Evaluation of Aortic Valve Replacement in Patients with Valvular Aortic Stenosis

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SUMMARY Echocardiographic and hemodynamic studies were obtained in 42 consecutive patients undergoing aortic valve replacement for isolated aortic stenosis. Concentric left ventricular (LV) wall thickening, the most common preoperative abnormality, occurred in 95% of patients. LV dilation with reduced fractional shortening was noted in approximately 25% of patients but was severe in only one patient. Six months after operation, LV wall thickness had decreased on average but had not returned to normal and fractional shortening was unchanged. Repeat measurements in 13 patients an average of 37 months after operation were unchanged compared with measurements made 6 months after operation. When patients were subdivided into those with LV dilatation and those without, we found that patients with dilated ventricles preoperatively had a greater decrease in LV internal dimension and mass than those without preoperative dilatation.

The patient data also were examined for possible association with mortality. One operative (2%) and five late cardiac (13%) deaths occurred. No preoperative or 6-month postoperative echocardiographic or hemodynamic measurement was strongly associated with these deaths, nor were any late deaths due to congestive heart failure.

Compared with preoperative measurements in symptomatic patients who were operated for isolated aortic regurgitation, patients with aortic stenosis had smaller left ventricles with less depression of systolic function, as well as less aortic root and left atrial dilatation. Our data do not support the concept that the aortic valve should be replaced before the onset of symptoms to prevent irreversible LV damage in patients with isolated aortic stenosis.

ALTHOUGH MOST PATIENTS who undergo aortic valve replacement for aortic valve disease survive operation and are symptomatically improved, some die despite an apparently successful operation. In patients with aortic regurgitation, late death often is related to irreversible left ventricular dysfunction that had developed before operation. To determine whether preoperative left ventricular dysfunction could also account for some of the late postoperative deaths in patients with aortic stenosis, we prospectively studied patients undergoing operation for this condition.

One goal of the study was to identify preoperative measurements associated with either operative or late mortality. Patients were also examined to determine the alterations in cardiac structure and function that develop in response to a severe left ventricular pressure load and to assess the changes that occur after the pressure load is relieved by operation. Finally, measurements obtained in patients with aortic stenosis were compared with those obtained in patients with aortic regurgitation.

Methods

Patients

The patient population consisted of all patients undergoing aortic valve replacement for long-standing valvular aortic stenosis who were operated on between January 1972 and June 1976. Patients included in the study population had an aortic valve index of less than 0.80 cm²/m² and less than 1+/4+ aortic regurgitation visualized by aortic root cineangiography (34 patients) or no murmur of aortic regurgitation on physical ex-
amination (eight patients). Patients were excluded if they had dysfunction of other heart valves severe enough to require valve replacement or if valvular surgery had been performed. Before operation, all patients had severe exertional dyspnea, overt congestive heart failure, angina pectoris or syncope. The presence of left ventricular dysfunction or coronary artery disease were not used to exclude patients from analysis.

Forty-two patients met the selection criteria and were included in the present study. There were 30 men and 12 women, ages 29–76 years (mean 56.8 years). Thirty patients had either 2320 Series (27 patients) or 2400 Series (three patients) Starr-Edwards prosthetic valves, 10 had Björk-Shiley valves and two had porcine heterograft valves placed at operation. Coronary artery perfusion was used during cardiopulmonary bypass in 21 patients, coronary perfusion plus topical iced saline was used in eight patients and iced saline alone was used in seven patients. Six patients had neither coronary artery perfusion nor iced saline.

Patient Studies

History, physical examination, 12-lead ECG, echocardiogram and cardiac catheterization were obtained before operation in all 42 patients. In seven patients, the left ventricle could not be entered at catheterization because of a heavily calcified aortic valve. Therefore, preoperative data on aortic valve gradient and area were available in 35 of 42 patients (83%). Thirty-eight patients returned for a 6-month postoperative evaluation. Four patients had embolic events between operation and the 6-month study and were not recatheterized. Thus, 34 patients had cardiac catheterization at the 6-month evaluation and left ventricular pressures were measured in all.

Left ventricular cineangiography was obtained before operation in 31 patients and 6 months after operation in 23 patients. Coronary artery anatomy was assessed in 36 of 42 patients (86%) by preoperative coronary arteriography (30 patients), 6-month postoperative coronary arteriography (four patients) and autopsy examination (two patients).

Echocardiograms satisfactory for analysis were obtained preoperatively in 40 of 42 patients. Repeat study was attempted in all 38 patients who returned for the 6-month postoperative evaluation. The two patients with unsatisfactory preoperative echocardiograms also had unsatisfactory studies 6 months after operation. Thus, 36 patients had acceptable-quality echocardiograms 6 months after operation. Echocardiograms were also obtained early (10–23 days) after operation in 12 patients and late (15–67 months) after operation in 16 patients.

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. Left ventricular transverse dimensions at end-diastole and end-systole and ventricular septal and left ventricular posterior free wall thicknesses were measured echocardiographically by directing the ultrasound beam through the left ventricle caudal to the tips of the mitral leaflets. Aortic root and left atrial dimensions were measured before operation in all patients, but were not obtained after operation because of the presence of the prosthetic aortic valve. 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.

The mortality rate was evaluated by testing the association between the patient measurements and overall mortality using Cox's method of life-table analysis. The preoperative measurements were the independent variable and death from any cause was the end point. This analysis was repeated using the data obtained 6 months after operation. Operative mortality was not tested separately.

Results

Follow-up

Operative death occurred in one of the 42 patients, for an operative mortality of 2%. This patient did not have associated coronary artery disease. Forty-one patients survived operation and were discharged from the hospital. Two of the 41 patients (5%) had poor-quality echocardiograms before and after operation and were excluded from analysis; both are still alive. Three patients had no postoperative echocardiographic or hemodynamic studies and are still alive. Thirty-six patients with good-quality preoperative echocardiograms returned approximately 6 months after operation for repeat echocardiographic and hemodynamic study.

Six of the 41 survivors of operation (15%) died during late follow-up. One patient developed lymphocytic leukemia and died 3 years after operation. One patient with coronary artery disease had a myocardial infarction 10 months after operation, developed congestive heart failure after the infarct and died 3 months later. Another patient with coronary artery disease died suddenly 4 years after operation. Three patients died of complications related to the prosthetic valve; one due to an infected valve, another due to a sudden poppet malfunction (confirmed at autopsy) and a third due to a perivalvular leak. This latter patient developed congestive heart failure and died suddenly before the leak could be repaired. Two patients required a second operation, one because of a perivalvular leak and one because of poppet malfunction; both are still alive.

Thirty-five patients are still alive (mean follow-up 52.9 months). Thirty had good-quality postoperative echocardiograms and are alive (mean follow-up 53.4 months). Excluding the patient who died of leukemia, the overall mortality (operative and late) was six of 42 patients (14%) and late mortality was five of 41
patients (12%), giving an average annual late mortality of 3.5% per year.

Seven patients, all with known coronary artery disease, have mild or moderately severe angina pectoris after operation. One other patient with hemolytic anemia has moderate dyspnea on exertion and one patient has presyncope postoperatively. The other patients have minimal or no postoperative symptoms.

Information about coronary artery anatomy was available in 36 patients. Fourteen of the 36 patients (39%) were found to have coronary artery disease, defined as greater than 50% narrowing of at least one major coronary artery. One of the 14 patients had saphenous vein bypass grafts placed at the time of aortic valve replacement. Myocardial infarction related to operation (detected by the development of new Q waves on the postoperative ECG) occurred in four of the 36 patients (11%). Of the four events, three occurred in patients with coronary artery disease (three of 14 patients or 21%) and one occurred in a patient without coronary disease (one of 22 patients or 5%). In addition to the one leukemic and the three valve-related late deaths, two other late deaths occurred in patients with coronary artery disease. One of the deaths was clearly related to an acute myocardial infarction; the other was sudden. If all coronary events (operative infarction, late infarction and death) were considered, coronary events occurred in five of 14 patients (36%) with documented coronary artery disease.

Preoperative Evaluation

The echocardiographic measurements obtained before operation in the 40 patients with satisfactory echocardiograms are shown in figures 1 and 2. These data are expressed as a percentage of the expected value obtained using regression equations derived from a large series of younger and older normal subjects.

The internal dimensions of the left ventricle at end-diastole and end-systole were above the normal range in 11 patients (28%) (fig. 1). In contrast, the thickness of the left ventricular free wall (and the ventricular septum) was increased in 38 of 40 patients (95%). The ratio of ventricular septal thickness to left ventricular free wall thickness ranged from 0.93–1.21 (mean ± SEM 1.06 ± 0.01). Although no patient had a ratio greater than 1.3, the mean value was significantly greater than normal (p < 0.001). Estimated left ventricular mass was above the normal limit in 31 of 40 patients (78%) (fig. 1). Fractional shortening of the left ventricle was below the normal limit in nine of 40 patients (23%) and above the normal limit in four of 40 (10%) (fig. 2). The results were similar when ejection fraction was used. Three of the nine patients (33%) with reduced fractional shortening had coronary artery disease.

The aortic root dimension was above the normal range in six of 40 patients (15%), and the left atrial dimension was above normal in five of 40 patients (13%). Although the increases were small, the mean values of both aortic root and left atrial dimensions were significantly (p < 0.01) increased compared with normal (fig. 2).

Six-month Postoperative Evaluation

Thirty-six patients had acceptable-quality echocardiographic studies both preoperatively and 6 months after operation. Two of these patients required reoperation because of an unsatisfactory operative result. Data from the other 34 patients are shown in figures 3 and 4 and summarized in table 1. Left ventricular dimensions at end-diastole and end-systole and left ventricular fractional shortening were unchanged after operation (p > 0.05) (fig. 3). In contrast, ventricular septal and left ventricular free wall thicknesses at study 6 months after operation had decreased significantly (p < 0.01) (fig. 4). Primarily as
a result of the change in wall thickness, estimated left ventricular mass decreased after operation ($p < 0.01$). The decreases in wall thickness and mass paralleled a decrease in left ventricular systolic pressure (fig. 4).

The echocardiographic measurements of the left ventricle obtained at 6-month postoperative study are summarized in figure 5 and expressed as a percentage of the expected value.

The hemodynamic and echocardiographic changes after operation are summarized in table 1. Left ventricular systolic and end-diastolic pressures, pulmonary artery systolic, diastolic and wedge pressures and aortic valve gradient all decreased, while aortic valve index and area increased significantly.

The preoperative and 6-month postoperative data were also analyzed to determine whether the magnitude and direction of the change in echocardiographic measurements after operation were different in the 10 patients with dilated left ventricles preoperatively (i.e., left ventricular end-diastolic dimension $\geq 52$ mm) compared with the 24 patients without preoperative left ventricular dilatation. The results are summarized in table 2.

**Figure 2.** Echocardiographic measurements obtained from the same patients shown in figure 1. See legend to figure 1 for explanation of symbols and abbreviations. Aortic root measurements from the five patients who required aortic root reconstruction are indicated by the diagonal line through the data point.

**Figure 3.** Echocardiographic measurements obtained in 34 patients with both preoperative and 6-month postoperative studies. Data from two patients who required reoperation are excluded from this graph. LV = left ventricular.

The diastolic and systolic dimensions of the left ventricle decreased significantly after operation in the patients who had dilated ventricles before operation. In contrast, these dimensions increased after operation in the patients without left ventricular dilatation. Wall thickness decreased postoperatively in both groups. Although left ventricular mass also decreased significantly in both groups, the magnitude of the decrease was greater in the patients with preoperative left ventricular dilatation.

**Serial Echocardiographic Evaluation**

To evaluate the time course of echocardiographic changes, we reviewed studies obtained early (10–23 days) and late (1–6 years) after operation. Twelve early echocardiographic studies were available. Two
patients who had significant postoperative peri-
valvular aortic regurgitation and one who had an
operative myocardial infarction were excluded. These
three patients were the only patients who had an in-
crease of 4 mm or greater in the left ventricular end-
systolic dimension between the preoperative and early
postoperative studies.

Sixteen patients had repeat echocardiographic
studies after the 6-month postoperative evaluation.
These late studies were performed 15–67 months
(mean 30 months) after operation. Three of the 16
patients developed severe hemolytic anemia during
late follow-up and were excluded from analysis. All
two patients had increases of 3 mm or greater in the
left ventricular end-systolic dimension between the 6-
month and late postoperative evaluations. Of the
remaining 13 patients (mean follow-up 31 months),
two had increases of 3 mm or greater in the end-
systolic left ventricular dimension during the late
follow-up studies. Both patients had coronary artery
disease, and one subsequently died suddenly.

The early and late postoperative data were com-
pared with preoperative and 6-month postoperative
measurements in the same patients. The results are
summarized in table 3. The p values included in table 3
were obtained using a paired t test. Two separate
columns are indicated in this table for both early
postoperative measurements and 6-month post-
operative measurements. These separate columns are
necessary because the patient population with both
pre- and early postoperative measurements were
slightly different from the patient population with
both early and 6-month postoperative data.

The only echocardiographic measurements that had
changed significantly at study 6 months after opera-
tion were left ventricular wall thickness and mass.
Table 1. Mean Values Before and After Operation

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Preop value</th>
<th>6-month postop value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV dimension (diastole) (mm)</td>
<td>48.2 ± 10.3</td>
<td>48.4 ± 6.9</td>
<td>NS</td>
</tr>
<tr>
<td>LV dimension (systole) (mm)</td>
<td>32.0 ± 9.8</td>
<td>32.7 ± 6.9</td>
<td>NS</td>
</tr>
<tr>
<td>Septal thickness (mm)</td>
<td>16.2 ± 2.0</td>
<td>14.2 ± 1.9</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>LV free wall thickness (mm)</td>
<td>15.4 ± 1.8</td>
<td>14.0 ± 1.6</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>34.4 ± 7.3</td>
<td>32.8 ± 6.8</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>70.8 ± 9.6</td>
<td>68.7 ± 9.6</td>
<td>NS</td>
</tr>
<tr>
<td>Estimated LV mass (g)</td>
<td>425 ± 147</td>
<td>359 ± 94</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>76.4 ± 12.6</td>
<td>74.7 ± 10.3</td>
<td>NS</td>
</tr>
<tr>
<td>Rohlilt-Estes score</td>
<td>4.5 ± 2.5</td>
<td>3.6 ± 2.7</td>
<td>p = 0.05</td>
</tr>
<tr>
<td>LV systolic pressure (mm Hg)</td>
<td>217 ± 28.4</td>
<td>149 ± 21.0</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>LV end-diastolic pressure (mm Hg)</td>
<td>17.8 ± 8.6</td>
<td>14.4 ± 3.7</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Aortic systolic pressure (mm Hg)</td>
<td>134 ± 30.9</td>
<td>133 ± 19.0</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic diastolic pressure (mm Hg)</td>
<td>69 ± 9.3</td>
<td>67 ± 9.7</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>5.1 ± 1.6</td>
<td>4.7 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac index (l/min/m²)</td>
<td>2.8 ± 0.8</td>
<td>2.6 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>Aortic valve peak gradient (mm Hg)</td>
<td>81.4 ± 23.9</td>
<td>15.7 ± 13.6</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.56 ± 0.23</td>
<td>1.05 ± 0.31</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Aortic valve index (cm²/m²)</td>
<td>0.32 ± 0.14</td>
<td>0.61 ± 0.20</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Pulmonary systolic pressure (mm Hg)</td>
<td>33.4 ± 11.2</td>
<td>27.9 ± 6.9</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>Pulmonary diastolic pressure (mm Hg)</td>
<td>14.1 ± 4.6</td>
<td>12.4 ± 3.6</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Pulmonary wedge pressure (mm Hg)</td>
<td>13.3 ± 5.8</td>
<td>10.1 ± 3.4</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

Abbreviation: LV = left ventricular.

Table 2. Changes in Echocardiographic Measurements After Operation in Patients With and Without Left Ventricular Dilatation

<table>
<thead>
<tr>
<th>LV dimension (dia)</th>
<th>Preop</th>
<th>6-month postop</th>
<th>Change</th>
<th>Preop</th>
<th>6-month postop</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 52 mm</td>
<td>43.0 ± 3.9</td>
<td>45.7 ± 5.1</td>
<td>2.7†</td>
<td>60.7 ± 10.1</td>
<td>54.8 ± 6.6</td>
<td>-5.9†</td>
</tr>
<tr>
<td>≥ 52 mm</td>
<td>27.5 ± 4.3</td>
<td>30.5 ± 4.8</td>
<td>3.0†</td>
<td>42.9 ± 11.1</td>
<td>38.0 ± 8.6</td>
<td>-4.9†</td>
</tr>
<tr>
<td>LV free wall thickness</td>
<td>15.4 ± 1.9</td>
<td>14.1 ± 1.7</td>
<td>-1.3†</td>
<td>15.1 ± 1.7</td>
<td>13.6 ± 1.4</td>
<td>-1.5†</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>36.2 ± 6.9</td>
<td>33.4 ± 6.3</td>
<td>-2.8†</td>
<td>39.2 ± 7.9</td>
<td>31.3 ± 7.9</td>
<td>1.1</td>
</tr>
<tr>
<td>Estimated LV mass (g)</td>
<td>361 ± 89</td>
<td>334 ± 94</td>
<td>-27*</td>
<td>578 ± 148</td>
<td>420 ± 67</td>
<td>-158†</td>
</tr>
</tbody>
</table>

*p < 0.05.
†p < 0.01.

Abbreviations: LV = left ventricular; dia = diastole; sys = systole.

Wall thickness was not changed at the early postoperative study but had decreased significantly by 6 months after operation (table 3). However, the left ventricular internal dimensions decreased, on average, early after operation but had returned to preoperative values by the 6-month postoperative study. As a result of the decrease in left ventricular dimensions early after operation, left ventricular mass decreased. Although these changes were not quite statistically significant, nevertheless, they suggest that most of the decrease in left ventricular mass occurred between the preoperative and early postoperative studies. No further change in wall thickness or mass was found between the 6-month postoperative study and late postoperative evaluation. No significant change was found in any other echocardiographic measurement between the preoperative, early, 6-month and late postoperative studies.
It is not clear whether any important selection factors determined which patients had early or late postoperative echocardiographic studies. However, comparison of the preoperative echocardiographic and hemodynamic data from these patients with the preoperative data from the rest of the patient population failed to reveal any statistically significant difference.

**Mortality Experience**

The association between the various measurements and death is summarized in table 4 using both preoperative and 6-month postoperative values. Although the data shown in this table included all deaths, similar results were obtained when the operative death and the late death due to leukemia were excluded. Of the 23 preoperative variables, only pulmonary artery systolic pressure was significantly \( p < 0.05 \) associated with death. When 20 tests for association are performed, one would expect on the average to find one significant association by chance alone. This expectation, coupled with the relatively weak association \( p = 0.03 \), suggests that none of the preoperative measurements can be used to predict the likelihood of a poor operative result. Examination of the mortality experience using the 6-month postoperative data also failed to reveal a strong association between any measurement and overall mortality. Three related measurements — the peak aortic valve gradient, the aortic valve area and the aortic valve index — showed borderline association with death, perhaps indicating that patients with significant prosthetic valvular gradients are at increased risk of dying during late follow-up. Again, the relatively weak association and the large number of measurements evaluated makes this inference speculative.

**Discussion**

The preoperative echocardiographic measurements show that left ventricular wall thickening is the most common abnormal echocardiographic finding in symptomatic patients who come to operation with severe valvular aortic stenosis. In the present series, wall thickening above the normal range was present in 95% of patients. Wall thickness averaged 16 mm and exceeded 20 mm in only one of the 40 patients. Patients with aortic stenosis have a chronic and severe elevation of left ventricular systolic pressure that equals or exceeds that found in any other disease. Therefore, this finding suggests that maximum pressure stimulus to secondary left ventricular thickening rarely produces a wall thickness that exceeds 20 mm. This corresponds to an increase in wall thickness of approximately 75%.

In contrast, the internal dimensions of the left ventricle in diastole and systole were increased above normal in only 25% of patients. Moreover, marked ventricular dilatation (i.e., end-diastolic dimension greater than 50% above normal) was present in only one patient, whose left ventricular end-diastolic dimension was 86 mm and who also had coronary artery disease and a history of very heavy alcohol intake for several years before operation.

Systolic function of the left ventricle, as assessed by the percent fractional shortening of the base of the ventricle, was at or above the lower limit of normal in 31 of 40 patients (78%). In the other nine patients, the left ventricular fractional shortening was mildly or moderately reduced. These nine patients also had mild or moderate increases in left ventricular end-diastolic and end-systolic dimensions. A marked reduction in left ventricular systolic function (i.e., fractional shortening below 20%) was not seen in any patient. Thus, the left ventricle appears to respond to a severe and chronic pressure overload primarily by thickening its walls. Ventricular dilatation is uncommon and, when present, is usually mild or moderate. Systolic function is well preserved in most patients, despite the marked increase in left ventricular systolic pressure.

These findings are in agreement with several angiographic studies that have shown increased left ventricular wall thickness with normal or only mildly

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**Table 3. Serial Changes in Echocardiographic Measurements**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Preop</th>
<th>Early postop</th>
<th>Early postop</th>
<th>6-month postop</th>
<th>6-month postop</th>
<th>Late postop</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV dimension (dia) (mm)</td>
<td>47.0</td>
<td>44.2</td>
<td>44.7</td>
<td>47.0</td>
<td>50.3</td>
<td>51.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 7.4</td>
<td>± 4.8</td>
<td>± 4.8</td>
<td>± 6.4</td>
<td>± 8.8</td>
<td>± 9.4</td>
<td>0.24</td>
</tr>
<tr>
<td>LV dimension (sys) (mm)</td>
<td>29.3</td>
<td>28.7</td>
<td>29.3</td>
<td>30.0</td>
<td>34.7</td>
<td>35.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 5.8</td>
<td>± 4.5</td>
<td>± 5.5</td>
<td>± 4.3</td>
<td>± 9.4</td>
<td>± 10.0</td>
<td>0.46</td>
</tr>
<tr>
<td>LV wall thickness (mm)</td>
<td>15.0</td>
<td>15.0</td>
<td>15.0</td>
<td>13.6</td>
<td>13.5</td>
<td>13.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 1.7</td>
<td>± 1.0</td>
<td>± 1.5</td>
<td>± 1.5</td>
<td>± 1.3</td>
<td>± 1.45</td>
<td>0.59</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>397</td>
<td>340</td>
<td>350</td>
<td>338</td>
<td>360</td>
<td>374</td>
<td></td>
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<tr>
<td></td>
<td>± 154</td>
<td>± 89</td>
<td>± 89</td>
<td>± 113</td>
<td>± 97</td>
<td>± 106</td>
<td>0.22</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
<td>37.7</td>
<td>35.1</td>
<td>34.5</td>
<td>36.0</td>
<td>31.8</td>
<td>32.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 5.9</td>
<td>± 9.8</td>
<td>± 9.5</td>
<td>± 5.4</td>
<td>± 7.7</td>
<td>± 8.4</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>73.6</td>
<td>84.7</td>
<td>84.2</td>
<td>71.3</td>
<td>73.1</td>
<td>69.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 9.4</td>
<td>± 11.2</td>
<td>± 10.6</td>
<td>± 9.7</td>
<td>± 11.2</td>
<td>± 11.9</td>
<td>0.28</td>
</tr>
</tbody>
</table>

*p ≤ 0.01.*

Abbreviations: LV = left ventricular; dia = diastole; sys = systole.
abnormal left ventricular volume and ejection fraction in the majority of patients with isolated aortic stenosis.8, 21-23 These studies have also shown that a relatively small percentage of patients with aortic stenosis have mild or moderate left ventricular dilatation and reduced ejection fraction.6, 22, 23 McDonald obtained similar results using echocardiography.24 The reduction in left ventricular systolic function found in the present study could not be ascribed to the presence of coexistent coronary artery disease, as reported by Liedtke et al.25 Although other studies have not quantitatively examined aortic root and left atrial size, measurements in the present study indicate that only minimal increases occur.

Comparison of echocardiographic measurements in the same patients before and after operation revealed that left ventricular wall thickening decreased significantly after left ventricular systolic pressure was reduced by aortic valve replacement. Specifically, the mean ventricular septal thickness decreased approximately 2 mm and free wall thickness decreased approximately 1.5 mm after operation. Because the mean internal dimension of the left ventricle at end-diastole was unchanged 6 months after operation, a significant reduction in estimated left ventricular mass was noted 6 months postoperatively that reflected the decrease in wall thickness. As judged by the percent fractional shortening, systolic function of the base of the left ventricle, on average, was unchanged after operation.

When patients with and without left ventricular dilatation were compared, it was noted that patients with preoperative left ventricular end-diastolic dimensions greater than 52 mm had a significant decrease in left ventricular internal dimensions, wall thickness and mass after operation, but wall thickness and mass usually remained abnormal. In contrast, patients without left ventricular dilatation had a slight postoperative increase in left ventricular dimension that accompanied the decrease in wall thickness. As a result, the patients without left ventricular dilatation had a smaller decrease in left ventricular mass after operation than patients with preoperative dilatation.

Left ventricular systolic function (as assessed by fractional shortening) decreased slightly after operation in patients without preoperative left ventricular dilatation. In contrast, systolic function increased slightly in patients whose preoperative left ventricular dimension was above normal (although the postoperative increase was not quite statistically significant). Using contrast angiography, Kennedy et al.28 reported little or no change in ejection fraction after operation in patients with aortic stenosis and normal preoperative ejection fractions. However, contrast angiographic studies by Kennedy et al.,28 Croke et al.,29 and Smith et al.,27 and radionuclide cineangiographic studies performed in our laboratory28 have shown significant increases in resting ejection fraction after operation in some patients with aortic stenosis who had dilated ventricles and low preoperative ejection fractions. This larger increase in resting systolic function after operation (compared with the present echocardiographic study) may relate in part to the fact that most of the patients described in these angiographic studies appear to have had more severe depression of left ventricular systolic function than the patients reported in the present series. Changes in the eccentricity of the left ventricle between diastole and systole, as well as between preoperative and postoperative studies, may also explain some of the differences between the echocardiographic and

<table>
<thead>
<tr>
<th>Table 4. Measurements Associated with Overall Mortality</th>
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<tbody>
<tr>
<td><strong>Measurement</strong></td>
</tr>
<tr>
<td>LV dimension (dis) (mm)</td>
</tr>
<tr>
<td>LV dimension (sys) (mm)</td>
</tr>
<tr>
<td>Septal thickness (mm)</td>
</tr>
<tr>
<td>LV free wall thickness (mm)</td>
</tr>
<tr>
<td>Aortic root dimension (mm)</td>
</tr>
<tr>
<td>Left atrial dimension (mm)</td>
</tr>
<tr>
<td>LV fractional shortening (%)</td>
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<tr>
<td>LV ejection fraction (%)</td>
</tr>
<tr>
<td>Estimated LV mass (g)</td>
</tr>
</tbody>
</table>

**Electrocardiography**
- Heart rate (beats/min) 0.46 0.65
- Romhilt-Estes score 0.35 0.83

**Hemodynamics**
- LV systolic pressure (mm Hg) 0.65 0.85
- LV end-diastolic pressure (mm Hg) 0.51 0.91
- Aortic systolic pressure (mm Hg) 0.56 0.96
- Aortic diastolic pressure (mm Hg) 0.92 0.64
- Cardiac output (l/min) 0.92 0.24
- Cardiac index (l/min/m²) 0.56 0.31
- LV peak gradient (mm Hg) 0.15 0.05*
- Aortic valve area (cm²) 0.43 0.05*
- Aortic valve index (cm²/m²) 0.30 0.06
- Pulmonary systolic pressure (mm Hg) 0.03* 0.32
- Pulmonary diastolic pressure (mm Hg) 0.12 0.83
- Pulmonary wedge pressure (mm Hg) 0.12 0.98

* p ≤ 0.05.

Abbreviations: LV = left ventricular; dis = diastolic; sys = systolic.
angiographic assessments of the postoperative change in left ventricular systolic function.

These data indicate that the major change in the left ventricle after aortic valve replacement (and consequent reduction in left ventricular systolic pressure) was a decrease in wall thickness. Although left ventricular systolic pressure decreased markedly, it did not return completely to normal, partly because of the small residual gradient across the aortic valve. Likewise, left ventricular wall thickness and mass did not return to normal by 6 months after operation (fig. 6).

Measurements from a small number of patients early (10–23 days) after operation suggest that the decrease in wall thickening occurred 2 weeks to 6 months after operation. However, left ventricular end-diastolic dimension, though unchanged 6 months postoperatively, had decreased slightly at the early postoperative study. Because of this early postoperative decrease in left ventricular internal dimension, estimated left ventricular mass had decreased by the time of the early postoperative study. Repeat echocardiographic evaluation of 13 patients an average of 31 months after operation showed no further reduction in either left ventricular wall thickness or mass compared with the 6-month postoperative study. Thus, it appears that most of the regression of left ventricular wall thickness and mass takes place during the 6 months immediately after operation, and that little further regression occurs during subsequent follow-up. Moreover, much of the decrease in left ventricular mass appears to occur early after operation. Although changes in heart rate that occurred between the preoperative, early and 6-month postoperative studies could have influenced the echocardiographic measurements, the observations just discussed are consistent with studies on the time course of regression of hypertrophy in experimental animals.

Several hemodynamic measurements were significantly altered by operation. In addition to the expected reductions in left ventricular systolic pressure and increases in aortic valve area and index, the left ventricular end-diastolic pressure and the pulmonary artery systolic, diastolic and wedge pressures all decreased significantly. These latter changes may reflect an increase in left ventricular compliance due to the regression in left ventricular wall thickening after operation.

In addition to detecting abnormalities of several measurements of structure and function of the heart in patients with a marked elevation in left ventricular pressure, we analyzed the data to determine whether any preoperative measurements were highly associated with mortality and hence predictive of a good or poor operative result. Because only one operative death occurred in the series and because the six late deaths were related to several different causes, only overall mortality was examined. Of the 23 preoperative measurements, only pulmonary artery systolic pressure was associated with overall mortality. This association was weak (p = 0.03) and possibly due to chance. We found no explanation for findings reported from our institution and others that radiographic heart size was inversely related to prognosis in patients undergoing operation for isolated aortic stenosis. Specifically, left ventricular internal dimension and wall thickness and left atrial dimension were not associated with overall mortality. Although our series is small, preoperative evaluation of a single echocardiographic, electrocardiographic or hemodynamic measurement does not appear useful as a method for identifying patients with isolated aortic stenosis who are at risk of a poor operative result.

The preoperative echocardiographic findings in symptomatic patients with aortic stenosis are considerably different from those in patients undergoing aortic valve replacement at our institution for aortic regurgitation during approximately the same time period (figs. 1 and 2). The results of the operative experience in patients with isolated aortic regurgitation are reported in detail elsewhere. Although the prevalence of the various types of symptoms in the two groups of patients was different, the indications for operation were the same for patients with aortic regurgitation as for those with aortic stenosis, i.e., the development of severe dyspnea on exertion, congestive heart failure, angina or syncope.

In symptomatic patients with aortic stenosis, left ventricular end-diastolic and end-systolic dimensions were rarely greater than 50% of the expected value. In symptomatic patients with aortic regurgitation, these dimensions (particularly the end-systolic dimension) were greater than 50% of expected in most patients (fig. 1). Also, only patients with aortic regurgitation had a markedly reduced left ventricular fractional shortening (i.e., < 20%). Although left ventricular free
wall thickness was slightly greater in patients with aortic stenosis, the amount of left ventricular dilatation was much less. As a result, the estimated left ventricular mass was less in patients with aortic stenosis than in patients with aortic regurgitation\(^\text{[11, 29]}\) (fig. 1).

Aortic root and left atrial dimensions were smaller in patients with aortic stenosis than in patients with aortic regurgitation (fig. 2). Part of the difference in aortic root dimensions is explained by the fact that some patients with aortic regurgitation had aortic root disease (and hence markedly dilated aortic roots), while those with aortic stenosis did not. Even when patients with aortic root disease are excluded, aortic root dimension is still less in patients with aortic stenosis and above the upper limit of normal in only a relatively small percentage of patients.

The relatively normal aortic root size observed in this study appears to conflict with angiographic data, which suggest that most patients with aortic stenosis have significant poststenotic dilatation of the aorta. However, this poststenotic dilatation is most marked above the aortic annulus. Therefore, it may be underestimated by an echocardiographic measurement of aortic root dimension obtained at the level of the aortic leaflets. In contrast, aortic root dilatation in patients with aortic regurgitation usually is marked at the base of the aorta and, therefore, is likely to be detected by an aortic root measurement at the level of the aortic valve.

The poor association between preoperative or postoperative measurements and death in patients with valvular aortic stenosis is in marked contrast to our experience in patients with aortic regurgitation. In these latter patients, a reduced fractional shortening and a markedly increased end-systolic dimension of the left ventricle were strongly associated, both preoperatively and 6 months postoperatively, with late death from congestive failure.\(^\text{[11]}\) Moreover, over half of the late postoperative deaths in patients with prior aortic regurgitation were due to congestive heart failure.

In contrast, left ventricular fractional shortening was not markedly reduced and end-systolic dimension was not markedly increased in patients with aortic stenosis. In fact, only one patient with aortic stenosis fell into the high-risk group (identified in the patients with aortic regurgitation\(^\text{[11]}\)) characterized by both a preoperative left ventricular end-systolic dimension greater than 55 mm and a fractional shortening less than 25\% (fig. 6). Also, patients with aortic stenosis appear to have a very low incidence of late death due to congestive heart failure. These factors probably account for our inability to predict late postoperative outcome in aortic stenosis.

Thus, it appears that some symptomatic patients with aortic valve disease who have a severe left ventricular volume overload may develop irreversible left ventricular dysfunction before operation, while those with an isolated severe pressure overload only rarely develop this complication. This observation is consistent with ultrastructural evidence of degenerated cardiac muscle cells found in patients with aortic regurgitation but not in patients with isolated aortic stenosis,\(^\text{[84]}\) and may explain differences in the survival experience after aortic valve replacement in these two conditions.

Reports of early operative experience (including one from our institution)\(^\text{[4]}\) indicated no difference in the late survival in patients undergoing operation for isolated aortic stenosis compared with those who had operation for isolated aortic regurgitation.\(^\text{[4, 34-36]}\) However, operative mortality and valve-related complications in this earlier experience produced a relatively high incidence of early and late morbidity and mortality compared with more recently reported series,\(^\text{[6, 5, 10, 36]}\) in most of which, patients with isolated aortic regurgitation had a poorer late survival after operation.\(^\text{[5, 10, 36]}\)

In our two recent operative series, we found a greater late mortality for patients undergoing operation for isolated aortic regurgitation\(^\text{[11]}\) compared with data presented in this paper from those who underwent operation for isolated aortic stenosis (fig. 7).

In our experience, this greater late mortality could be accounted for by the late deaths due to congestive heart failure in patients who had an operation for isolated aortic regurgitation (fig. 7).

These observations are particularly relevant to the issue of whether earlier operative intervention is warranted in patients with aortic valve disease. In aor-
tic regurgitation, it may be possible to use echocardiography to identify a subgroup of patients who are at high risk of subsequently developing irreversible left ventricular dysfunction and may benefit from operative intervention before ominous symptoms occur.\(^{11, 37}\) However, early operative intervention for the purpose of preventing irreversible left ventricular dysfunction is not warranted in patients with aortic stenosis because irreversible damage occurs only rarely, if at all.

Most of the late deaths in patients with aortic stenosis, as well as most of the late deaths not due to congestive heart failure in patients with aortic regurgitation, were related to coexistent coronary artery disease or to prosthetic valve complications. Moreover, many of our postoperative patients who did not die suffered significant prosthesis-related complications or had acute myocardial infarctions (table 5). Our data do not predict which patients will be at high risk of developing prosthetic valve problems. Also, we cannot definitively conclude from our data that late events related to coronary artery disease could have been prevented or appreciably delayed by coronary bypass operation at the time of aortic valve replacement.

Prophylactic operation could possibly be justified to prevent sudden death in asymptomatic patients with aortic stenosis. Overall 5-year mortality in a recently reported series of patients with aortic stenosis who were followed medically was considerably higher than either the 5-year mortality of patients with aortic regurgitation\(^{38}\) or the 5-year postoperative mortality in our present series of symptomatic patients with aortic stenosis who had operation. Most of the patients in this medical series, presumably, were symptomatic. It is not known whether the 5-year survival during medical follow-up of asymptomatic patients with hemodynamically significant aortic stenosis would be greater or less than the 5-year survival of symptomatic patients who were followed medically or who had operation. Therefore, we do not recommend prophylactic operation in asymptomatic adult patients with isolated aortic stenosis.

### References

3. Isom WO, Dembrow JM, Glassman E, Pasternack BS, Sackerl JP, Spencer FS: Factors influencing long-term survival after

### Table 5. Comparison of Mortality and Late Postoperative Complications in Patients with Aortic Stenosis and Those with Aortic Regurgitation

<table>
<thead>
<tr>
<th></th>
<th>Aortic stenosis</th>
<th>Aortic regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall cardiac mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>6/42 (14%)</td>
<td>18/55 (33%)</td>
</tr>
<tr>
<td>Excluding:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Aortic root reconstruction</td>
<td>6/42 (14%)</td>
<td>13/50 (26%)</td>
</tr>
<tr>
<td>b) Aortic root reconstruction and CHF deaths</td>
<td>6/42 (14%)</td>
<td>6/43 (14%)</td>
</tr>
<tr>
<td>Late cardiac mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) CHF</td>
<td>0/41 (0%)</td>
<td>7/44 (16%)</td>
</tr>
<tr>
<td>b) CAD</td>
<td>2/41 (5%)</td>
<td>2/44 (5%)</td>
</tr>
<tr>
<td>c) Prosthetic valve</td>
<td>3/41 (7%)</td>
<td>0/44 (0%)</td>
</tr>
<tr>
<td>Valve complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Poppet malfunction or perivalvular leak</td>
<td>4/41 (10%)</td>
<td>3/44 (7%)</td>
</tr>
<tr>
<td>Secondary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Infection</td>
<td>1/41 (2%)</td>
<td>0/44 (0%)</td>
</tr>
<tr>
<td>b) Anemia</td>
<td>6/41 (15%)</td>
<td>2/44 (5%)</td>
</tr>
<tr>
<td>c) CVA</td>
<td>4/41 (10%)</td>
<td>5/44 (11%)</td>
</tr>
<tr>
<td>Total number of patients with valve complications</td>
<td>11/41 (27%)</td>
<td>9/44 (20%)</td>
</tr>
<tr>
<td>Including postop gradient &gt;30 mm Hg</td>
<td>14/41 (34%)</td>
<td>12/44 (27%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early postop (survived)</td>
<td>3/41 (7%)</td>
<td>3/47 (6%)</td>
</tr>
<tr>
<td>Late postop</td>
<td>3/41 (7%)</td>
<td>2/44 (5%)</td>
</tr>
</tbody>
</table>

Abbreviations: CHF = congestive heart failure; CAD = coronary artery disease; CVA = cerebrovascular accident.
W L Henry, R O Bonow, J S Borer, K M Kent, J H Ware, D R Redwood, S B Itscoitz, C L McIntosh, A G Morrow and S E Epstein

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