonstrated that catheter-based ultrasound imaging can be used to identify cardiac structures and to assess their function.8-17 A potential advantage of ultrasound is its ability to continuously monitor cardiac structures and function without the risk of contrast-related adverse effects. If intracardiac ultrasonic (ICUS) imaging can provide accurate and reliable measurements of LV volumes, EF, and regional wall motion, then this technique may provide an alternative to left ventriculography in the cardiac catheterization laboratory in many groups of patients in whom the...
Calculation of LV Volume:

\[ \text{LV volume} = \sum A \times h. \]

Fig 1. Schematic display of intracardiac ultrasound (ICUS) catheter in left ventricular (LV) cavity to image the ventricle in cross section at different levels from apex (A) to base (F) and the equation for volume calculation using Simpson’s rule as shown at top. Bottom, Example of a series of ICUS cross-sectional images of the LV from the apex (A) to the aortic annulus (F) at 1-cm intervals from an experimental stage. The calibration between two dots on the ICUS images is 4 mm. LV in top diagram indicates left ventricular cavity; RV, right ventricle; RA, right atrium; AO, ascending aorta; and LA, left atrium.

angiographic assessment of mitral regurgitation is not required. Current ICUS equipment can image the LV in a cross-sectional or tomographic format at all levels along the long axis (Fig 1), and LV volumes can be calculated from the images by Simpson’s rule.

Therefore, in the first part of this study, a canine model was used to determine (1) the feasibility and accuracy of ICUS imaging for measurements of LV volumes and EF in a rigidly controlled experimental preparation in which instantaneous LV volume can be directly measured in the beating heart; (2) the comparative accuracy of several algorithms for calculation of LV volumes; and (3) the influence of LV infarction and/or aneurysm on the accuracy of LV volume and EF calculations. In the second part of this study, using dogs and pigs catheterized via the femoral artery, this technique was used to examine the applicability of the ICUS method in an intact animal.

Methods

Test in Canine Model For Direct Measurement of LV Volumes

Animal Preparation

The study conformed to the guidelines outlined by the American Heart Association for animal research. Eight adult mongrel dogs (27 to 36 kg) were anesthetized with sodium pentobarbital 30 mg/kg IV, intubated, and ventilated with a Harvard respirator.

A model permitting direct measurement and alteration of instantaneous LV volume was modified from the preparation originally described by Suga and Sagawa18,19 and has been used extensively in our laboratories and previously described in detail.20 Briefly, after a left thoracotomy, the animal was placed on cardiac pulmonary bypass. All venous return was drained, filtered, warmed, and oxygenated and then pumped by a calibrated roller pump back into the distal ascending aorta and coronary arteries. The sinoatrial node was destroyed, and right atrial pacing (80 to 100 beats per minute) was initiated to maintain a constant heart rate throughout each stage of the experiment. A high-compliance latex balloon was introduced into the LV through the aortic valve via the proximal ascending aorta. The balloon was connected to a calibrated extracardiac reservoir, which is a rigid calibrated polyurethane column of 3/4-in internal diameter. The mitral leaflets were sutured to ensure that no blood went through the mitral orifice during diastole or systole. Thus, the LV cavity was isolated from the remainder of the circulation. To ensure that the balloon conformed maximally to the contour of the LV, chordae tendineae attaching the papillary muscles to the mitral valve were removed. The thebesian venous return into the LV was drained by a small cannula (24 gauge) inserted through the apex. This ensured that in all cases the balloon was contiguous with the endocardium. The balloon reservoir system was sutured to the aortic annulus, and the column was maintained in a vertical position. A port of the short side arm (5 mm in length) at the lower end of the column allowed known amounts of fluid to be added or withdrawn and the ICUS catheter to be introduced. Therefore, the ultrasound catheter was introduced to follow a small curve. The balloon reservoir system was filled with saline. The LV volume was determined by subtracting the instantaneous volume of the fluid in the column from the volume of fluid transfused into the system. The systolic volume was determined at the highest level of the fluid in the column and the diastolic volume at the lowest level. The height of the fluid in the column was assessed by continuous video recording of the column and later off-line analysis. For each measurement of column height, the mean value from
five consecutive beats was recorded. The resistance to ventricular contraction could be controlled by altering the diameter of the outlet of the tubing attached to the top of the column. LV contractility was also altered pharmacologically by propranolol or dobutamine.

**Intracardiac Ultrasound**

A 10F, 10-MHz catheter-based ultrasound transducer (CVIS) was used. The imaging catheter consists of an ultrasonic transducer (single crystal) and rotating mirror enclosed within an acoustic housing at the distal segment of the catheter. The distance between the mirror and tip of the catheter was 0.7 cm. The catheter assembly houses a flexible drive cable that was used to rotate the mirror. A one-way valve and a Luer assembly were used to fill the lumen with sterile saline and to flush air from the catheter before use. This provided an acoustic medium for ultrasound imaging. The one-way valve helps retain saline in the acoustic housing. The catheter was connected to the CVIS INSIGHT system to produce an imaging field of 360° for a cross-sectional cardiac image with the catheter in the center (Fig 1). The axial resolution was 0.30 mm, and the lateral resolution was 0.37 mm. The frame rate used in this study was 20 to 30 frames per second. The ICUS catheter was introduced via a sheath through the side arm into the reservoir system and then through the aortic annulus into the apex of the LV. The tip of the catheter was advanced to the most distal part of the apex. After the apical position of the tip of the catheter was confirmed by direct visual inspection of the catheter tip pushing the apical wall, the junction of the catheter and the sheath was marked, and the catheter was pulled back gradually into the ascending aorta in a calibrated fashion while the ICUS images were continuously recorded. The calibrated pullback was conducted either by a device that produced a constant withdrawal speed in the first two experiments or later by hand. In both cases, the pullback was stopped at 5-mm intervals, and the distance withdrawn was noted on the corresponding ICUS LV image.

**Study Protocol**

After baseline withdrawal, the ventricle was imaged at a series of different LV volumes. To vary volume, known amounts of saline were added to or removed from the system. The range of volume varied with the size of the animal. At each volume stage, ICUS imaging was performed simultaneously with the recording of systolic and diastolic column height and hemodynamics. To determine the accuracy of measurement of LV volume using ICUS imaging in deformed and asymmetric LV cavities, either by inducing anterior (2 dogs) or inferior (1 dog) myocardial infarction by coronary artery ligation or by creating an LV apical aneurysm (1 dog). The LV aneurysm was created by replacing the apex with a tissue patch, producing an apical aneurysmal sac. Three to 8 stages at different volumes and EF were obtained in each animal, and a total of 35 stages were obtained. Of 35 stages, 15 stages were studied with LV infarction or aneurysm, producing LV shape distortion.

**Application in Intact Animals**

Since left cardiac catheterization is often performed via a femoral or brachial artery, applicability of the ICUS method in a setting similar to the catheterization laboratory was tested in 10 intact animals (6 pigs and 4 dogs) by inserting the ultrasound catheter through a femoral or carotid artery. A total of 19 experimental stages of different LV volumes and EF in 10 animals were obtained at baseline or after intervention with dobutamine (in 3 animals) or esmolol infusion (in 2 animals) or ligation of the left anterior descending coronary artery (in 4 animals). In 9 experimental stages in 5 pigs, the effect of the use of different paths (femoral versus carotid artery) to introduce and withdraw the ultrasound catheter on the calibration of ICUS LV volumes, EF, and stroke volume was examined by comparing ICUS measurements from the femoral approach with those from the carotid approach at the same experimental stage. A 10F arterial sheath was placed in a femoral and/or carotid artery, and the ICUS catheter was introduced through the sheath by use of a 0.021 guide wire with a soft J-curve tip. After the ultrasound catheter was placed in the LV, the catheter was advanced gradually into the LV apex with a J-tip guide wire. Continuous monitoring of ICUS LV image was used to indicate the catheter tip in the apex, which was characterized by the smallest LV cavity without an adjacent right ventricular cavity. In every case, this sign was confirmed by visual inspection of the push of the apex by the tip of the catheter, by direct hand palpitation if there was uncertainty about the visual inspection, or by x-ray fluoroscopy. After the catheter tip was confirmed in the LV apex, the following steps were taken to ensure that there was no bending or slack of the catheter either in the LV or in the aorta. To do this, the catheter was pulled back slightly while the ICUS image was continuously monitored. When a change in the ICUS imaging plane with gradual increase in the LV cavity size was observed, indicating that the catheter followed the pullback, the catheter was then advanced slightly back to the apical position. In one case in which no significant change in the LV image was observed during the initial pullback of the catheter, a slack of the catheter in the aorta or LV cavity was considered. In this case, the catheter was withdrawn to the LV outflow tract and readvanced into the apex. After confirmation of both apical position and no slack of the catheter in the LV or aorta, continuous sequential ICUS images were recorded during the calibrated pullback as described earlier in the canine model. In 16 experimental stages in 7 animals, modulation technique or a transit time flowmeter (Transonic Systems Inc) was used simultaneously to determine cardiac output during pullback of the ultrasound catheter. Biplane left ventricular angiography was performed in 10 experimental stages in 5 animals in anteroposterior and lateral projections. A 7F pigtail catheter was placed in the LV for contrast (Angiovit, Berlex) injection at 3 to 5 mL/s for 3 seconds. Calibration with a metal ball of known diameter was performed to determine the magnification factor for each angiographic plane. LV angiograms were recorded on a 1/2-in videotape for later analysis.

**Data Analysis**

**ICUS Measurements**

Cross-sectional ICUS images of the LV were reviewed off-line to identify the end-diastolic (the largest LV cross-sectional area) and the end-systolic (the smallest LV cross-sectional area) frames. The end-diastolic and end-systolic outlines of the LV cavities at each 5-mm interval were traced manually along the inner border of the endocardial/cavity interface and digitized with a commercially available computer system (SUM 1010, Sony). The papillary muscles were not excluded when the endocardial interface was traced. The luminal area at each interval from apex to aortic valve was thus obtained. Special attention was paid to trace LV outflow tract area, which is enclosed by the LV wall and anterior mitral leaflet and is adjacent to the left atrium and right ventricle (Fig 2).

**Algorithm for Calculation of ICUS Volumes and EF**

Sequential ICUS images during each calibrated pullback divided the LV into numerous (n) segments (Fig 1) at a fixed segmental interval (h) from the apex to the aortic valve. Summation of the segmental volumes using Simpson's rule yielded LV volume:

\[
LV \text{volume} = h_1 A_{apex} + h_2 \sum A_s + h_3 A_{LVOT}
\]
where \( A \) was mean cavity area of each LV cross section, which was calculated by averaging the LV cross-sectional area at the beginning of the segment and the area at the end of the segment. Since the transducer was not mounted at the very tip of the catheter but rather 7 mm proximal to the tip, \( h_1 \) was 0.7 cm and apical volume was calculated by mean apical cross-sectional area \( (A_{cav}) \) multiplied by 0.7 cm. The mean area for this apical segment was calculated by dividing the first apical cross-sectional area (at the end of this segment) by 2, assuming the area at the beginning of the apical segment, which cannot be obtained by use of this ICUS catheter, to be 0. The \( h_2 \) was the actual pullback distance from the last segment to the left ventricular outflow tract (LVOT) just below aortic annulus. In Equation 1, \( h_3 \) is the fixed segmental interval (or height) of the remaining segments. Mathematically, the smaller the segments (segmental height), the more accurate the estimate. Different segmental intervals (5, 10, and 15 mm) were tested in this study to determine the effect of segmental height (slicing interval) on the accuracy of calculated volumes. Summation of end-diastolic segmental LV volumes of all segments from the apex to aortic valve yielded end-diastolic LV volume and, similarly, summation of end-systolic segmental LV volumes yielded end-systolic LV volume. LV EF was calculated by subtracting end-systolic volume from end-diastolic volume divided by end-diastolic volume and expressed in percent. For application in intact animals, a 5-mm segmental height was used to calculate the end-diastolic and end-systolic volumes. The stroke volume was calculated by subtracting end-systolic volume from end-diastolic volume.

Since simultaneous recording of a single section of ICUS image and LV pressure curve allows reconstruction of the LV pressure-volume loop and parameters derived from the pressure-volume loop have been proposed for measurement of LV work and function, we also examined the accuracy of volume calculated from the single segmental area at the tip of papillary muscles. The volume was calculated by assuming prolated ellipsoidal LV

\[
(2) \quad \text{LV volume} = D^3
\]

where \( D \) is the minor-axis diameter of the ellipsoid.

**Calculation of Actual Stroke Volume and Angiographic Volumes**

The actual LV stroke volume was calculated by cardiac output determined by the thermodilution technique (in 9 stages) or a flowmeter (in 7 stages) divided by heart rate. Angiographic LV end-diastolic and end-systolic volumes were calculated according to the biplane area-length method with the correction equation that was derived from canine hearts by Graham et al.\(^22\). Angiographic EF and stroke volume were then calculated.

**Variability Study**

For interobserver variability of volume and EF measurements, two experienced echocardiographers measured all ICUS images independently in 9 stages of 3 animals. To test the intraobserver variability, the measurements of LV volume and EF were performed by the same observer in 9 stages after an interval of 1 week. For interobserver variability, volume measurement (both end-diastolic and end-systolic volume) by ICUS was 38.2±14.9 mL by observer 1 and 37.6±14.6 mL by observer 2 (\( P=\text{NS} \)). Correlation between the two measurements was excellent \((r=.98)\), with an SEE of 1.77 mL. A similarly good correlation was found for interobserver measurements of EF \((r=.98, \text{SEE}=2.3\%)\). For intraobserver variability, there was similarly an excellent correlation between two measurements by the same observer at 1-week intervals \((r=.99, \text{SEE}=1.44 \text{mL})\). The absolute interobserver difference between two measurements of volume was 1.22±1.18 mL. The correlation between two measurements of EF by the same observer in 1 week was also excellent \((r=.99, \text{SEE}=2.1\%)\).

**Statistical Analysis**

Data were expressed as mean±SD. Comparisons of continuous variables between actual (or angiographic) and ICUS mea-
Agreement plots

Ventricular Volumes

two
lines

Table 1. Intracardiac Ultrasound Calculations of Volume and Ejection Fraction Using Different Segmental Heights Compared With True Measurements

<table>
<thead>
<tr>
<th></th>
<th>True Value</th>
<th>5-mm Segment</th>
<th>10-mm Segment</th>
<th>15-mm Segment</th>
<th>Single Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV, mL</td>
<td>55.4±13.8</td>
<td>56.3±13.7</td>
<td>56.6±14.0</td>
<td>56.0±13.3</td>
<td>71.1±24.5*</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>32.1±12.3</td>
<td>32.8±11.8</td>
<td>33.0±12.6</td>
<td>32.5±13.0</td>
<td>34.0±16.5</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>42.6±13.4</td>
<td>42.1±12.8</td>
<td>42.3±13.3</td>
<td>43.5±14.3</td>
<td>56.3±15.6*</td>
</tr>
</tbody>
</table>

LVEDV indicates left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; and LVEF, left ventricular ejection fraction.

*P<.05.

measurements were performed with univariate linear regression analysis and ANOVA. The difference between regression line and the line of identity was examined for each data set. If there was a significant difference by ANOVA, paired data were examined by Student's t test. Agreement between ultrasound measurement and actual (or angiographic) value was assessed by the mean and SD of the difference between actual (or angiographic) and ICUS-based measurements for each method. Absolute measurement error was calculated by use of the absolute value of the difference between actual and intracardiac measurements for each method and compared by univariate analysis and paired Student's t test. The absolute error for each ICUS method in LVs with infarction/aneurysm was compared with that in LVs without infarction/aneurysm by paired Student's t test. A value of P<.05 was considered statistically significant.

Results

Canine Model for Direct Measurement of Ventricular Volumes

Adequate quality of ICUS images for calculation of LV volumes was obtained in a total of 35 stages in 8 animals. No perforation of the ventricle or latex balloon was observed. The time required to obtain a complete set of LV sequential images at 5-mm intervals for calculation of LV volume was usually 2 to 3 minutes.

LV End-Diastolic Volume

There was no significant difference between actual true end-diastolic volumes and end-diastolic LV volumes determined by ICUS with 5-, 10-, or 15-mm segments (Table 1). The correlation and agreement between true and ICUS-measured volumes were excellent for 5-mm segments (P<.001) and for 10-mm segments (P<.001) (Fig 3). There was no difference between the regression line and the line of identity for 5- and 10-mm segments (P>.5). The absolute error of ICUS measurement was 2.5±0.35 mL for 5-mm segments, which was not different from that for 10-mm segments (2.9±0.4 mL) (P>.05). A less strong correlation between the true volume and that by 15-mm...
segments was observed ($y=0.81x+11.1$, $r=.84$, $P<.001$, $\text{SEE}=7.39\text{ mL}$), with a significant difference between the regression line and the line of identity ($P<.05$ for slope and $P<.01$ for intercept). The absolute measurement error was $6.4\pm0.7\text{ mL}$ with 15-mm segments, which was significantly greater than that using 5-mm segments ($P<.05$) or 10-mm segments ($P<.05$). The LV volume determined by single-section ICUS image deviated significantly from the true volume ($P<.001$, Table 1), and there was only a moderate correlation between the true volumes and those derived by the single section ($y=1.32x+1.81$, $r=.74$, $P<.01$, $\text{SEE}=16.7\text{ mL}$). The regression line was significantly different from the line of identity ($P<.05$ for slope and intercept). The absolute error was $18.8\pm2.28\text{ mL}$.

**LV End-Systolic Volume**

There was no difference between true and ICUS LV end-systolic volumes calculated with 5-, 10-, or 15-mm segments or even a single section (Table 1). True end-systolic volume correlated very well with ICUS end-systolic volume measured with 5- or 10-mm segments (Fig 4). A similar correlation was found for 15-mm segments ($y=0.97x+0.94$, $r=.91$, $P<.001$, $\text{SEE}=5.4\text{ mL}$), but there was a slightly greater data scatter, with an absolute measurement error of $4.13\pm3.3\text{ mL}$, which was significantly greater than the absolute error of $2.21\pm1.71\text{ mL}$ calculated by 5-mm segments or of $2.78\pm1.92\text{ mL}$ by 10-mm segments. The end-systolic volume calculated by ICUS single section correlated only fairly well with true end-systolic volume, with significant data scatter ($y=1.19x-6.27$, $r=.77$, $P<.01$, $\text{SEE}=12.3\text{ mL}$) and an absolute measurement error of $9.44\pm8.2\text{ mL}$, which was significantly greater than any of the ICUS calculations using multiple segments ($P<.01$). The regression lines were not different from the line of identity for all segmental heights selected and even single section ($P>.05$).

**LV EF**

ICUS-derived EF using 5- or 10-mm segments were almost identical to actual true ejection fractions without systematic underestimation or overestimation (Fig 5, Table 1). The absolute error of ICUS measurement of EF was $3.91\pm2.59\%$ for 5-mm segments and $4.13\pm2.79\%$ for 10-mm segments. An excellent correlation was also found between EF by ICUS 15-mm segments and true EF ($y=0.95x+2.97$, $r=.89$, $P<.0001$, $\text{SEE}=6.61\%$), with slightly greater data scatter. The absolute ICUS measurement error of EF was slightly greater by 15-mm segments ($5.35\pm3.76\%$) than by 5-mm segments ($P<.05$). The regression lines were not different from the line of identity for 5-, 10-, and 15-mm segments selected. EF calculated by single ICUS section was significantly different from true EF (Table 1). The correlation between ICUS-derived EF by single ICUS section and true EF was only moderate, with significant data scatter ($y=0.82x+2.21$, $r=.66$, $P<.01$, $\text{SEE}=12.69\%$) and an absolute measurement error of $14.8\pm12.2\%$. The regression line for the single segment
was significantly different from the line of identity (P<.01 for slope, P>.2 for intercept).

Influence of LV Infarction/Aneurysm on the Accuracy of Volume and EF Calculations
The presence of LV infarction or aneurysm significantly increased the measurement error of the end-diastolic volume, end-systolic volume, or EF calculation with the single ICUS section (Table 2). The presence of LV infarction or aneurysm, however, did not significantly increase ICUS measurement error for end-diastolic or end-systolic volume measurement with 5-, 10-, or 15-mm segments (Table 2). There was a tendency toward greater absolute ICUS measurement error of EF in the presence of LV infarction/aneurysm. A significant difference in the measurement error was found between EF in the LVs with infarction/aneurysm and those without infarction/aneurysm when 15-mm segments or single sections were used (Table 2).

Application in Intact Animals
Stroke volumes determined by ICUS (29.56±10.20 mL) with the catheter introduced via a femoral artery were not different from the actual stroke volumes by thermodilution technique or flowmeter measurements (28.16±10.87 mL, P>.05) in 16 experimental stages in 7 animals. Correlation between stroke volumes by ICUS and the actual stroke volumes was excellent, with a regression line almost identical to the line of identity (Fig 6). Correlations and agreements between ICUS volumes or EF and biplane angiographic measurements in 10 experimental stages in 5 animals are depicted in Fig 7. The regression lines were not different from the line of identity (P>.1). There was a tendency toward underestimation of angiographic volume (41.15±24.69 mL, n=20, including end-systolic and end-diastolic volumes) by ICUS measurements (40.44±24.42 mL), but the difference was not statistically significant. No difference between ICUS (42.18±19.14%, n=10) and angiographic (42.68±19.06%) EF was observed (P>.05). Different paths to introduce the ultrasound catheter did not affect the accuracy of ICUS determination of volumes. Stroke volume by ICUS with the catheter introduced via a femoral artery (34.8±7.41 mL) was not different from that via a carotid artery (33.6±7.85 mL, P>.05, n=9). Similarly, end-diastolic volume (72±18 mL, n=9), end-systolic volume (37±12 mL), and EF (48±8%) determined by ICUS with the catheter introduced via a femoral artery were not significantly different from the end-diastolic volume (71±17 mL), end-systolic volume (36±17 mL), and EF (47±9%) via a carotid artery (P>.05).

Discussion
The feasibility of imaging cardiac structures with an ICUS device has been shown previously. However, ICUS measurements of LV volumes and EF must be shown to be highly accurate before this technique can compete in the cardiac catheterization laboratory with contrast ventriculography. This study demonstrates that
ICUS imaging with a 10-MHz transducer mounted on a 10F catheter tip reliably and accurately measures LV volumes and EF with Simpson’s rule in a canine beating-heart model in which instantaneous true LV volume can be directly measured. In intact animals, stroke volumes and EF could also be reliably and accurately measured by an ICUS catheter introduced via a femoral or carotid artery.

Since the accuracy of calculating LV volumes by Simpson’s rule depends on the height of the segments, the optimal segment height, i.e., the height that requires the minimal number of segments while still maintaining accuracy, was explored. Both 5- and 10-mm slices provided adequate accuracy for calculating LV volumes. The presence of LV infarction and aneurysm did not affect the accuracy of the ICUS measurement of volumes and EF when a segmental height ≤10 mm was applied.

### Table 2. Comparison of Absolute Measurement Errors of Intracardiac Ultrasound in Normal and Distorted LV Shapes Using Different Methods

<table>
<thead>
<tr>
<th>Absolute Measurement Errors</th>
<th>Distorted LV Shape</th>
<th>Normal LV Shape</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDV, mL</td>
<td>5-mm segment</td>
<td>1.96±±2.01</td>
<td>1.99±±1.47</td>
</tr>
<tr>
<td></td>
<td>10-mm segment</td>
<td>2.88±±2.18</td>
<td>2.57±±1.75</td>
</tr>
<tr>
<td></td>
<td>15-mm segment</td>
<td>5.07±±3.03</td>
<td>3.07±±3.13</td>
</tr>
<tr>
<td></td>
<td>Single section</td>
<td>12.80±±8.70</td>
<td>5.07±±3.72</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>5-mm segment</td>
<td>5.30±±2.59</td>
<td>3.72±±2.21</td>
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<tr>
<td></td>
<td>10-mm segment</td>
<td>5.65±±2.90</td>
<td>3.42±±2.26</td>
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<td></td>
<td>15-mm segment</td>
<td>6.98±±4.28</td>
<td>4.54±±2.94</td>
</tr>
<tr>
<td></td>
<td>Single section</td>
<td>21.97±±15.60</td>
<td>10.07±±6.07</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; LVEDV, LV end-diastolic volume; LVESV, LV end-systolic volume; and LVEF, LV ejection fraction.

**Measurement of LV Volumes and EF**

Simpson’s rule for volume calculations has theoretical advantages, especially in an LV with a distorted shape. However, several studies with transthoracic echocardiography or contrast ventriculography have demonstrated only a minor improvement in measurement error over other algorithms, such as the area-length method, although in an isolated heart model, integration of serial multiple echocardiographic LV cross sections with a 3-mm segmental height has been reported to be very accurate for calculation of LV volumes. This method may be partly because Simpson’s rule has to be modified for application in angiographic or conventional echocardiographic calculations. The commonly used modified Simpson’s rule assumes that the length of one of the two orthogonal angiographic or echocardiographic planes represents the true long axis of the LV and that the shape of the LV cross section is elliptical/circular. In fact, the long-axis length of one angiographic or echocardiographic plane may differ from another and is often foreshortened, and LV cross section may not be circular or elliptical when myocardial infarction or LV aneurysm is present. Another modified Simpson’s rule for conventional two-dimensional echocardiographic calculation uses several (usually four) LV cross sections and assumes that distances between them are equal. However, these distances are not equal and may vary from one patient to another, especially when LV infarction or aneurysm is present.

An ICUS catheter with the transducer mounted on the tip can image the LV in serial cross sections. In this study, the LV volumes were calculated by integrating all cross-sectional areas along the LV long axis multiplied by segmental height. This approach requires no assumptions about cross-sectional LV geometry or LV length. ❍
The average of the areas at the beginning and end of the segment is assumed to be representative of the mean segmental area. This minor assumption is valid if the segments are sufficiently short. Mathematically, the shorter the segments, the more accurate the calculation; in practice, however, measuring too many short slices is tedious and time-consuming. The choice of a 10-cm segment produced only a minimal measurement error compared with using a 5-mm segment. The presence of an LV aneurysm or myocardial infarction tended to decrease the accuracy of the ICUS measurements of end-systolic volume, and thus EF, using a segmental height of 15 mm or the single section, as shown in Table 2. Obviously, the single section misses apical infarcts and aneurysms.

Comparison With Prior Studies

Although catheter-based two-dimensional ultrasound imaging has been investigated since the early 1960s and LV dynamics were assessed in previous reports,8-12 few studies have systematically and quantitatively evaluated LV volumes and EF.13-15 In a preliminary report, Wolfberg et al15 compared LV volumes from ICUS calculated by a Simpson's rule algorithm with LV volumes determined by single-plane angiography calculated by a prolate elliptical model in pigs. Although a good correlation ($r = .95$) was observed for LV end-diastolic volumes, end-systolic volumes correlated only moderately well ($r = .71$). Our results may differ from those of Wolfberg et al because, instead of single-plane angiography, we measured true volumes or used blipane angiography with a correction factor for small hearts. We also used different ultrasound catheters (10F, 10 MHz compared with 6F, 12.5 MHz). The absolute accuracy of ICUS cannot be determined by comparison with single-plane angiography because calculations of LV volumes from single-plane angiograms may vary significantly with different projection angles, especially in LVs with deformed shapes.6 Even with blipane angiography, a correction factor should be applied to account for papillary muscles and trabecular carnae as well as the inadequacy of the ellipsoid reference figure to describe a chamber with irregular shape and margins.6 For canine hearts or small hearts in a pediatric population, a different regression equation has been proposed for the correction.22

In our study, a regression equation22 derived from small canine hearts was chosen to correct for angiographic overestimation of LV volumes. This equation avoided the problem of overcorrection of end-systolic volume when the LV volume was <15 mL by conventional equations for adult human hearts.22 In several experimental stages in our study, the end-systolic angiographic volumes were from 8 to 15 mL before the correction and would have been close to zero or even a negative value had the correction equation for human adult hearts been applied. This study proportionally corrected end-diastolic and end-systolic volumes using the correction equation proposed by Graham et al.22 Therefore, the correlation between angiographic and ICUS measurements for end systole or for EF was not different from the correlations for end diastole. The improvement in the imaging quality with the 10-MHz ultrasound catheter was strikingly obvious and probably contributed to the high correlations in our study.

Developmental Needs and Future Clinical Applications

Although ICUS sequential fixed-interval LV cross-sectional images provide a practicable approach for precise determination of LV volumes in experimental settings, several important technical improvements are required before this technique can be routinely applied in cardiac catheterization laboratories. The maximal total imaging field of the current catheter-based ultrasound equipment is 12.8 cm in diameter with the ultrasound catheter in the center of the image, or a depth of 6.4 cm around the catheter. When the catheter is placed eccentrically, this limited depth may prevent complete visualization of LV cross-sectional circumference in patients with severely dilated LVs. A future generation of ultrasound catheters with lower-frequency transducers will increase the depth of penetration and may even permit LV imaging from the right ventricle.

On pullback, the catheter may follow a curvilinear course, resulting in measurement error; fluoroscopy can be used to avoid this problem. Ideally, at each cross section of the LV, the part of the catheter on which the transducer is mounted should be parallel to the long axis of the LV to ensure that a perpendicular ultrasound beam slices the LV wall in its short axis. The 10F catheter used in the present study has a relatively rigid section on which the ultrasound crystal is mounted that appears to help maintain a perpendicular position. However, if a thinner and softer catheter were devel-
oped, an adjustable catheter tip, similar to an Inoue balloon catheter, would help to keep the section of the ultrasound catheter on which the transducer is mounted at the desired angle, maintaining the ultrasound beam perpendicular to the LV long axis. Movement of the catheter in a medial-lateral direction may cause off-angle imaging when the catheter does not move parallel to the LV long axis. A computer simulation of ICUS measurement errors from an off-angle image is included in the “Appendix.”

More significant error may be produced by the movement of the catheter in the basal-apical direction; however, this did not appear to occur with the 10F housing catheter used in this study. If the catheter is bent or trapped in the LV wall, which could be observed by fluoroscopy, catheter movement in the apical-basal direction could theoretically occur, but this was not observed in our study. It is also possible that systolic shortening of the LV long axis could affect the catheter position when the tip is at the very apex. In our model, less than 2 to 5 mm of systolic retraction of the catheter was observed when the tip was at the very apex. Obliteration of the LV apical cavity with catheter entrapment during systole was usually observed, indicating that the small LV long-axis shortening seen at angiography or two-dimensional echocardiography may be partly due to obliteration of the apical cavity. This may explain why only a minimal systolic retraction of the catheter was observed in this study, whereas 1 to 2 cm of shortening in the LV long axis is usually observed by angiography.

In the case of significant systolic retraction of the ultrasound catheter, the imaging planes may differ from diastole to systole, causing one diastolic section in the LV apex to be missed. The consequences may be minimal because the apex is obliterated during systole and because the apical diastolic cross-sectional area is small, ranging from 1.5 to 4.7 cm² in our study. A smaller catheter of sufficient rigidity or one with an adjustable tip to maintain its form during the cardiac cycle would certainly improve clinical utility. The ability of ICUS to assess the extent and location of LV regional wall motion abnormalities is currently being explored, and preliminary results have recently been reported.16,17

Summary

ICUS using a 10-MHz transducer mounted on a 10F housing catheter can image the entire LV circumferential endocardium and wall in beating animal hearts. LV end-diastolic and end-systolic volumes can be accurately derived from a series of sequential ICUS images of LV cross section at each 5- to 10-mm interval by Simpson’s rule. This technique allows reliable determination of parameters derived from LV volume such as LV EF and stroke volume. Technical improvements such as an extended imaging field by means of a lower-frequency transducer and smaller catheters may be required before use of this technique becomes routine.

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Appendix

Mathematical Modeling of LV Volume and EF in Normal Ventricles

To explore the impact of slice thickness and malalignment on the accuracy of LV volume measurements by ICUS, mathematical modeling was performed. The ventricle was modeled as a prolate ellipsoid with major axis a (directed along the z axis) and minor axes b, with the ellipsoid truncated at the equator (z=0), given by the manifold

\[ \frac{x^2}{b^2} + \frac{y^2}{b^2} + \frac{z^2}{a^2} = 1 \]

The ICUS image was modeled as a plane crossing the z axis at z0, tilted by an angle θ from the x-y plane, rotated about the y axis. For a point at a distance r from the center of the catheter and at an angle θ from the ICUS x’ axis, the coordinates in the x,y,z system are

\[ x=r \cos \theta \cos \phi; y=r \sin \theta; z=r \cos \theta \sin \phi + z_0 \]

To obtain a description of the endocardial border as seen by the ICUS plane, Equations 4 are substituted into Equation 3 to yield a quadratic equation,

\[ r^2 \left( \frac{\cos^2 \theta \cos^2 \phi + \sin^2 \theta \cos^2 \phi \sin^2 \phi}{b^2} + \frac{2z_0 \cos \theta \sin \phi}{a^2} \right) + r \left( \frac{2z_0 \cos \theta \sin \phi}{a^2} \right) + \left( \frac{z_0^2}{a^2} - 1 \right) = 0 \]

which can be solved for r(θ). For a series of N slices spaced Δz apart, LV volume is given by

\[ V(a, b, z, \phi) = \sum_{z=0}^{N} \left( \int_{z}^{z+\Delta z} \frac{r^2(\theta)}{2} d\theta \right) \Delta z \]

Equation 5 was solved for all combinations of a = 6, 8, and 10 cm; b = 1 and 2; Δz = 0.5 and 1 cm; θ (the misalignment parameter) = 0°, 10°, 20°, and 30° to yield the end-systolic volume (ESV), with endocardial excursions of 0.5, 1.0, and 1.5 cm used to model end-diastolic volume and calculate the EF (144 simulations in all). These were compared with the true volume, 2πab²/3, and derived EF.

Results

For φ=0°, the error in ESV was minuscule, a 0.1% overestimation, with overestimations of 1.5%, 5.0%, and 12.1% for φ=10°, 20°, and 30°, respectively. EF was barely affected by ICUS malalignment and was underestimated by only 0.7%, even for φ=30°. Linear regression demonstrated that the error was significantly (P=.01), although only slightly, affected by slice thickness, with the ESV overestimation falling by about 10% when the slice thickness was reduced from 1.0 to 0.5 cm.

Because this mathematical model used a prolate ellipsoid in its analysis, the results are strictly applicable only to the symmetrical, normal ventricle. However, since the numerical integration was performed around
the full perimeter of the ellipsoid without any assumption of symmetry, these data may actually be valid in other circumstances. Overall, these findings support the accuracy of ICUS-determined LV volume and EF as demonstrated in this article.

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