Effect of Preoperative Ejection Fraction on Survival and Hemodynamic Improvement Following Aortic Valve Replacement

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SUMMARY Ninety-three patients with aortic valve disease were evaluated to determine the effect of the preoperative left ventricular ejection fraction (EF) on the results of aortic valve replacement (AVR). Forty-six patients had aortic stenosis (AS), 16 had aortic insufficiency (AI), and 31 had mixed aortic stenosis and insufficiency (MX). Immediate and long-term survival curves in AS and MX, and in AS patients with adequate preoperative EF (≥ 0.50) and those with depressed preoperative EF (< 0.50), were compared. There was a trend toward a greater early mortality rate (0–1 month after AVR), but this difference did not reach the level of statistical significance (P > 0.05). In patients surviving the one-month preoperative period there was no significant difference in the long-term survival between the EF groups.

Thirty-two surviving patients, 18 with EF ≥ 0.50 and 14 with EF < 0.50, were further evaluated clinically and hemodynamically at an average interval of 29 months (range 9–66 months) after surgery. All AS and MX patients stayed at or improved to New York Heart Association (NYHA) class I or II. Six of the AS or MX patients with depressed EF had distinctly abnormal arteriovenous oxygen (A-VO₂) difference (> 6 vol%) preoperatively. Surgery resulted in normalization of the A-VO₂ difference in four. The preoperative mean pulmonary arterial (PA) pressure was elevated to > 20 mm Hg in five of the AS or MX patients with depressed EF. Postoperatively, four of the five showed significant decreases (> 10 mm Hg) in the mean PA pressure, but most (four-fifths) of the patients remained abnormal (mean PA > 20 mm Hg). Hemodynamics obtained during 300 kg-m/min exercise showed gross abnormalities of pressure and flow in seven of eight patients with depressed EF. Stress-induced hemodynamic abnormalities were also present in six of 12 with EF ≥ 0.50, but the abnormality was limited to moderate rises in the mean PA pressure in five of the six. Similar clinical and hemodynamic changes were seen in the eight restudied patients with AI, except that two patients with depressed EF were not improved clinically (remained NYHA class III postoperatively) and continued to have marked hemodynamic abnormalities postoperatively.

We conclude that a depressed preoperative EF may cause a moderate increase in the perioperative mortality rate, with little effect on subsequent long-term survival in patients with AS or MX undergoing AVR. Resting hemodynamic abnormalities seen in the depressed EF group often show significant improvement after surgery.

CONFLICTING RESULTS have been reported in the literature on the effect of preoperative heart size on survival after aortic valve replacement (AVR). Two series have suggested that the most significant factor influencing long-term survival after AVR was the degree of preoperative cardiac enlargement on chest x-ray.1, 2 This observation was supported by Barnhorst et al., who noted that advanced stages of ventricular enlargement were associated with increased early and late mortality.3 However, in the series reported by Hirshfield and coworkers, the preoperative cardiothoracic ratio did not influence survival in aortic insufficiency (AI), and in aortic stenosis (AS) it was correlated with survival in an inverse way, i.e., there were more sudden, unexplained postoperative deaths in those who had a normal heart size before surgery.4

The left ventricular ejection fraction (EF) is also used as an index of preoperative left ventricular dysfunction. Using this parameter instead of cardiac enlargement on the chest x-ray to predict survival, it is not clear whether a reduced preoperative EF is associated with a greater early and late mortality rate after AVR.

While the relation between the left ventricular EF and the risk of surgery is a major consideration, equally important is whether antecedent left ventricular dysfunction affects improvement after AVR. An early report by Hultgren and coworkers noted that neither preoperative congestive heart failure nor the specific aortic valve lesion affected the capacity to obtain a good clinical and hemodynamic result.5 However, a limitation of this study was that patients were selected because they had demonstrated excellent clinical results from AVR. Because congestive heart failure can result from an elevated left ventricular end-diastolic pressure with maintenance of a good left ventricular EF, several investigators have looked at the effect of the preoperative left ventricular EF on the results of AVR. Cohn et al. believe that the EF is probably the single most useful of the readily ob-

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tangible hemodynamic measurements to predict the outlook for patients undergoing cardiac surgery, including valvular replacement. Yet Hildner et al. noted that the preoperative EF did not parallel clinical improvement in their patients undergoing AVR. Most recently, Kennedy and coworkers and Pantely et al. reported that reduced preoperative EFs were largely reversible after AVR.

In this study we assessed the effect of the preoperative left ventricular EF on both survival and long-term hemodynamic response to isolated AVR.

Materials and Methods

The records of all patients who underwent isolated AVR at Presbyterian University Hospital between January, 1970 and December, 1976 were evaluated. We studied only those patients having single plane left ventriculograms in the right anterior oblique (RAO) projection, allowing objective determination of the preoperative EF. There were 93 such patients (71 males and 22 females), ranging in age from 18–78 years. The aortic valve was replaced in 88 patients with a Bjork-Shiley prosthesis and five patients with a Magovern aortic prosthesis. Forty-six had isolated AS, 16 had isolated AI, and 31 were considered to have mixed aortic valve lesions (MX), defined as a systolic gradient across the aortic valve of at least 30 mm Hg associated with a minimum of 1 out of 4+ AI. Thirty-two of these patients were not specifically studied for associated coronary artery disease. Thirty of the 32 were under the age of 35 years and were considered low risk for significant coronary lesions. Of the 61 patients undergoing selective coronary arteriography, 12 were found to have significant disease, defined as 70% or greater narrowing in at least one major coronary artery. Patients with associated disease involving any other cardiac valve were excluded from this series. All patients were operated on because of the presence of one or more of the following symptoms: angina, syncope, functional class III or IV dyspnea or congestive heart failure. Follow-up on these patients was either done by personal interview and examination by one of the authors or obtained by talking directly to the patient or his private physician.

The preoperative EF could be calculated in 93 patients. In all cases, left ventriculography was performed before coronary arteriography. The end-diastolic and end-systolic ventricular silhouettes were traced from the first beat with adequate opacification that did not represent or immediately follow an extrasystole. The EF was determined and calculated according to the method of Kasser and Kennedy, however, a magnification correction was not used, since this parameter cancels out in the equation that was used. The calculated EF was reduced to biplane data by the regression equation developed by these workers. Repeat right heart catheterization was performed on 32 of the 93 patients. The 32 patients, 27 males and five females, had undergone uncomplicated AVR. The distribution of valvular lesions and EFs is as shown in table 1. The patients with AI have been listed separately because they represent a different pathological process and may well behave differently. Patients with AS and MX aortic valvular disease have been grouped together and divided according to their preoperative EF. The average age of the restudied patients was 52 years (range 19–81 years). Several patients had short early systolic murmurs, but none were suggestive of significant hemodynamic obstruction. One patient was noted to have a short, high-pitched blowing diastolic murmur consistent with hemodynamically mild AI. The average interval between surgery and repeat catheterization was 29 months (range 9–66 months). The preoperative cardiac outputs were done either by the indocyanine green dye technique or the Fick method using previously described techniques. Oxygen content of the blood samples was determined by the Van Slyke method.

Follow-up catheterization procedures were accomplished on an outpatient basis without interruption of the patients' anticoagulant therapy. The right heart catheterization was carried out using a Lehman catheter; a 20 gauge, 1½-inch polyethylene catheter was inserted in the left radial artery. The resting pulmonary artery wedge (PAW) pressure, pulmonary artery (PA) pressure, systemic arterial pressure, arterial venous oxygen (A-VO2) difference, and cardiac output were measured. The cardiac outputs were performed by indocyanine green dye technique using the same method used preoperatively. Twenty patients also performed supine exercise on a bicycle ergometer at a constant external workload of 300 kg-m/min. During exercise, the mean PA pressure was continually monitored while A-VO2 differences and duplicate cardiac outputs were obtained between 3–6 minutes of exercise.

Out of the 93 total patients, 28 were excluded from determination of survival data. The exclusions consisted of the 16 patients with isolated AI who were excluded because of insufficient numbers and 12 patients with associated significant coronary artery disease (10 with AS and two MX both evenly distributed between EFs). Two patients with AS and adequate EF died of noncardiac causes (cancer of the lung and an automobile accident). In the survival curves, they were treated as alive and withdrawn at the last preceding period of observation. The remaining late deaths consisted of autopsy proven or clinically diagnosed cardiac causes, most commonly sudden death.

Exclusion of the patients with AI and associated significant coronary artery disease left a total of 65 patients with objectively determined EF. This total consisted of 36 patients with AS and 29 with MX. Cumulative survival curves for the 36 patients with AS vs the 29 with MX were calculated according to the method described by Colton. The AS and MX patients were then combined and divided into two groups with preoperative EF ≥ 0.50 and those with an EF < 0.50. Cumulative survival curves were
TABLE 1. Hemodynamic Data Before and After Aortic Valve Replacement

<table>
<thead>
<tr>
<th>Pt/Age/Sex</th>
<th>EF</th>
<th>Lesion</th>
<th>Cor</th>
<th>Preoperative</th>
<th>Postoperative (Resting)</th>
<th>Postoperative (Exercise)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A-V</td>
<td>CI</td>
<td>PA</td>
<td>PAW</td>
<td>A-V</td>
<td>CI</td>
</tr>
<tr>
<td>Preoperative EF &lt; 0.50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/57/M 0.21 AS -</td>
<td>6.48</td>
<td>1.40</td>
<td>28</td>
<td>24</td>
<td>6.39</td>
<td>1.70</td>
</tr>
<tr>
<td>2/69/M 0.26 AS -</td>
<td>6.50</td>
<td>-</td>
<td>20</td>
<td>14</td>
<td>6.67</td>
<td>1.96</td>
</tr>
<tr>
<td>3/60/M 0.27 AS +</td>
<td>4.86</td>
<td>2.44</td>
<td>12</td>
<td>4</td>
<td>5.09</td>
<td>-</td>
</tr>
<tr>
<td>4/29/M 0.30 MX</td>
<td>7.38</td>
<td>-</td>
<td>40</td>
<td>34</td>
<td>-</td>
<td>5.08</td>
</tr>
<tr>
<td>5/63/M 0.33 AS</td>
<td>8.32</td>
<td>1.46</td>
<td>46</td>
<td>32</td>
<td>5.49</td>
<td>2.05</td>
</tr>
<tr>
<td>6/55/M 0.40 AS -</td>
<td>4.81</td>
<td>3.14</td>
<td>17</td>
<td>8</td>
<td>-</td>
<td>6.60</td>
</tr>
<tr>
<td>7/23/M 0.42 MX</td>
<td>6.71</td>
<td>2.27</td>
<td>32</td>
<td>34</td>
<td>-</td>
<td>4.31</td>
</tr>
<tr>
<td>8/60/M 0.45 AS +</td>
<td>3.42</td>
<td>3.70</td>
<td>18</td>
<td>7</td>
<td>4.65</td>
<td>2.76</td>
</tr>
<tr>
<td>9/67/M 0.47 AS -</td>
<td>8.45</td>
<td>2.20</td>
<td>42</td>
<td>32</td>
<td>4.77</td>
<td>1.98</td>
</tr>
</tbody>
</table>

Preoperative EF ≥ 0.50

| 10/51/M 0.50 AS - | 5.07 | 1.65 | 12 | 7 | - | 4.06 | 2.33 | 14 | 4 | 9.82 | 3.74 | 40 |
| 11/57/M 0.52 AS - | 5.15 | 2.46 | 12 | 7 | 4.47 | 2.34 | 12 | 5 | 9.89 | 4.46 | 18 |
| 12/63/M 0.52 MX | 4.81 | 3.05 | 40 | 22 | 5.72 | 2.17 | 26 | 6 | 12.29 | 5.05 | 50 |
| 13/30/M 0.54 AS | 5.68 | 2.58 | 11 | - | - | 2.58 | 11 | 6 | - | - | - | - |
| 14/52/M 0.55 MX | 7.78 | 1.87 | 37 | 26 | 5.07 | 2.37 | 15 | 10 | 10.35 | 5.30 | 42 |
| 15/51/M 0.56 AS | 5.70 | 2.82 | 17 | 9 | 5.44 | 2.08 | 13 | 10 | 12.12 | 3.90 | 24 |
| 16/67/F 0.56 MX | 4.51 | 2.07 | 17 | 12 | 4.78 | 2.99 | 13 | 5 | 12.08 | 5.18 | 24 |
| 17/46/M 0.57 MX | - | 1.46 | 19 | 14 | 6.15 | 2.10 | 12 | 6 | - | 12.65 | 3.44 | 28 |
| 18/64/M 0.38 AS + | 4.95 | 2.63 | 16 | 8 | 5.24 | 1.73 | 20 | 13 | 13.06 | 3.61 | 45 |
| 19/55/M 0.68 AS | - | 3.08 | 10 | 5 | - | 5.53 | 2.38 | 11 | 6 | - | - | - |
| 20/32/M 0.69 AS | 4.86 | 2.61 | 14 | 8 | 4.18 | 3.76 | 15 | 8 | 9.77 | 6.66 | 34 |
| 21/48/M 0.72 AS | 4.23 | 2.27 | 20 | 10 | 4.40 | 3.31 | 18 | 12 | 8.97 | 5.20 | 32 |
| 22/59/M 0.72 MX | - | 2.96 | - | - | 5.00 | 2.25 | 14 | 5 | 9.30 | 4.33 | 30 |
| 23/93/F 0.73 AS | 4.49 | 2.17 | 18 | 16 | 5.36 | 2.27 | 16 | 9 | - | - | - | - |
| 24/62/M 0.77 MX | - | 4.51 | 2.50 | 14 | 4.90 | 2.50 | 21 | 13 | 9.70 | 4.53 | 28 |

Aortic insufficiency

| 25/92/M 0.42 AI | - | 8.57 | 1.63 | 50 | 32 | 5.27 | 2.42 | 45 | 33 | 12.26 | 2.98 | 80 |
| 26/57/M 0.32 AI | - | 8.12 | 1.73 | 35 | 25 | 5.46 | 2.35 | 20 | 8 | 10.18 | 3.54 | 60 |
| 27/92/M 0.36 AI | - | 8.63 | 1.39 | 38 | 20 | 9.29 | 1.55 | 50 | 40 | 11.78 | 4.63 | 25 |
| 28/90/M 0.58 AI | - | 4.55 | 2.80 | 12 | 7 | 5.32 | 2.90 | 12 | 7 | - | - | - |
| 29/23/F 0.48 AI | - | 5.52 | 2.27 | 18 | 9 | 4.27 | 2.86 | 27 | 22 | 10.33 | 3.97 | 35 |
| 30/19/F 0.63 AI | - | 4.33 | 2.46 | 16 | 10 | 3.34 | 3.52 | 12 | 6 | 8.59 | 6.08 | 20 |
| 31/55/F 0.63 AI | - | 4.27 | 3.39 | 18 | 12 | 3.43 | 3.11 | 12 | 5 | 10.30 | 5.66 | 35 |
| 32/64/M 0.70 AI | - | 8.67 | 1.80 | 8 | - | 5.43 | 2.24 | 10 | 4 | 11.38 | 4.25 | 22 |

Abbreviations: EF = ejection fraction; Cor = coronary artery lesion; (+) = number of major coronary vessels involved; A-V = arteriovenous oxygen difference in vol%; CI = cardiac index (l/min/m²); PA = mean pulmonary artery pressure (mm Hg); PAW = mean pulmonary artery wedge pressure (mm Hg); AS = aortic stenosis; AI = aortic insufficiency; MX = mixed aortic stenosis and insufficiency.

calculated for these two EF subsets comparing the EF ≥ 0.50 with an EF < 0.50. Survival curves were then done on just the AS patients divided according to preoperative EF of ≥ 0.50 and < 0.50. These survival curves were compared at one and three months and each year for five years, as well as for overall differences in cumulative survival using the method described by Peto et al.14, 15

Statistical comparisons were performed using paired and grouped data. The significance of differences was assessed using the two-tailed t test or chi square analysis without the Yates continuity correction.16 P values < 0.05 were considered significant.

The change (Δ) in mixed venous oxygen transport (MVOT) with exercise was calculated from the relation:

\[ \Delta \text{MVOT} = \text{MVOT}_{\text{ex}} - \text{MVOT}_{\text{rest}} \]

where: MVOT = cardiac index × PA oxygen content in vol% during rest or exercise (EX).17

Results

The distribution of the EFs for the 93 patients in this series is given in table 2. The patients with AI or associated significant coronary artery disease were excluded from calculations of the survival data. Immediate and long-term survival rates were evaluated for the remaining 36 patients with AS who had a mean EF of 0.49 ± 0.15 (sd) and 29 patients with MX who had a mean EF of 0.54 ± 0.15 (P > 0.10) (fig. 1). This shows no statistical difference in immediate or long-term survival between these groups of patients. These AS and MX patients were then pooled and immediate and long-term survival curves were determined for patients with EF ≥ 0.50 and EF < 0.50, as shown in figure 2. The survival curves for the EF < 0.50 patients shows a higher, early mortality rate, but the curves are essentially parallel after this. While the difference in early mortality did not reach the level of statistical significance, it may have done so if there were a larger number of
There were curves calculated for the patients divided according to a preoperative EF of $\geq 0.50$ or $< 0.50$, as shown in figure 3. Again, a higher, though not statistically significant, early mortality rate was found. The last two years of the survival curve for AS patients contains too few patients to be meaningfully interpreted.

In this series, there were 15 patients (10 with AS and five with MX) with preoperative EF $\leq 0.35$ and no associated significant coronary artery disease. There were three perioperative deaths occurring within one month of AVR in these 15 patients, and all three deaths were AS patients. One patient with MX died three years after AVR. The remaining 11 patients continue to survive anywhere from one to five years after AVR.

There were 12 patients in this series with associated significant coronary artery disease (six with EF $\geq 0.50$ and six with EF $< 0.50$). Seven patients had coronary artery bypass surgery as well as AVR, and five did not. Seven of these 12 patients died within one year of their operation (four had coronary bypass surgery as well as AVR), and five of these patients also had EFs $< 0.50$. Of the surviving five patients with associated coronary artery disease, three had bypass surgery and two did not.

Late cardiac deaths were defined as those occurring more than three months after AVR. There were six late deaths in the EF $\geq 0.50$ group and five of the six were sudden, without a definite cause determined. In the EF $< 0.50$ group there were four late deaths; two were sudden (one had a thrombus preventing opening of the prosthesis), one was due to acute myocardial infarction and one was due to intractable congestive heart failure.

There were 32 restudied patients. The clinical improvement in the 24 AS or MX patients divided according to their preoperative EFs are shown in figure 4. All improved to New York Heart Association (NYHA) functional class I or II, but statistically more of the EF $\geq 0.50$ group improved to or stayed at functional class I ($P < 0.01$). Six of the eight restudied AI patients also improved their postoperative func-

### Table 2. Breakdown of Patients with Quantitative EFs

<table>
<thead>
<tr>
<th>Total no. patients</th>
<th>Ejection fraction Range</th>
<th>Mean</th>
<th>No. with valvular lesion AS</th>
<th>No. with associated CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>$\geq 0.60$</td>
<td>0.67</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>26</td>
<td>0.50-0.59</td>
<td>0.54</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>28</td>
<td>0.31-0.49</td>
<td>0.40</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>$\leq 0.30$</td>
<td>0.26</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations: AS = aortic stenosis; MX = mixed aortic stenosis and insufficiency; AI = aortic insufficiency; CAD = coronary artery disease.

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**Figure 1.** Cumulative survival rates for all aortic stenosis (AS) and mixed aortic stenosis and insufficiency (MX) patients who underwent aortic valve replacement (AVR) plotted as a function of the time after operation. In this and the two subsequent survival curves the time intervals plotted are one month, three months, and one to five years after AVR. Brackets indicate mean ± SEM. The number of patients under observation at the beginning of each follow-up interval is adjacent to each curve.
Figure 2. Cumulative survival rates for combined aortic stenosis (AS) and mixed aortic stenosis and insufficiency (MX) patients plotted as a function of time after operation. The solid line represents patients with a preoperative ejection fraction (EF) $\geq 0.50$ and the dotted line an EF $< 0.50$. More early deaths (0-1 month) occurred in the depressed EF group, but this difference was not statistically significant.

Figure 3. Cumulative survival rates for patients with isolated aortic stenosis (AS) divided into preoperative ejection fraction (EF) $\geq 0.50$ and $< 0.50$ and plotted as a function of time after AVR. More early deaths (0-1 month) occurred in the depressed EF group, but this difference was not statistically significant.
shows the pre-to-postoperative changes in A-VO₂ differences in AS and MX patients with EF ≥ 0.50 and EF < 0.50. The A-VO₂ difference was higher in EF < 0.50 compared to EF ≥ 0.50 both pre- and postoperatively, but these differences were not statistically significant. Neither group showed significant change after surgery. Since surgery is unlikely to produce improvement in patients with a normal preoperative A-VO₂, only those patients with a distinctly abnormal A-VO₂ difference (> 6 vol%)* were further evaluated. One out of 11 patients with preoperative EF ≥ 0.50 and six out of nine with preoperative EF < 0.50 had such distinctly abnormal values. The one patient with EF ≥ 0.50 improved, (narrowed the A-VO₂ > 1 vol% and decreased the absolute value to < 6 vol%) after surgery. Four of the six patients with EF < 0.50 showed this amount of improvement. One patient in the EF < 0.50 group showed significant deterioration, with the A-VO₂ difference postoperatively > 6 vol%. For the eight patients with isolated AI, six showed postoperative decreases in A-VO₂ difference, one deteriorated postoperatively but remained within the normal range, and one remained markedly abnormal at 9.29 vol%. The directional changes in the cardiac index (CI) were as expected from the changes in A-VO₂ differences, with few exceptions.

The effect of the preoperative EF on the pre-to-postoperative change in the mean PA pressure for the AS and MX patients is shown in figure 6. The mean PA pressure was significantly higher in patients with EF < 0.50 than in patients with EF ≥ 0.50 preoperatively (P < 0.05), but not postoperatively. The decrease in the PA pressure following surgery was not significant in either EF group. Since surgery would not be expected to improve those patients with normal mean PA pressures before surgery, only those patients with elevated mean PA pressure (> 20 mm Hg) were further examined. Two of 13 patients with EF ≥ 0.50 showed this abnormality and both showed significant improvement, with one returning to normal range. Five of the nine patients with preoperative EF < 0.50 had mean PA pressures > 20 mm Hg. Four of the five decreased the mean PA pressure postoperatively; however, it still remained abnormally elevated. Three of the five patients with AI and EF < 0.50 showed deterioration in the mean PA pressure following surgery. The remaining five patients with AI showed changes similar to those demonstrated for the patients with AS and MX. The changes in the mean PA pressure were similar in direction and magnitude to the changes in the mean PA pressure.

Since the normal physiological response to moderate supine exercise is for the CI to be increased out of proportion to the decrease in mixed venous oxygen content, the product (MVOT) of CI times the mixed venous oxygen content remains the same or increases. A decrease in MVOT is defined as an abnormal response to exercise. With regard to the mean PA pressure, an elevation above 30 mm Hg with exercise was considered abnormal. The cross-hatched area in figure 7 denotes the normal response as defined by these criteria.

The response to 300 kg-m/min supine exercise for the AS and MX patients is shown in figure 7. Only one of the eight patients with preoperative EF < 0.50 fall

*The average A-VO₂ difference in 68 normal patients from our laboratory was 4.30 ± 0.50 vol%. To identify distinctly abnormal patients we have taken values that were more than three standard deviations above the mean.
Within the hatched area, while six of the 12 patients with preoperative EF $\geq 0.05$ fall within this area, a difference which is statistically significant ($P > 0.05$). Only one patient with EF $\geq 0.50$ decreased the MVOT with exercise and this was an 81-year-old male. All patients with postoperative resting hemodynamic abnormalities, regardless of their EF group, fell outside the limits of the hatched area except for one patient with EF $\geq 0.50$. This patient had a wide A-VO$_2$ difference but normal mean PA pressure at rest. Exercise-induced hemodynamic abnormalities were also noted in one patient with EF $\leq 0.50$ and four of the 12 patients with EF $\geq 0.50$ who had normal resting hemodynamics (A-VO$_2$ difference $< 5.5$ vol% and mean PA pressure $\leq 20$ mm Hg). All six with EF $\leq 0.50$ and stress-induced abnormalities showed abnormal elevation of the mean PA pressure, but only one of them had decreased MVOT.

The seven patients with AI who performed the same exercise showed similar exercise responses. One of the four with EF $\leq 0.50$ had a normal exercise response, while two of the three with EF $\geq 0.50$ showed this response. The sole exercise abnormality in the EF $\geq 0.50$ group was a borderline elevation of the mean PA pressure to 35 mm Hg.

**Discussion**

Our data support the observation$^{20}$ that the preoperative left ventricular EF does not dramatically affect survival following AVR. However, there was a trend for patients with a preoperative EF < 0.50 to have lower one-month survival rates. While this trend did not reach the level of statistical significance, it may indicate that in a larger series, the combination of AS or MX with a depressed preoperative EF may be associated with a greater risk of early mortality following AVR. While these data indicate that a reduced preoperative EF may increase the early mortality rate with AVR, once beyond the one-month survival period, the mortality is about the same for both EF groups.

The similarity of late survival rates for the two EF groups is related to the high occurrence of late sudden death in the EF $\geq 0.50$ group (five out of six deaths). This high occurrence of late unexpected sudden deaths

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**Figure 5.** Pre- to postoperative changes in the resting arteriovenous oxygen (A-VO$_2$) difference found in the two ejection fraction (EF) groups for aortic stenosis (AS) or mixed aortic valvular lesion (MX) patients. Shown are the pre- and postoperative mean and SEM for both EF groups. The dashed line separates values above and below 6 vol%. The (x) represents AS patients and the (X) the MX patients.

**Figure 6.** Pre- and postoperative changes in the resting mean pulmonary artery (PA) pressure for aortic stenosis (AS) and mixed aortic valvular lesions (MX) patients. Given are the pre- and postoperative mean and SEM for both ejection fraction (EF) groups. The dashed line separates values above and below 20 mm Hg. $\Delta = \text{AS}$ and $X = \text{MX}$. 
in patients who have undergone AVR has been noted by previous workers, and this study did not clarify the mechanism responsible for this.

Twelve patients undergoing AVR had associated significant coronary artery disease. Seven of the 12 patients died within one year of AVR and five of the seven had EFs < 0.50. While the numbers are too small for definitive conclusions, they suggest that the combination of a reduced preoperative EF together with significant coronary artery disease may carry a less favorable prognosis.

While a reduced preoperative EF did not markedly increase early or late mortality after AVR, it is equally important to know what effect the EF had on the clinical and hemodynamic response after surgery. On the basis of the NYHA functional classification, 24 patients with AS or MX who were restudied stayed at or were symptomatically improved to class I or II by their surgery, and none showed deterioration. This finding — that the majority of patients improved clinically after cardiovascular surgery despite a depressed EF — is similar to findings noted in an earlier report. Two follow-up patients who did not improve (both were in class III) had EFs < 0.50 and had AI as an underlying lesion. This is consistent with reports that patients with AI who have evidence of preoperative impaired ventricular performance or depressed EF may not significantly improve following AVR.

The changes in A-VO2 differences indicative of changes in flow were similar to findings of Bristow, Ross and Lee and coworkers, which showed no significant change following AVR. In their series, as well as ours, most of the patients had normal A-VO2 differences and/or normal CIs preoperatively and therefore would be unlikely to show significant improvement following surgery. Since we were interested in whether patients with low CI and wide A-VO2 differences preoperatively show improvement after surgery, and whether the preoperative EF had any bearing on it, we looked selectively at this subgroup of patients. In patients with AS or MX, AVR may result in significant improvement (fig. 5). The eight patients with AI had results similar to six of the eight showing postoperative decreases in their A-VO2 differences. The remaining two who had increased postoperative A-VO2 differences also had EF ≤ 0.50. In the present series, although hemodynamic improvement occurred in most patients regardless of the preoperative EF, the patients with depressed EFs had higher mean A-VO2 values both pre- and postoperatively.

Several previous studies have indicated significant decreases in the mean PA and/or PA wedge pressures following AVR. These studies did not differentiate their patients on the basis of an initial PA pressure or EF. Our study indicates that patients with AS or MX with preoperative EF ≥ 0.50 generally have normal mean PA pressures preoperatively, and they generally remain so postoperatively. The patients with depressed preoperative EFs had statistically higher mean PA pressures preoperatively (P < 0.05). Four of five with abnormal preoperative elevations showed decreases of at least 10 mm Hg, but in four this parameter remained abnormally elevated at rest. The eight patients with AI had similar results, with three of the six with preoperative EFs < 0.50 con-
Continuing to show abnormally elevated mean PA pressures postoperatively. The study results indicate that while improvements in the resting mean PA pressure occur in both EF groups, significant abnormalities persist in half of the depressed EF groups.

As with the resting postoperative hemodynamic findings, which tended to be incompletely reversed in patients with depressed preoperative EFs, the exercise results showed greater abnormalities of flow and pressure in this group. Although resting hemodynamic abnormalities were almost completely normalized in patients with $EF \geq 0.50$, approximately half showed moderate elevations of PA pressures associated with relatively appropriate increases in flow. This abnormality may be partly related to persistent changes in left ventricular compliance induced by long-standing valvular lesions. Thus, even years after AVR, these patients continue to develop an abnormal hemodynamic pattern in both EF groups, significant abnormalities of pressure resulting in pulmonary hypertension. An alternate explanation for these findings is that the stress-induced abnormalities of pressure and flow were related to moderately depressed EFs within a broad group of patients with $EF \geq 0.50$. Unfortunately, this study did not contain a sufficient number of patients to resolve this point.

Recent reports, have indicated that reduced preoperative EFs may markedly improve or return to normal after AVR for AS or MX. However, this optimistic report should be tempered. Eight of the 10 patients with AS in the report by Pantely and coworkers had normal preoperative EFs. The report by Kennedy and coworkers had selected patients who had a good response to surgery and excluded patients with a poor clinical result. No such selection was made in our series, and although most patients with preoperatively depressed EFs showed hemodynamic improvement, significant resting or stress-induced hemodynamic abnormalities were demonstrable in nearly all members of this group. Patients not adequately represented in these series are ones with depressed preoperative EFs who had only a fair to poor clinical result from AVR. Whether significant hemodynamic improvement occurs in a particular patient will depend on whether left ventricular dysfunction was too far advanced before valve replacement. There does not seem to be a reliable clinical means of determining which patient with a depressed EF has advanced left ventricular dysfunction, and thus may not show appreciable hemodynamic improvement after AVR.

This study shows: 1) a moderate increase in the immediate or perioperative mortality rate, with little effect on subsequent long-term survival in patients with AS or MX and depressed preoperative EF undergoing AVR; 2) patients whose preoperative evaluations disclose both a reduced EF and resting hemodynamic abnormalities often are stable or significantly improved after surgery. Thus, a low preoperative EF should not be the only reason for deciding against AVR, at least in patients with AS or MX.

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Asymptomatic Coronary Artery Disease: 
Angiographic Assessment of Diabetics 
Evaluated for Renal Transplantation 

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SUMMARY Twenty-one insulin-dependent diabetics with azotemic nephropathy were evaluated for renal transplantation by selective coronary angiography and cine left ventriculography. All had hypertension, retinopathy, neuropathy, and required salt restriction plus diuretics for volume overload. There was no clinical or electrocardiographic evidence of ischemic coronary artery disease in twenty.

Ten patients (five males, five females, mean age 29.3 years; mean duration of diabetes 18.9 years; mean serum cholesterol 264 mg%) had no significant coronary artery disease and no ventricular wall motion abnormalities.

Nine patients (seven males, two females; mean age 38.7 years; mean duration of diabetes 21.9 years; mean serum cholesterol 239 mg%) had significant coronary artery disease, seven demonstrating focal abnormalities in left ventricular wall motion.

Two patients (one male, one female; mean age 36.5 years; mean duration of diabetes 28.5 years; mean serum cholesterol 250 mg%) had no significant coronary artery disease, but demonstrated diffusely abnormal left ventricular wall motion with diminished ejection fraction.

Thirty-eight percent had significant coronary artery disease unpredictable by electrocardiographic or clinical data. The finding of no significant coronary artery disease in 52% of a group with severe renal-hypertensive complications of diabetes is surprising. Two patients had a demonstrated cardiomyopathy.

ATHEROSCLEROTIC CARDIOVASCULAR disease is the most common cause of death among patients with severe renal disease. In a group of diabetic patients under evaluation for renal transplantation, the major non-renal cause of morbidity and mortality would be ischemic cardiovascular complications. In order to clarify the risks of surgery in those diabetic patients in whom severe coronary artery disease might raise serious doubts about the possibility of renal transplantation, a prospective study using cardiac catheterization with angiography was begun. The initial angiographic and hemodynamic results are reported in this paper.

Patients

Twenty-one insulin-dependent diabetics with severe renal insufficiency were admitted for evaluation for renal transplantation. Table 1 lists the background information on these patients, 13 males and eight females with a mean age of 34 years (range 22-48 years) and a mean duration of diabetes of 20.6 years. All had diabetic retinopathy and neuropathy. All were hypertensive and anemic. Sixteen patients had a functioning arteriovenous fistula and eight were on maintenance hemodialysis. The evaluation process followed a strict protocol developed by the Dialysis-
Effect of preoperative ejection fraction on survival and hemodynamic improvement following aortic valve replacement.
J D O'Toole, E A Geiser, P S Reddy, E I Curtiss and R M Landfair

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