Serial Echocardiographic Evaluation of Left Ventricular Function in Valvular Disease, Including Reproducibility Guidelines for Serial Studies

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SUMMARY Longitudinal echocardiographic studies of left ventricular (LV) function in valvular disease were evaluated in 24 medically treated patients followed for 6 months to 3 years (mean 16.3 months) and in 22 surgically treated patients before and at least 1 year after operation (mean 14 months). In initial reproducibility studies of enlarged hearts (mean end-diastolic dimension [EDD] 6.6 ± 0.2 cm [± SEM], range 4.8–8.8 cm), serial changes in LVEDD exceeding ± 0.3 cm and in the percentage of minor diameter systolic shortening (%D) greater than ± 5.5% were considered biologically significant (outside the range of measurement and temporal variability). Guidelines for serial echocardiographic tracking of the left ventricle are presented. Medically treated patients were divided into three categories according to EDD and %D: (1) stable or improved LV size and function (seven patients); (2) progressive LV dilatation with stable function (seven patients), in which EDD increased by 0.5–1.2 cm (mean EDD 5.8 ± 0.4 to 6.6 ± 0.4 cm, p < 0.001), with no significant change in %D; and (3) LV decompensation (10 patients), with %D declining by 6–20% (mean %D 38 ± 2.0% to 28 ± 1.8%, p < 0.001), usually associated with an increasing EDD (mean EDD 6.0 ± 0.3 to 6.7 ± 0.3 cm, p < 0.001). In 15 surgical patients EDD decreased postoperatively by 0.4–2.2 cm (mean EDD 6.3 ± 0.2 to 5.2 ± 0.2 cm, p < 0.001), while seven patients had either no postoperative change or an increase in EDD of 0.4–1.0 cm (mean EDD 7.0 ± 0.5 to 7.2 ± 0.6 cm). In 17 of 24 medical (70%) and 17 of 22 surgical patients (77%), the results of serial echocardiographic assessment of the EDD and %D were in agreement with the results of other noninvasive methods of evaluating the left ventricle. Echocardiographic evidence of progressive LV dysfunction was otherwise clinically silent in six medical patients. The preoperative findings of an EDD greater than 8.0 cm, ESD greater than or equal to 6.4 cm and low %D (≤ 22%) were noted only in three patients with aortic insufficiency who had postoperative heart failure probably secondary to irreversible myocardial damage sustained before surgery.

Thus, echocardiography is valuable in longitudinal pre- and postoperative evaluation of LV function in patients with valvular disease, and may aid in recognition of early, otherwise undetected, or irreversible LV dilatation and dysfunction.

VALVULAR INSUFFICIENCY and stenosis may produce a burden on the left ventricle that has the potential of causing insidious, sometimes irreversible, deterioration of left ventricular (LV) function. Echocardiography is well suited for serially assessing the left ventricle in valvular disease to characterize the degree, the mechanism and the time course of myocardial change and function more exactly, and for detecting signs indicative of irreversible myocardial decompensation. Although preoperative echocardiographic evaluation of LV function in valvular disease has been reported, only recently has this technique been used for serial examination of myocardial changes after valvular surgery, with conflicting results.

The present study was undertaken to evaluate the role of M-mode echocardiography in the longitudinal evaluation of LV function in aortic insufficiency, aortic stenosis and mitral regurgitation. Serial long-term echocardiographic assessment of LV function was studied in patients with these valvular lesions treated either medically or surgically. Serial echocardiographic assessment of LV function was compared with the evaluation of LV performance by other noninvasive clinical methods. In addition, we studied the limits of reproducibility for serial echocardiographic evaluation of LV dimensions and function in valvular disease and defined changes that seemed statistically and biologically significant.

Methods

Patient Groups

The study group consisted of 46 patients admitted for evaluation of valvular heart disease, including 24 medically treated patients (group 1), of whom 14 patients had aortic insufficiency, three had aortic stenosis and seven had mitral regurgitation, and 22 surgically treated patients (group 2), of whom nine had aortic insufficiency, seven had aortic stenosis and six had mitral regurgitation. The medically treated patients were studied serially with two or more echocardiograms over a period of 6 months to 3 years (mean 16.3 months); surgically treated patients had echocardiograms before and at least 1 year after surgery (mean 14 months). All patients in the surgical group received gluteraldehyde-treated porcine heterografts. Each patient had hemodynamic studies, including cardiac catheterization and left ventricular cineangiography. Multiple valvular abnormalities or combined stenosis and insufficiency, clinical or angiographic evidence of coronary disease with segmental...
disorders of LV contraction, and technically unacceptable echocardiograms were the criteria for exclusion. The subjects were 23-77 years old (mean 50 years). Echocardiographic data were also collected in our laboratory on 53 normal subjects without clinical evidence of heart disease to establish control values of echocardiographic measurements.

Etiology of the valvular disease was determined by echocardiographic, hemodynamic, surgical, and pathologic analysis. In the 10 patients with pure valvular aortic stenosis, the aortic valve area estimated by the Gorlin formula averaged 1.06 cm² (range 0.8-1.55 cm²) in group 1 and 0.49 cm² (range 0.3-0.6 cm²) in group 2. Of 23 patients with isolated aortic insufficiency, six patients had acute or subacute regurgitation related to infective endocarditis (three in group 1 and three in group 2). The remaining 17 patients with aortic regurgitation were judged on historical, clinical, surgical or pathologic grounds to have chronic valvular disease related to rheumatic disease in 11, lues in one, Marfan’s syndrome in two, bicuspid aortic valve in two and unknown etiology in one.

The 13 patients with mitral regurgitation included two with mitral valve prolapse and intact chordae tendineae (group 1), nine with flail mitral valve due to ruptured chordae tendineae (four in group 1 and five in group 2) and two with rheumatic mitral regurgitation (one each in the medical and surgical groups).

Clinical Analysis

Patients in both groups were also evaluated serially throughout their follow-up period by other non-invasive clinical means; progression or regression of clinical signs and symptoms of congestive heart failure, any change in heart size or in pulmonary vasculature on chest x-ray and any significant change in the ECG were noted for each patient. Medically treated patients were judged to have progression of their disease if deterioration occurred in any one of these clinical variables, whereas surgically treated patients were thought to show regression of disease if improvement occurred in any of these variables.

Echocardiographic Analysis

M-mode echocardiograms were done in the standard manner, with the patient in the supine position with the head of the bed elevated 30°. The left ventricle was recorded just distal to the tip of the anterior mitral leaflet from the standard interspace, as defined by Popp et al. Special efforts were made to record from the same intercostal space with the patient’s upper body and the head of the bed always elevated to the same degree (30°) and the patient in a similar degree of left lateral tilt by placing a 30° angled wedge behind the patient’s back. In addition, tracings were selected for measurement from similar places in the left ventricle by reviewing previous echocardiograms.

Tracings were obtained using an Ekoline 20A (Smith-Kline Instruments) ultrasonoscope and 2.25-MHz, 0.5-inch diameter transducers collimated to 5 cm or 7.5 cm, and were recorded on an Electronics-for-Medicine DR6 strip-chart recorder at 50 or 100 mm/sec. Specific measurements were made by averaging three or more cycles for sinus rhythm and five cycles for atrial fibrillation.

Measurements of LV dimensions are shown in figure 1. Internal LV end-diastolic minor dimension (EDD) was measured between the septal and posterior wall endocardium at the onset of the QRS complex. Left ventricular end-systolic dimension (ESD) was measured as the perpendicular distance between the LV posterior wall endocardium at its most anterior position during systole and the interventricular septal endocardium. Left ventricular posterior wall amplitude was obtained from the maximum excursion of the posterior wall endocardium during systole. Interventricular septal amplitude was measured analogously. LV posterior wall thickness was measured as the narrowest endocardial–epicardial distance in mid-diastole just before the presystolic thinning dip. Similarly, interventricular septal thickness was measured from the right ventricular endocardium to the LV endocardium in mid-diastole just before presystolic thinning.

Derived echocardiographic ejection indexes of LV

![Figure 1. Echocardiographic measurements of the left ventricle (paper speed 50 mm/sec). EDD = end-diastolic dimension; ESD = end-systolic dimension; PWA = posterior wall amplitude; PWT = posterior wall thickness; IVSA = interventricular septal amplitude; IVST = interventricular septal thickness.](image-url)
performance included percentage change of the minor diameter during systole (%D):

\[
\%D = \left( \frac{EDD - ESD}{EDD} \right) \times 100
\]

and ejection fraction (EF):

\[
EF = \left( \frac{EDV - ESD}{EDV} \right) \times 100
\]

using the method of Teichholz \(^{22}\) to calculate end-diastolic and end-systolic volumes; %D and EF are collectively referred to as echocardiographic ejection phase indexes.

**Determination of Limits of Reproducibility**

To determine what magnitude of change in the echocardiographic measurements should be considered significant, we evaluated reproducibility in terms of measurement variability (i.e., how much each measurement varied when made repeatedly on the same echocardiogram) and of temporal variability (i.e., how much change occurred secondary to physiologic or technical factors when echocardiographic studies were repeated in the same patient on different days) (fig. 2). Measurement variability was tested by having three experienced observers make blind, duplicate measurements on two separate occasions on a series of 15 randomly selected abnormal echocardiograms. Each response consisted of the average of three to five measurements. Temporal variability was evaluated by recording and measuring two to five echocardiograms in each of 12 stable patients over 1 week. Each type of variability was determined in patients with significant cardiomegaly. The mean EDD was 6.9 ± 0.2 cm (range 5.6–8.1 cm) in the patients with valvular disease who were used for determining measurement variability, and 6.1 ± 0.4 cm (range 4.8–8.8 cm) in the nine patients with valvular disease and the three patients with cardiomyopathy who were used for determining temporal variability. By analyzing all of these reproducibility measurements, both types of variability were then evaluated by the coefficient of variation, defined as the standard deviation of all the repeated measurements in a given case divided by the mean of those measurements. Two standard deviations on either side of the mean were calculated from the estimates of reproducibility, and the 95% confidence interval was determined for each echocardiographic measurement: the actual value by which each measurement can vary secondary to technical reasons in serial echocardiographic studies was then calculated.

Reproducibility is also influenced by repeat readings of the same echocardiogram, either by one or more interpreters. To evaluate the effect of multiple readings on reproducibility, the percentage of echocardiographic responses falling within the 95% confidence interval on a given tracing were analyzed with one interpreter making single and duplicate readings, with two interpreters making one and two readings and with three interpreters making one reading each. All these responses were made on separate days and consisted of the average of three to five measurements for each reading, depending on the cardiac rhythm.

**Statistical Analysis**

The statistical significance of differences in echocardiographic measurements and group means was tested by paired and nonpaired \(t\) tests.

**Results**

**Limits of Reproducibility of Serial Echocardiographic Measurements**

The coefficient of variation was 2.6–2.9% when EDD was measured either repeatedly on the same tracing (measurement variability) or on different tracings obtained over a period of time (temporal variability) (fig. 2). Variability is somewhat larger, about 10%, when %D was measured. From these estimates of reproducibility, the 95% confidence interval (±2 S.D.) for each measurement was used to determine what change should be considered significant (fig. 2). Thus, on serial echocardiograms, changes in EDD exceeding ±0.3 cm or in %D greater than ±5.5% were considered to be outside the range of technical error.

![Diagram](http://circ.ahajournals.org/)

**Figure 2.** Evaluation of the reproducibility of serial echocardiography. Measurement and temporal variability in serial echoes can produce variation in end-diastolic dimension (EDD) of ±0.3 cm and in the percentage of minor diameter systolic shortening (%D) of ±5.5%.
and, therefore, biologically and statistically significant.

Figure 3 depicts the percentage of responses falling within the 95% confidence interval, when made by one, two and three interpreters making either single or duplicate readings on separate occasions. Each response consisted of the average of three to five measurements. A single interpreter making one reading has only a 79% probability of falling within the 95% confidence interval for a given echocardiographic measurement. Increasing the number of readers or the number of readings made on separate occasions increases this probability, such that two interpreters making duplicate readings or three interpreters making one reading each have greater than a 90% chance that their responses, when averaged, will fall within the 95% confidence interval.

Serial Echocardiographic Measurements in Group 1

Because both echocardiographic LV ejection indexes provided approximately the same results, analysis of LV function in the medical patients is presented in terms of EDD and %D.

An echocardiographic measurement was judged changed only if it increased or decreased by more than could be attributed to temporal or measurement variability (EDD ± 0.3 cm and %D ± 5.5%). Serial changes less than these amounts were not considered biologically significant, and the echocardiographic measurement was judged stable.

The 24 medically treated patients followed for 6 months to 3 years (mean 16.3 months) were divided into three categories on the basis of EDD and %D.

Stable or Improved LV Dynamics (fig. 4)

Seven medically treated patients had no progression of LV disease during the follow-up period in that they showed stable or improved LV dynamics. With medical therapy, EDD decreased significantly by 0.4–0.9 cm in four of these patients, and remained stable (varied by less than 0.3 cm) in three. %D either showed no biologically significant change (i.e., varied by less than 5.5%) or improved (increased 7% in one patient). Mean values of EDD and %D were not significantly changed (EDD 6.8 ± 0.4 [SEM] to 6.5 ± 0.4 cm, p < 0.001; %D 31 ± 2.4 to 31 ± 2.9%, p < 0.001). Three patients in this category had aortic insufficiency, two had aortic stenosis and two had mitral regurgitation.

Progressive LV Dilatation with Stable Function (fig. 5)

Despite progressive LV dilatation, ventricular function was maintained stable or compensated, as defined by a stable %D, in seven medically treated patients. In these patients, the EDD increased by 0.5–1.2 cm (mean EDD 5.8 ± 0.4 to 6.6 ± 0.4 cm, p < 0.001), whereas %D did not change significantly (mean %D 37 ± 1.3 to 35 ± 1.5%, p < 0.001). Four patients in this category had aortic insufficiency, one had aortic stenosis and two had mitral regurgitation.
LV Decompensation (fig. 6)

LV decompensation, characterized by a significant decline of 6–20% in %D (mean 38 ± 2.0 to 28 ± 1.8%, p < 0.001), developed in 10 medically treated patients. In all but two of these patients, EDD increased concomitantly 0.6–1 cm (mean EDD 6.0 ± 0.3 to 6.7 ± 0.3 cm, p < 0.001). In the two patients in whom EDD did not change significantly, the %D fell 10% and 12%, indicating the development of significant LV dysfunction. Seven of these 10 patients had aortic insufficiency and three had mitral regurgitation.

Clinical vs Echo Analysis in Group 1

In these 24 medically treated patients, echocardiographic evidence of progressive LV dysfunction was compared with other clinical evidence of deterioration, as judged as a change in signs, symptoms, chest x-ray or ECG (fig. 7). There was a striking concordance between echocardiographic measurements of EDD and %D and the results of other clinical methods of assessing the state of the left ventricle in 17 of these 24 patients. Ejection phase indexes and other clinical methods suggested no progression in six patients and progressive deterioration in 11 patients. In six medically treated patients (indicated by an asterisk in figure 7), echocardiographic evidence of progressive LV dysfunction, as judged by a significant increase in EDD or a decrease in %D, was otherwise clinically silent, with no change in the patient's signs, symptoms, chest x-ray or ECG.

Serial Echocardiographic Measurements in Group 2

Because placement of prosthetic valves often produces abnormal septal motion, and because under such circumstances the septum may not be representative of the other cardiac walls, estimates of ejection phase indexes, including %D, may be misleading in the postoperative state. Similarly, postoperative ESD, which is directly affected by such abnormal septal motion, may not accurately reflect the patient's clinical course. As a consequence, EDD is considered the principal means of evaluating LV change after valvular surgery.

Among the 22 surgically treated patients studied before and 1 year after valvular surgery (mean follow-up 14 months) (fig. 8), 15 patients had a significant decrease in EDD of 0.4–2.2 cm postoperatively, with the mean EDD decreasing from 6.3 ± 0.2 to 5.2 ± 0.2 cm (p < 0.001). By this measurement, these patients were improved with regression of LV size. Five of
these patients had aortic insufficiency, four had aortic stenosis and six had mitral regurgitation. However, in seven surgically treated patients EDD did not change significantly or increased 0.4–1.0 cm (mean EDD 7.0 ± 0.5 to 7.2 ± 0.6 cm). These patients were unimproved with no regression of LV size. Four of these unimproved patients had aortic insufficiency and three had aortic stenosis. None of the patients with postoperative regression had a preoperative EDD greater than 8.0 cm and all three patients with a preoperative EDD greater than this value showed no regression after valvular surgery (fig. 8).

In the 15 surgical patients who had regression in LV size as judged by a significant decrease in the postoperative EDD, preoperative ESD ranged from 2.0–5.0 cm, and the mean ESD after operation was not significantly changed (3.9 ± 0.2 to 3.7 ± 0.2 cm, p < 0.001). In the seven surgical patients with no regression of LV size, preoperative ESD was 2.8–6.6 cm, and the mean preoperative ESD was significantly greater than in the patients with postoperative LV regression (3.9 ± 0.2 vs 5.0 ± 0.6 cm, p < 0.001). In these patients with no regression, the mean ESD actually increased postoperatively (5.0 ± 0.6 to 5.4 ± 0.7 cm, range 0–1.7 cm).

Clinical vs Echocardiographic Analysis in Group 2

Among the 22 surgically treated patients, echocardiographic EDD and other noninvasive clinical methods of assessing the LV were in agreement in 17 patients, with improvement suggested in 14 patients and lack of improvement in three patients (fig. 9).

The seven patients with no regression in LV size by echocardiographic EDD postoperatively are marked by asterisks in figure 9 and are further analyzed in figure 10. Four of these patients were improved by other methods of clinical assessment, and three were unimproved by echocardiography or other methods. Four of these seven patients had aortic insufficiency and three had aortic stenosis. Preoperatively, three of these patients had exceptionally large EDDs (8.0, 8.2 and 8.4 cm) and ESDs (6.4, 6.5 and 6.6 cm), and four patients had especially low %D (17, 19, 20 and 22%) (fig. 10). Postoperatively, four of these seven patients with no regression in LV size by echocardiography had significant congestive heart failure. Three of these patients with significant postoperative heart failure had a very large EDD (≥ 8.0 cm) and a large ESD (≥ 6.4 cm) associated with a low %D (≤ 22%) preoperatively. All three of these patients had properly functioning prosthetic valves documented on repeat cardiac catheterization and no apparent operative complication; the remaining patient had significant paraprosthetic aortic insufficiency. All other patients in the surgical group, including the 15 patients with postoperative regression of LV dimension and the other four patients with no regression of LV dimension, had preoperative EDDs and ESDs less than those in these three patients with postoperative failure, i.e., EDD ≤ 7.6 cm and ESD ≤ 5.6 cm in all the other surgical patients. Only one other patient had a reduction in preoperative %D similar to that in these three patients. In two of the seven patients (fig. 10), both of whom had aortic stenosis, preoperative echo-
cardiographic measurements were normal, and did not change postoperatively.

**Individual Serial Echocardiographic Studies**

Figure 11 (case A) depicts longitudinal echocardiographic studies in a patient with aortic regurgitation secondary to endocarditis. Initially, the EDD increased and the ESD decreased, resulting in a compensatory increase in %D. Although over the ensuing 17 months, LV dilatation continued with only slight decrease in %D, significant LV dysfunction then appeared with a dramatic fall in %D. After aortic valve replacement, an impressive decline to a normal EDD occurred over the next 6 months.

In contrast, the serial echocardiographic studies in a 52-year-old patient with chronic rheumatic aortic insufficiency (fig. 11, case B) revealed progressive and marked LV dilatation (EDD 8.0 cm, ESD 6.3 cm) and a decrease in %D during the initial 6 months of follow-up. After apparently uncomplicated surgery, ventricular size failed to regress over the next 19 months, even though the aortic prosthesis was functioning normally by clinical assessment and on repeat cardiac catheterization. Clinically, this patient continued in congestive heart failure after valve replacement, presumably because of irreversible preoperative myocardial damage.

Figure 12 shows longitudinal echocardiographic studies in three medically treated patients. Case A illustrates a case of aortic insufficiency in a 29-year-old patient with a bicuspid aortic valve in whom EDD and ESD increased progressively and LV function (%D) remained stable over a 20-month period. Cases B and C illustrate two adult patients with mitral regurgitation secondary to prolapse with intact chordae tendineae in whom ventricular dimensions increased progressively during long-term follow-up. In patient B the %D remained stable for 34 months, whereas in patient C the %D decreased significantly during a 31-month period.

**Discussion**

The left ventricle undergoes a series of changes when exposed to excessive pressure or regurgitant volume. Hypertrophy, without a great deal of dilatation, is the more common response to aortic stenosis whereas combined dilatation and myocardial hypertrophy invariably develop when aortic or mitral insufficiency is of significant magnitude. Initially, such changes are considered physiologic and compensatory, in that they allow maintenance of normal cardiac output and LV filling pressure. With time, however, and especially in the presence of increasingly severe valvular dysfunction, myocardial decompensation begins. The ventricle becomes unable to achieve normal resting and exercise flows and maintain normal diastolic pressures; signs, symptoms and hemodynamic evidence of heart failure supervene. Cardiac failure consequent to valvular disease is, in its early stages, a reversible phenomenon, and correcting the valvular defect by leaflet repair or replacement generally restores normal or nearly normal LV dynamics. If valvular disease is permitted to persist too long, however, an irreversible phase of myocardial dysfunction occurs, where alleviation of a pressure or volume load may fail to alleviate ventricular failure. Biochemical changes and structural alterations of LV muscle, including fibrosis and possibly mitochondrial changes, in all likelihood, subserve these hemodynamic alterations and account for their irreversibility.

Of utmost importance in management of patients with stenotic and regurgitant valvular lesions, therefore, is the serial tracking of ventricular size and func-

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**Figure 9.** Comparison of echocardiographic measurements of end-diastolic dimension (EDD) and other clinical means of assessing the left ventricle, such as a change in signs and symptoms, chest x-ray or ECG, in the 22 surgically treated patients. The cross-hatched boxes indicate concordance between echocardiographic and other methods of clinical assessment. The patients with no postoperative regression of left ventricular size by echocardiography are marked with asterisks. See text and figure 10 for further analysis.

**Figure 10.** Analysis of seven patients who had no regression of end-diastolic dimension (EDD) after valve replacement. The preoperative combination of a markedly elevated EDD, significantly increased end-systolic dimension (ESD) and abnormal percentage of minor diameter systolic shortening (%D) are boxed. Postoperatively, patients who continued to have congestive heart failure (F) and who had these preoperative findings are also boxed. AI = aortic insufficiency; AS = aortic stenosis.
tion, primarily to detect early evidence of progressive cardiac hypertrophy, dilatation and dysfunction. Echocardiography lends itself well to this aim, and provides a means of longitudinally evaluating LV function in aortic stenosis and insufficiency and mitral regurgitation. This approach should facilitate detection of early functional changes in the left ventricle, thereby guiding the clinician in determining the optimal timing for cardiac catheterization and valvular surgery.

Reproducibility Guidelines for Serial Echocardiographic Studies (figs. 2 and 3)

All techniques, including echocardiography, have an inherent variability on being repeated. It is thus necessary, in any study that focuses on serial changes in a measurement, to minimize variation and to define the limits of reproducibility of the technique being used. In serial echocardiographic studies, the left ventricle should always be recorded from the standard interspace, just distal to the tip of the mitral valve. The patient's upper body should always be elevated to the same degree and positioned in a similar degree of left lateral tilt by always using a certain degree of elevation of the head of the bed measured with a protractor and by placing a standard angled wedge behind the patient's back. The details of the intercostal space used, the degree of elevation of the patient's upper body and the degree of left lateral tilt should be noted in the chart of a patient whose left ventricle is being followed serially by echocardiography and consulted before each recording. In addition, efforts should be made to study the patient in a basal state to minimize

**Figure 11.** Case A: Serial preoperative and postoperative studies in a patient with aortic insufficiency secondary to endocarditis. Note progressive increase in the end-diastolic (EDD) and end-systolic (ESD) dimensions and the acute fall in percentage of minor diameter systolic shortening (%D) before surgery. Postoperatively, -EDD returned to normal within 6 months. Case B: Serial echocardiographic studies in a patient with aortic insufficiency. Note the marked left ventricular dilatation and depressed %D preoperatively, with failure of the EDD to regress during the 6 months after valve replacement.

**Figure 12.** Case A: Echocardiographic studies in a patient with aortic insufficiency who had a progressive increase in end-diastolic (EDD) and end-systolic (ESD) dimensions, with maintenance of a stable percentage of minor diameter systolic shortening (%D) over 19 months. Cases B and C: Serial echocardiographic studies in two patients with mitral regurgitation. EDD and ESD increased progressively in both patients. Patient B maintained a stable %D during 34 months of follow-up, while patient C had a significant decline in %D over a 31-month period.
the effect of heart rate on LV measurements. Although not done in this study, measuring LV dimensions at a consistent part of the respiratory cycle, as determined by a respirometer, will improve reproducibility. Finally, by reviewing previous records, similar places within the left ventricle should be selected for serial measurement. Even when all these precautions are observed, a certain amount of variability occurs in serial echocardiographic measurements.

In the current study, we took these steps to standardize the echocardiographic recordings and then evaluated measurement variability and temporal variability. By determining the 95% confidence interval (the range of two standard deviations for all repeated measurements) for each echo measurement, we quantified the technical error of serial echocardiographic studies. Using this approach, we showed that serial changes in EDD greater than 0.3 cm and changes in %D greater than 5.5% are outside the range of technical error and therefore represent biologically and statistically significant changes.

Reproducibility is also enhanced by repeat readings on separate occasions. To have greater than a 90% chance that averaged measurements will fall within the 95% confidence interval requires that at least two readers make a certain measurement averaging three to five cardiac cycles (fig. 3). To enhance reproducibility, all serial echocardiographic studies should be performed with the safeguard of having two or more experienced readers independently analyze each tracing. In our laboratory, serial echocardiographic studies are analyzed in duplicate, and a third independent observer is consulted when a discrepancy arises.

Appropriate Echocardiographic Measurements in Serial Evaluation

Although a variety of echocardiographic measurements were reviewed to ascertain those best suited for serial evaluation of patients with valvular disease, only the degree of LV dilatation (EDD and ESD), and the LV ejection phase indexes (%D and ejection fraction) proved to be sufficiently reproducible and valuable. The EDD, ESD and %D were most easily and reproducibly measured and are not subject to as many assumptions and errors as the ejection fraction.

A technical problem encountered in the present study was our inability to determine myocardial contractility accurately in the postoperative patients echocardiographically. Cardiac surgery and the placement of rigid valvular prostheses usually results in paradoxical, akinetic or hypokinetic septal motion. Because such septal motion may not be representative of overall ventricular performance, postoperative LV function may be significantly underestimated by echocardiography. In the majority of patients in this study evaluated after surgery, the ejection phase indexes determined by echocardiography decreased compared with the preoperative reading due to this abnormal septal motion, whereas other indexes of improvement, such as regression in symptoms, decrease in LV size on x-ray and improved angiographic ejection fraction, indicated that the left ventricle was benefited by surgery. Therefore, postoperative measurements of LV ejection phase indexes, based on the limited "ice-pick" view of the heart provided by M-mode echocardiography were discarded as potentially misleading.

We also hypothesized that serial changes in the amplitude or velocity of posterior wall motion might be an alternative means of assessing postoperative ventricular function. However, posterior wall amplitude and velocity showed little or no correlation with ejection phase indexes in the medical group (r < 0.50), and thus are considered unreliable means of assessing postoperative ventricular function. Likewise, because the degree and presence of abnormal septal motion postoperatively directly affects ESD and because such abnormal motion is present for a variable period of time and is secondary to several etiologies, including conduction abnormalities, postoperative ESD was considered less likely to reflect a patient's course after surgery than EDD, which is unaffected by these variables. Based on these observations, we considered left ventricular EDD the most reliable measurement for echocardiographic assessment of postoperative ventricular function.

Other measurements considered to reflect cardiac output, myocardial hypertrophy, or LV compliance — including aortic and anterior mitral leaflet amplitudes, posterior wall and septal thickness, PR-AC interval and EF slope — were also analyzed, but, as previously reported, were of little value in defining LV function in individual patients.

The most reliable and reproducible echocardiographic measurements for preoperative serial evaluation of LV function in patients with valvular disease are EDD, ESD and %D. Postoperatively, EDD is the most reliable echocardiographic measurement.

Serial Studies in Unoperated Patients with Valvular Disease (figs. 4-7)

Several echocardiographic patterns of LV dilatation and function were defined. In patients treated medically, a group with stable LV dimensions and ejection phase indexes was delineated (fig. 4), emphasizing that even hemodynamically severe valvular lesions may be commensurate with a stable clinical and hemodynamic course over a long period of time. In one medically treated patient who had stable ventricular function, %D increased from 41 to 48%; this patient had subacute mitral regurgitation due to myxomatous change and valve prolapse. Such augmentation in contractility probably represents a physiologic, compensatory response to ventricular volume overload. Another patient in this group had regression of LV dilatation as his congestive heart failure and rheumatic mitral regurgitation were treated medically (EDD decreased from 7.7 to 6.8 cm). Regression of dilatation was seen most often after valvular surgery.

Progressive LV dilatation was another serial echo-
cardiographic pattern observed in the medically treated patients (figs. 5 and 6). In many instances, LV dimensions enlarged significantly over only 4–6 months. Such dilatation, perhaps compensatory, was observed in acute and subacute aortic and mitral regurgitation, as well as in more chronic valvular disease. In some patients it led to extreme degrees of LV enlargement, with EDD in excess of 7.3 cm. Such LV dilatation occurred in combination with stable LV function, %D remaining normal and unchanged, and with deteriorating or decompensating LV function, where %D and ejection fraction decreased. LV decompensation, manifested by a progressive decrease in the ejection indexes, usually associated with other signs of clinical deterioration, in all likelihood heralds a downhill course and may be an indication for more aggressive intervention, i.e. cardiac catheterization, more frequent follow-up studies and possibly even valvular surgery. In six medically treated patients who had a progressive increase in EDD or a decrease in %D by echocardiography, no change was detected by history, physical examination, chest x-ray or ECG. These patients appeared to have clinically silent LV dilatation. The significance of this echocardiographic pattern and whether echocardiography can detect myocardial change before other noninvasive tests are both uncertain and must await further study.

Correlation of Serial Echocardiograms and Other Clinical Assessment

A significant finding of this study was the high degree of correlation between serial echocardiographic assessment of EDD and %D and other clinical methods (signs and symptoms of failure, chest x-ray and ECG) in both groups. These findings help establish the clinical reliability and usefulness of significant, longitudinal change in LV size and function as detected by echocardiography in valvular disease.

Serial Studies after Valvular Surgery (figs. 8–10)

Fifteen of 22 surgically treated patients had a regression in LV dilatation after valve surgery, and all but one of these were improved by signs, symptoms, chest x-ray or ECG. LV dilatation, therefore, is a potentially reversible state, assuming that surgical intervention is timed optimally before an inordinate degree of myocardial damage occurs. Such reduction in echocardiographically determined EDD after successful valvular surgery for volume overload states is in agreement with the results of other studies.11, 14, 15, 17

Nonregression in LV dimension was detected by echocardiography in seven patients postoperatively (fig. 10). Two of these patients had aortic stenosis without failure and maintained their previously normal ventricular size and function. All five of the remaining patients with no regression postoperatively had failure before surgery. Three of these patients with aortic regurgitation were clinically unimproved and had persistent LV failure after surgery despite a properly functioning prosthetic valve, as determined by repeat cardiac catheterization, and no evidence of perioperative myocardial infarction. The other patient with postoperative failure had persistent aortic insufficiency with significant paraprosthetic regurgitation. The final patient with no regression of LV size seemed to improve clinically once the stenotic lesion was relieved, even though the ventricle remained enlarged. In some of these patients, irreversible ventricular dilatation and myocardial damage probably led to persistent clinical failure, whereas in others, alleviation of the volume or pressure load permitted clinical improvement despite continued myocardial abnormality. These echocardiographic findings of continued LV abnormalities despite clinical improvement after uncomplicated aortic valve replacement are similar to the findings from hemodynamic and angiographic studies reported by Gault,31 Hildner32 and Pantely33 and their colleagues.

All three patients with aortic regurgitation who had persistent cardiac failure after uncomplicated aortic valve replacement with a properly functioning prosthesis at the time of long-term follow up had preoperative echocardiographic findings of a markedly dilated left ventricle (EDD ≥ 8.0 cm and ESD ≥ 6.4 cm), associated with depressed ejection indexes (%D ≤ 22%). The other 19 patients in the surgical group, 15 with regression and four without regression of LV dimensions, had a preoperative EDD ≤ 7.6 cm and ESD ≤ 5.6 cm, and all but two had a %D ≥ 26%.

Such preoperative echocardiographic findings in patients with valvular disease are in accord with findings from other studies of echocardiographic signs predictive of poor surgical results.11, 14, 15, 17 Gaasch and co-workers44 serially studied 19 patients with chronic aortic regurgitation from 1 week to 24 months after valvular surgery. All four of their patients without paravalvular aortic regurgitation in whom LV dimension was not significantly reduced postoperatively had a markedly enlarged LV dimension preoperatively (EDD ≥ 8.0 cm) and a tendency toward reduced %D (≤ 30% in two patients). In addition, these investigators found that the single preoperative echocardiographic measurement that best differentiated patients with chronic aortic regurgitation who had poor surgical results from those with successful surgery (defined as reduction in LV internal diastolic diameter to within two standard deviations of the normal value) was a disproportion between preoperative LV end-diastolic radius (R) and posterior wall thickness (Th). In their series, the four patients with a preoperative R/Th ratio ≥ 4.0 failed to return to normal LV internal dimension after surgery, whereas the 12 patients with a R/Th ratio < 4.0 regained a normal LV internal diameter after aortic valve replacement.

Using serial echocardiographic measurements, Bonow et al.11 followed 37 patients with aortic regurgitation over a mean of 34 months and reported that a LV systolic diameter > 55 mm identified patients at high risk of developing congestive heart failure or dying late postoperatively, and was the most sensitive predictor of patients who eventually came to
aortic valve replacement. These authors recommended that surgery be considered in asymptomatic patients with aortic insufficiency and left ventricular systolic diameters > 55 mm. In the present study, all 15 patients with clinical improvement and regression in EDD after surgery had a preoperative ESD < 50 mm, and only the three patients with postoperative heart failure on the presumed basis of irreversible preoperative myocardial dysfunction had a preoperative ESD > 56 mm.

In another study, Bonow et al. found that five of eight patients who died of congestive heart failure within 1 month of aortic valve replacement for symptomatic aortic regurgitation had a preoperative echocardiographically determined ejection fraction of less than 54%, whereas only two of 21 such patients with ejection fractions greater than 54% died from congestive heart failure within 1 month of surgery. Cunha and colleagues used serial echocardiograms to study 80 patients who had undergone valve replacement for aortic regurgitation (mean follow-up 27 months), and found significant differences between patients with good and poor surgical results for preoperative %D, ejection fraction and ESD, but insignificant predictive differences for EDD. All patients who had echocardiographic %D less than 31% and ejection fraction less than 58% died. Clark et al. also reported the predictive value of a reduced preoperative echocardiographic ejection fraction as regards both increased mortality and the lack of reduction in LV end-diastolic volume and mass after aortic valve replacement in patients with aortic regurgitation.

In conclusion, the limits of reproducibility for serial echocardiographic evaluation of LV dimensions and function in valvular disease were studied, and changes considered to be statistically and biologically significant were defined (serial variations in EDD of ± 0.3 cm and in %D of ± 5.5%). Guidelines for serial echocardiographic tracking of the left ventricle in patients with valvular diseases treated medically and surgically were discussed. The correlation between longitudinal echocardiographic assessment of LV size and function and other currently used clinical techniques was excellent.

Several patterns of LV dilatation and function were delineated, including stability; compensatory LV dilatation, appearing early after the onset of acute regurgitation; chronic dilatation, ranging from mild to more marked and progressive varieties, the latter potentially ominous; and otherwise clinically silent LV dilatation. Myocardial decompensation, evidenced by a decrease in ejection phase indexes may accompany LV dilatation and is perhaps the most ominous danger sign. Improved LV dynamics, seen as a regression in EDD, sometimes occurred spontaneously or after medical therapy, but were usually observed after valve replacement. Finally, failure of regression of LV dimension after valvular surgery was recognized in several patients. Patients who failed to improve clinically after heart surgery, presumably due to irreversible myocardial changes, showed progressive, exceptionally large preoperative LV dimensions (EDD ≥ 8.0 cm and ESD ≥ 6.4 cm), and substantially depressed %D (< 22%). These echocardiographic warning signs may serve as indicators of irreversible myocardial damage in patients with valvular disease.

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