Observations on the Optimum Time for Operative Intervention for Aortic Regurgitation

II. Serial Echocardiographic Evaluation of Asymptomatic Patients

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SUMMARY A recent echocardiographic study of symptomatic patients who had aortic valve replacement for isolated aortic regurgitation indicated that patients in whom preoperative left ventricular end-systolic dimension [LVD(SYS)] exceeded 55 mm or fractional shortening (%FS) was less than 25% were at high risk of developing congestive heart failure and dying after an otherwise successful operation. Because indices of left ventricular systolic function might identify asymptomatic patients with aortic regurgitation who might benefit from earlier operation, 37 such patients were evaluated with serial echocardiograms (mean follow-up 34 months). Fourteen patients (38%) subsequently developed symptoms and were recommended for operation (SUBSQ OP). Twenty-three patients (62%) remain asymptomatic during follow-up (NON OP). LVD(SYS) and %FS were the most sensitive measurements for distinguishing on initial examination the patients who subsequently required operation from those who have not (LVD(SYS) 53.0 mm SUBSQ OP vs 44.3 mm NON OP, p = 0.001; %FS 28.8% SUBSQ OP vs 33.9% NON OP, p = 0.002). During serial studies, the maximum rate of change in end-systolic dimension exceeded 7 mm per year in only one patient. Four of five patients (80%) with end-systolic dimension greater than 55 mm developed symptoms and came to operation during a mean follow-up of 39 months. Of the 20 patients whose initial end-systolic dimension was 50 mm or less, only four patients (20%) developed symptoms and required operation, and none died during follow-up. Thus, an asymptomatic patient with aortic regurgitation whose end-systolic dimension is less than 50 mm appears to be at low risk and can be safely followed with echocardiograms at yearly intervals. Asymptomatic patients with end-systolic dimension of 50–54 mm are being followed with serial echocardiograms every 4–6 months. Operation is now being recommended to patients with end-systolic dimensions of 55 mm or greater, even in the absence of symptoms.

IT IS OFTEN DIFFICULT to decide when to intervene with operation in patients with long-standing aortic regurgitation.1 Although indications vary, many clinicians only recommend operation when certain symptoms are present. This approach is based on the observation that when angina, syncope or congestive heart failure develop, prognosis over the next several years is poor.2–7 A corollary of this concept is that by not recommending operation until these symptoms occur, operative risk will be postponed, as will the long-term morbidity and mortality associated with existing prosthetic valves. Also, by postponing operation, the patient may benefit from subsequent improvements in operative technique and prosthetic valve design.

The major drawback to this approach is that by the time angina, syncope or congestive heart failure develops, some patients have already suffered irreversible left ventricular dysfunction.1,8–18 Many of these patients develop severe congestive heart failure and die after operation, despite the elimination of aortic regurgitation. The present diagnostic challenge, therefore, is to identify the asymptomatic patient with aortic regurgitation just before irreversible left ventricular dysfunction occurs so that earlier operation can be undertaken.1, 9, 12, 14, 15, 17

Recently, we analyzed our experience with symptomatic patients who had aortic valve replacement for long-standing aortic regurgitation.18 This analysis indicated that patients who died postoperatively of congestive heart failure had preoperative echocardiographic evidence of poor left ventricular systolic function. These data suggested that echocardiography might be useful for identifying patients who would benefit from earlier operative intervention.

Recommendations for earlier “prophylactic” operation that are based on echocardiographic observations in patients who had operation because of symptoms must be applied with caution to the asymptomatic patient. For example, if asymptomatic patients in the subgroup who might benefit from earlier operation do not cross into the high-risk group or develop severe symptoms for many years, it is reasonable to question the wisdom of earlier operation. However, if such patients develop symptoms and come to operation within a few years, a significant decrease in operative mortality or valve-related complications would probably not be realized by postponing operation. Hence, it is important to know the changes in echocardiographic measurements and symptomatic status that occur during the natural history of initially asymptomatic patients with aortic regurgitation. The present study was designed to provide this information and to elucidate the role of echocardiography in managing the patient with long-standing aortic regurgitation.
Methods

Patient Population

The patient population consisted of all patients with aortic regurgitation who had been followed in the Cardiology Clinic of the National Heart, Lung, and Blood Institute in whom two or more serial echocardiograms had been obtained over at least a 1-year period. Patients were considered to have aortic regurgitation if they had a blowing diastolic murmur at the base of the heart on physical examination and a left ventricular end-diastolic dimension by echocardiography that was above the normal range. No patient had a decreased carotid upstroke suggestive of aortic stenosis or an apical holosystolic murmur of mitral regurgitation. Also, no patient had echocardiographic evidence of mitral or aortic stenosis. All but one patient had high-frequency diastolic fluttering of the anterior leaflet of the mitral valve.

Initial echocardiographic evaluation of these patients was performed between January 1972 and December 1975. The minimum potential follow-up for any patient in this study was 26 months. When the initial evaluations were performed (and during the course of the study), operation was recommended for patients with aortic regurgitation only when patients presented with or developed severe dyspnea on exertion, angina pectoris, syncope or congestive heart failure. Thus, none of the patients had these symptoms at the time of initial study. In addition, none developed these symptoms (and, therefore, none came to operation) within 1 year after the initial examination.

Patient Studies

History, physical examination, 12-lead ECGs and M-mode echocardiograms were obtained in all patients at the initial and subsequent evaluations. Romhilt-Estes scores were computed from the ECGs as previously described. Cardiac catheterization data were available in every patient who subsequently came to operation.

Echocardiographic examination was performed using either an Ekoline 20A or Hoffrel 201 ultrasound transceiver interfaced to a Honeywell 1856 strip-chart recorder. A 12.5-mm diameter, 2.25-MHz, unfocused ultrasound transducer was used. Echocardiographic measurements included left ventricular transverse dimensions at end-diastole and end-systole and ventricular septal and left ventricular posterior free wall thicknesses. These measurements were obtained using the T-scan technique with the ultrasound beam passing through the left ventricle caudal to the tips of the mitral leaflets. The left ventricular transverse dimensions at end-diastole and end-systole were taken as the maximum and minimum distance between the left side of the ventricular septum and endocardium of the left ventricular posterior free wall. Wall thickness measurements were made in late diastole but before atrial systole. Aortic root and left atrial dimensions were measured as previously described. A switched-gain circuit was used to simplify measurement of left ventricular wall thickness and left atrial dimension. From the primary echocardiographic measurements, left ventricular ejection fraction, fractional shortening of the left ventricle and estimated left ventricular mass were calculated.

Patients were subdivided into two groups based on whether they developed symptoms and required operation or remained asymptomatic. Measurements in the two groups were compared using an unpaired t test.

Results

Patient Experience

Thirty-seven patients met the selection criteria and were included in the present study. There were 20 men and 17 women, ages 16–64 years (mean 35 years). Fourteen of the 37 patients (38%) subsequently developed congestive heart failure, severe dyspnea on exertion, angina or syncope and were recommended for operation. These patients will be referred to as the "subsequent operation" group. In all 14 patients, aortic root cineangiography revealed aortic regurgitation severe enough to produce opacification of the left ventricle that failed to clear during the subsequent few cardiac cycles. No patient had an aortic valve gradient exceeding 20 mm Hg or evidence of significant disease of other heart valves. Two of the 14 patients (14%) had coexistent coronary artery disease. All 14 patients have had aortic valve replacement. One of the 14 patients required aortic root reconstruction in addition to aortic valve replacement. In these 14 patients, mean follow-up between the initial echocardiographic examination and the echocardiographic study immediately before operation was 28.2 months (range 13–57 months). Seven of the 14 patients (50%) came to operation within 30 months of the initial evaluation.

Twenty-three of the 37 patients (62%) have not developed severe dyspnea on exertion, congestive heart failure, angina or syncope, and operation has not been recommended. These patients will be referred to as the "nonoperative" group. In these 23 patients, the mean time between the initial and most recent echocardiographic examination was 38.7 months (range 26–64 months). All 23 patients are still alive. The time between initial echocardiographic examination and the most recent contact averaged 42.6 months (range 29–70 months).

Initial Evaluation

The electrocardiographic and echocardiographic measurements in the two groups are summarized in figures 1 and 2 and table 1. Left ventricular end-diastolic and end-systolic dimensions were larger, left ventricular fractional shortening was less, and the Romhilt-Estes score was greater in the subsequent operation group than in the nonoperative group. Of the four measurements, left ventricular end-systolic dimension and left ventricular fractional shortening most strongly distinguished the subsequent operation group from the nonoperative group. There were no significant race or sex differences between the two
FIGURE 1. Plot of left ventricular dimensions (LVD) at end-diastole (DIA) and end-systole (SYS) and left ventricular (LV) fractional shortening. Patients are subdivided into those who have remained asymptomatic during follow-up (NONOP) and those who developed symptoms and were recommended for operation (SUBSEQUENT OP). The mean values are indicated by open circles. The stippled area indicates the normal range of fractional shortening.

TABLE 1. Comparisons of Nonoperative and Subsequent Operation Patients

<table>
<thead>
<tr>
<th>Echo</th>
<th>Initial examination</th>
<th>Recent examination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonoperative</td>
<td>Subsequent operation</td>
</tr>
<tr>
<td>LV dimension (DIA) (mm)</td>
<td>66.7 ± 8.8</td>
<td>74.4 ± 7.9</td>
</tr>
<tr>
<td>LV dimension (SYS) (mm)</td>
<td>44.3 ± 7.6</td>
<td>53.0 ± 6.3</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>33.9 ± 4.2</td>
<td>28.8 ± 4.3</td>
</tr>
<tr>
<td>LV free wall thickness (mm)</td>
<td>12.6 ± 1.6</td>
<td>12.7 ± 1.3</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>515 ± 193</td>
<td>605 ± 175</td>
</tr>
<tr>
<td>Aortic root dimension (mm)</td>
<td>36.5 ± 5.4</td>
<td>36.1 ± 6.2</td>
</tr>
<tr>
<td>LA dimension (mm)</td>
<td>39.9 ± 6.0</td>
<td>41.5 ± 6.2</td>
</tr>
<tr>
<td>ECG</td>
<td>3.5 ± 2.5</td>
<td>5.2 ± 2.1</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>66 ± 9</td>
<td>69 ± 12</td>
</tr>
</tbody>
</table>

Data are mean ± sp.

Abbreviations: LV = left ventricular; DIA = end-diastole; SYS = end-systole; LA = left atrial.
groups. However, the mean age of the nonoperative group was significantly less than that of the subsequent operation group (35.5 ± 11.8 years vs 45.5 ± 13.1 years; p < 0.05).

The echocardiographic data from all 37 patients are summarized in figure 3 as a percentage of the expected value obtained using regression equations derived in our laboratory from a large group of younger and older normal subjects.

**Recent Evaluation**

The mean values obtained at the most recent evaluation are also summarized in table 1. In the nonoperative group, left ventricular end-systolic dimension did not change significantly during the average of 39 months that elapsed between the initial and recent evaluations (fig. 4). In the subsequent operation group, left ventricular end-systolic dimension increased significantly between the initial examination and the examination immediately before operation.

The data were examined to determine the rate of change of left ventricular end-systolic dimension during routine serial study. First, the absolute change was computed for each patient by subtracting the value obtained at initial examination from the value obtained at the most recent examination. The average rate of change was then computed by dividing the absolute change by the time period between the initial and the most recent examination. The results of the average rate of change in end-systolic dimension are also shown in figure 4. The average rate of change exceeded 4 mm per year in only one of the 37 patients (3%). The average rate of change for patients with left ventricular end-systolic dimension less than 50 mm (2.6 ± 1.2 mm per year) was similar to that for patients whose end-systolic dimension was 50 mm or greater (2.7 ± 1.1 mm per year).

The maximum rate of change of end-systolic dimension also was determined by computing the rate of change between sequential studies in each patient. For example, most patients had three or more sequential

**Figure 3.** Plot of echocardiographic measurements obtained at initial examination in 37 initially asymptomatic patients with isolated aortic regurgitation. Patients who subsequently developed symptoms and were recommended for operation are indicated by the filled circles; those who have not yet developed symptoms are indicated by the open circles. The echocardiographic measurements are expressed as a percentage of the expected value computed from the patient's age and body surface area. LVD = left ventricular dimension; SYM = end-systole; DIA = end-diastole; LVPW = left ventricular posterior wall thickness; AO = aortic root dimension; LV = left ventricular; LA = left atrial dimension.

**Figure 4.** Plot of left ventricular (LV) end-systolic dimension. Data in the four columns on the left show the measurements for the initial and most recent echocardiographic examinations for both the nonoperative and subsequent operation groups. The two columns on the right show the average and maximum rate of change in LV end-systolic dimension. See text for details of the method used to calculate the rate of change.
echocardiographic studies performed at intervals of 6–18 months. The most rapid change noted between these sequential studies was used as the maximum rate of change for that patient (fig. 4). The most rapid change observed between sequential studies exceeded 7 mm per year in only one patient.

The most recent data from the nonoperative and subsequent operation groups were compared with the echocardiographic and electrocardiographic measurements of 43 patients in our operative series who had good quality echocardiograms and who presented with symptoms and came to operation within 3 months of initial evaluation (table 2). These latter patients will be referred to as the “immediate operation group.” The mean values in the immediate operation patients were similar to the mean values in the subsequent operation group, except for heart rate and left ventricular free wall thickness, which were less in the subsequent operation group. In contrast, all measurements in the immediate operation group were significantly greater than those in the nonoperative group, except for fractional shortening, which was less, and aortic root dimension, which was not different.

Preoperative hemodynamic data from the 43 patients in the immediate operation group were compared with preoperative data in the 14 patients in the subsequent operation group. None of the hemodynamic measurements, including right- and left-heart pressures, aortic and pulmonary artery pressures, cardiac output and cardiac index, were significantly different between the two groups.

Relation of Left Ventricular End-systolic Dimension to Clinical Course

In figure 5, patients are divided into three subgroups based on the left ventricular end-systolic dimension measured at initial echocardiographic evaluation.

**End-systolic Dimension < 50 mm**

Four of the 20 patients (20%) whose left ventricular end-systolic dimension was less than 50 mm at initial evaluation developed symptoms and were recommended for operation. Left ventricular end-systolic dimension did not exceed 55 mm during follow-up in these four patients or in the 16 clinically stable patients who remained asymptomatic (figs. 4 and 5).

**End-systolic Dimension of 50–54 mm**

Six of 12 patients (50%) who were in this subgroup at initial evaluation developed symptoms requiring

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**TABLE 2. Comparison of Immediate Operation with Nonoperative and Subsequent Operation Patients**

<table>
<thead>
<tr>
<th>Echo</th>
<th>Nonoperative group</th>
<th>p</th>
<th>Immediate operation group</th>
<th>p</th>
<th>Subsequent operation group</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV dimension (DIA) (mm)</td>
<td>67.1 ± 8.4</td>
<td>0.02</td>
<td>72.1 ± 7.5</td>
<td>0.07</td>
<td>76.6 ± 7.6</td>
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<tr>
<td>LV dimension (SYS) (mm)</td>
<td>45.1 ± 7.2</td>
<td>0.002</td>
<td>52.5 ± 10.6</td>
<td>NS</td>
<td>56.4 ± 7.3</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>32.9 ± 4.4</td>
<td>0.004</td>
<td>28.2 ± 8.5</td>
<td>NS</td>
<td>26.4 ± 6.3</td>
</tr>
<tr>
<td>LV free wall thickness (mm)</td>
<td>12.8 ± 1.7</td>
<td>0.007</td>
<td>14.1 ± 1.8</td>
<td>0.03</td>
<td>12.9 ± 1.7</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>534 ± 193</td>
<td>0.01</td>
<td>656 ± 148</td>
<td>NS</td>
<td>642 ± 214</td>
</tr>
<tr>
<td>Aortic root dimension (mm)</td>
<td>37.6 ± 6.0</td>
<td>NS</td>
<td>37.6 ± 6.3</td>
<td>NS</td>
<td>36.7 ± 5.7</td>
</tr>
<tr>
<td>LA dimension (mm)</td>
<td>41.4 ± 6.0</td>
<td>NS</td>
<td>44.4 ± 7.0</td>
<td>NS</td>
<td>45.4 ± 6.5</td>
</tr>
</tbody>
</table>

ECG

| Romhilt-Estes score | 3.7 ± 2.8 | 0.001 | 6.6 ± 2.6 | NS | 5.9 ± 2.1 |
| Heart rate (beats/min) | 68 ± 12 | 0.001 | 83 ± 17 | 0.02 | 74 ± 10 |

Data are mean ± sd.

Abbreviations: LV = left ventricular; DIA = end-diastole; SYS = end-systole; LA = left atrial.
operation within 13–52 months (mean 23 months). Four of these six patients developed symptoms without the left ventricular end-systolic dimension exceeding 55 mm. The other two patients had left ventricular end-systolic dimensions greater than 55 mm by the time symptoms had developed (figs. 4 and 5).

End-systolic Dimension > 55 mm

Of the five patients in this subgroup at initial evaluation, four (80%) developed symptoms and were recommended for operation within 22–57 months (mean 39 months) after initial study. The percentage of patients with an end-systolic dimension of at least 55 mm who developed symptoms and came to operation was significantly greater than the percentage of patients with an end-systolic dimension less than 50 mm who required operation ($p < 0.05$ by Fisher’s exact test$^{27}$). An additional two patients crossed into the $> 55$ mm subgroup during the study (fig. 4). Both patients developed symptoms and came to operation, one patient in 9 months and the other in 16 months after crossover (figs. 4 and 5).

Discussion

Recently, we reviewed our experience with symptomatic patients who required operation to correct isolated aortic regurgitation.$^{18}$ This study showed that the left ventricular end-systolic dimension and the left ventricular fractional shortening (measured by echocardiography) are excellent measurements to use preoperatively to identify patients at high risk of having developed irreversible left ventricular dysfunction.$^{18}$ This conclusion is based on the observation that nine of 17 patients (53%) with a preoperative left ventricular end-systolic dimension greater than 55 mm either died at operation (two patients) or died late postoperatively of congestive heart failure (seven patients). Eleven of 13 patients (85%) who had both a preoperative left ventricular end-systolic dimension greater than 55 mm and a left ventricular fractional shortening below 25% either died at operation (two patients) or died late postoperatively of congestive heart failure (seven patients) or had moderate or severe residual systolic dysfunction postoperatively (two patients). In contrast, of the 32 patients with left ventricular end-systolic dimension of 55 mm or less, only one (3%) died late postoperatively of congestive heart failure. That patient suffered an intraoperative myocardial infarction and manifested markedly impaired left ventricular systolic function postoperatively.

These data strongly suggest that operation should be performed in patients with aortic regurgitation immediately before or shortly after the left ventricular end-systolic dimension exceeds 55 mm, regardless of symptomatic status. However, our previous study did not provide several important pieces of information. First, we did not know how long an asymptomatic patient with an end-systolic dimension greater than 55 mm would remain asymptomatic. If symptoms were to develop only after many years, the case for operating before the onset of symptoms would be weaker. Nor did we know how rapidly the end-systolic dimension changed during serial follow-up studies or whether this measurement could be used to identify patients who were likely to develop symptoms and require operation.

The results of the present study are relevant to these questions. We evaluated 37 patients who had isolated, chronic aortic regurgitation and had been followed for at least 1 year with two or more serial echocardiograms. At the initial evaluation, none of the patients had symptoms serious enough to warrant operation. Fourteen of the 37 patients (38%) subsequently developed either severe dyspnea on exertion, congestive heart failure, angina or syncope. Based on the development of symptoms, operation was recommended.

The echocardiographic and electrocardiographic measurements in these 14 patients were compared with measurements obtained in the 23 patients who have not developed symptoms and thus have not come to operation. Left ventricular end-systolic dimension and left ventricular fractional shortening were the measurements that on initial study most strongly distinguished patients who eventually required operation (table 1). These measurements are highly correlated and both reflect systolic function.$^{19}$ Left ventricular end-diastolic dimension and the Romhilt-Estes score also separated the two groups, but with lower statistical significance.

When patients were subdivided based on their left ventricular end-systolic dimension, operation was required in four of the five patients (80%) with a left ventricular end-systolic dimension greater than 55 mm. The time between initial study and operation in these four patients averaged 39 months. Operation was also required in six of 12 patients (50%) with an end-systolic dimension of 50–54 mm during an average follow-up of 23 months. In contrast, only four of the 20 patients (20%) whose end-systolic dimension was less than 50 mm required operation (fig. 5).

Findings in our operative series of symptomatic patients with isolated aortic regurgitation are pertinent to these observations.$^{18}$ Approximately two-thirds of the operative patients had left ventricular end-systolic dimensions of 50 mm or greater at the time they developed symptoms and came to operation. Of the 17 operative patients with an end-systolic dimension less than 50 mm, seven (41%) had associated coronary artery disease (fig. 6). In contrast, coronary disease was present in only three of the remaining 32 patients (9%) with end-systolic dimensions greater than 50 mm ($p < 0.05$ by Fisher’s exact test$^{27}$). Thus, when significant symptoms develop in patients with aortic regurgitation and left ventricular end-systolic dimension less than 50 mm, associated coronary disease is often present. Once this dimension is reached, half of initially asymptomatic patients with aortic regurgitation will develop symptoms and require operation during an average follow-up of 2–3 years.

Left ventricular end-systolic dimension may be markedly increased in some patients who do not complain of symptoms. Our experience with graded tread-
mill exercise testing is consistent with this observation in that exercise tolerance may be only mildly impaired in many patients with aortic regurgitation, even when the left ventricle is very large and its systolic function considerably depressed (Bonow RO, Borer JS, Rosing DR, Henry WL, Pearlman AS, McIntosh CL, Morrow AG, Epstein SE: unpublished observations).

The patients who remained asymptomatic during follow-up were significantly younger than those who developed symptoms and were recommended for operation. However, there was considerable overlap in the ages in the nonoperative and subsequent operation groups. Also, even relatively young patients (including two in their late twenties) presented with large, poorly contracting left ventricles.

The data in the present study were evaluated to determine the rate of change in left ventricular end-systolic dimension during routine clinical follow-up studies. These serial echocardiographic data demonstrated that it is very uncommon for the end-systolic dimension to increase more rapidly than 7 mm per year.

Before recommending that operation should be performed as soon as the end-systolic dimension exceeds 55 mm, it is important to examine the alternative, i.e., delaying operation until symptoms develop. One potential benefit of postponing operation is that improvements in operative techniques may reduce operative mortality. However, operative mortality was only 6% (excluding patients who required aortic root reconstruction) in our recent series of patients with isolated aortic regurgitation. This low operative mortality is similar to that noted in several other recent series. Because six of seven patients (86%) with end-systolic dimensions greater than 55 mm developed symptoms and came to operation during an average follow-up of 30 months (including the two asymptomatic patients whose end-systolic dimension increased to more than 55 mm during serial study), it does not appear that operative risk will be significantly decreased by waiting until asymptomatic patients with end-systolic dimensions greater than 55 mm develop symptoms. Moreover, there is evidence in our operative series that the risk of operative damage may be increased in patients with very large left ventricular end-systolic dimensions. By waiting until symptoms develop in patients with large end-systolic dimension, one runs the risk that the end-systolic dimension may increase further and, as a result, the chances of operative damage may be increased and the likelihood of left ventricular function improving postoperatively may be decreased.

Another potential benefit of postponing operation is that improvements in prosthetic valve design will decrease late morbidity and mortality after valve replacement. For instance, if the present mortality due to valve malfunction were greater than the risk of developing congestive heart failure and dying, early intervention would be difficult to justify. However, in our recent operative series of symptomatic patients with either isolated aortic regurgitation, or isolated aortic stenosis, only three of the combined total of 85 patients (4%) who survived operation died of valve-related complications. In contrast, nine of 17 sympto-

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**Figure 6.** Plot of left ventricular (LV) end-systolic dimension for the 49 patients reported in our operative series. The data shown in the left-hand column have been subdivided and are shown in the two columns on the right. Subdivision of the patients was based on whether they had coronary artery disease (CAD) in addition to aortic valve replacement. S = without.
matic patients (53%) operated upon for aortic regurgitation who had a preoperative left ventricular end-systolic dimension greater than 55 mm either died at operation or developed late postoperative congestive heart failure and died. These deaths occurred within 46 months of operation. If patients with both a preoperative end-systolic dimension greater than 55 mm and a fractional shortening less than 25% are considered, the likelihood of a poor result is further increased: 85% of such patients had a poor operative result.\(^8\)

Even if nonfatal valve complications, including anemia, cerebrovascular accidents, infection, poppet malfunction and perivalvular leak, are combined with the fatal valve complications (unpublished observations), the total incidence of all valve complications (20 of 85 patients or 24%) is still half (or less) of the congestive heart failure mortality in the high-risk groups. Therefore, it appears that postponing operation until symptoms develop in an asymptomatic patient with aortic regurgitation who has an end-systolic dimension greater than 55 mm results in a greater overall late mortality than the combined morbidity and mortality associated with prosthetic valve. Future improvements in prosthetic valve design will only strengthen this argument.

As a result of this information, we have changed our previous policy of recommending operation only to patients with aortic regurgitation who have severe dyspnea on exertion, congestive heart failure, angina or syncope. We still recommend operation to patients who present with or develop these symptoms during follow-up, regardless of the size or function of the left ventricle. Specifically, we do not withhold operation in patients with a left ventricular end-systolic dimension greater than 55 mm or a fractional shortening less than 25% for two reasons. First, a few patients with an end-systolic dimension greater than 55 mm had a significant increase in systolic function after operation. This was particularly true if preoperative fractional shortening was greater than 25%, but much less likely in patients whose fractional shortening was below 25%.\(^8\) Second, a few patients with low preoperative systolic function that did not improve postoperatively are still doing reasonably well after several years of follow-up.

In contrast to our previous policy of only recommending operation to symptomatic patients, we now perform an extensive inpatient evaluation in all asymptomatic or minimally symptomatic patients who have a left ventricular end-systolic dimension by echocardiography of 55 mm or greater. Unless left ventricular cineangiography and radionuclide angiography\(^9\) are in major conflict with the echocardiographic data (a situation that, in our experience, is uncommon in patients with aortic regurgitation), we recommend operation, even in the absence of severe dyspnea on exertion, overt congestive heart failure, angina or syncope.

Asymptomatic patients with aortic regurgitation who have a left ventricular end-systolic dimension less than 50 mm are followed medically. In our previous operative study, we found that none of the patients who were in this subgroup died at operation or during postoperative follow-up, which averaged 4 years.\(^16\) Therefore, there appears to be no reason to proceed with operation in such patients in the absence of symptoms, as long as patients are followed every 1–2 years. With this approach, some patients will develop symptoms requiring operation while maintaining good systolic function (fig. 5) and should have an excellent long-term postoperative prognosis. Alternatively, some patients will develop progressive impairment of left ventricular systolic function before the onset of symptoms. If these patients are followed closely by serial echocardiographic studies, operation can be performed as soon as the patient manifests an end-systolic dimension of 55 mm or fractional shortening of 25%.

Asymptomatic patients with severe aortic regurgitation who fall into the subgroup characterized by a left ventricular end-systolic dimension of 50–54 mm present a difficult therapeutic problem. If operation is performed in these patients, irreversible left ventricular dysfunction can probably be prevented. Only one of the 32 patients (3%) in our operative series\(^18\) who had preoperative left ventricular end-systolic dimension of 55 mm or less developed congestive heart failure in the late postoperative period, and that patient, as mentioned previously, suffered an intraoperative myocardial infarction resulting in severe left ventricular dysfunction.

However, operating on patients within this subgroup before symptoms develop would have been potentially advantageous for only two of the 12 patients (19%); i.e., those who developed a left ventricular end-systolic dimension greater than 55 mm before coming to operation (figs. 4 and 5). Moreover, although six of 12 patients (50%) came to operation during an average follow-up of 23 months after the initial echocardiographic study, the other six (50%) are still asymptomatic after a follow-up of 2–5 years. Operation in these latter six patients would have been of questionable benefit. They would have been subjected prematurely to the risks of operation (6% operative risk in our series), as well as to the hazards inherent in a prosthetic valve. Thus, while operating on asymptomatic patients with aortic regurgitation whose left ventricular end-systolic dimension is 50–54 mm is not an unreasonable approach, the majority of such patients can be followed with only a small risk of developing irreversible left ventricular dysfunction before symptoms occur. Therefore, we do not recommend operation to asymptomatic patients in this subgroup.

With these considerations in mind, our current approach to the clinical management of the asymptomatic patient with chronic aortic regurgitation is to assess left ventricular size and function by serial echocardiograms. The frequency of examination and
TABLE 4. Clinical Management and Left Ventricular (LV) Dimension

<table>
<thead>
<tr>
<th>LV dimension (systole)</th>
<th>Clinical management</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 45 mm</td>
<td>Medical therapy; echo exam every 2 years.</td>
</tr>
<tr>
<td>45-49 mm</td>
<td>Medical therapy; echo exam every year.</td>
</tr>
<tr>
<td>50-54 mm</td>
<td>Medical therapy; echo exam every 4-6 months.</td>
</tr>
<tr>
<td>≥ 55 mm</td>
<td>Operate, even without symptoms.</td>
</tr>
</tbody>
</table>

our clinical decisions are based on the left ventricular end-systolic dimension as shown in table 3.

Acknowledgments

The authors appreciate the cooperation and assistance of Cora Burn, Estelle Cohen and Joyce McKay, who performed the echocardiographic studies. The statistical analysis of the data was performed by Dr. James Ware, who was aided by Erica Britain. Their help was essential to the completion of the study. The authors also greatly appreciate the skillful assistance of Exa Murray, who typed the manuscript.

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Serial echocardiographic evaluation of asymptomatic patients.
W L Henry, R O Bonow, D R Rosing and S E Epstein

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