Aortic Valve Replacement in Patients With Aortic Stenosis and Severe Left Ventricular Dysfunction

David E. Powell, MD; Paul A. Tunick, MD; Barry P. Rosenzweig, MD; Robin S. Freedberg, MD; Edward S. Katz, MD; Robert M. Applebaum, MD; John L. Perez, MD; Itzhak Kronzon, MD

Background: The outcome of aortic valve replacement for severe aortic stenosis is worse in patients with impaired left ventricular function. Such dysfunction in aortic stenosis may be reversible if caused by afterload mismatch, but not if it is caused by superimposed myocardial infarction.

Methods: From our echocardiography database, 55 patients with severe aortic stenosis (valve area ≤0.75 cm²) and ejection fractions of 30% or lower who subsequently underwent aortic valve replacement were included. The operative mortality and clinical follow-up were detailed.

Results: There were 10 perioperative deaths (operative mortality, 18%). Twenty (36%) of the 55 patients had a prior myocardial infarction. In the 35 patients without prior myocardial infarction, there was only 1 death (3%). In contrast, 9 of 20 patients with prior myocardial infarction died (mortality rate, 45%; P = .001). The factors significantly associated with perioperative death on univariate analysis (functional class, mean aortic gradient, and prior myocardial infarction) were entered into a model for stepwise logistic regression. This multivariate analysis showed that only prior myocardial infarction was independently associated with perioperative death (odds ratio, 14.9; 95% confidence interval, 2.4-92.1; P = .004).

Conclusions: The risk of aortic valve replacement in patients with severe aortic stenosis and severely reduced left ventricular systolic function is extremely high if the patients have had a prior myocardial infarction. This information should be factored into the risk-benefit analysis that is done preoperatively for these patients, and it may preclude operation for some.

Arch Intern Med. 2000;160:1337-1341

T

HE OUTCOME of aortic valve replacement for severe aortic stenosis is worse in patients with impaired left ventricular function.1 The increasing prevalence of aortic stenosis2 and improved surgical techniques mandate continued interest in the determinants of surgical outcome in this high-risk group.

Left ventricular systolic dysfunction in patients with severe aortic stenosis may be caused by reversible afterload mismatch when increases in left ventricular pressure result in a decrease in stroke volume and ejection fraction.4 Alternatively, systolic dysfunction may be caused by the decreased contractility5 associated with myofiber loss and fibrosis due to hypertrophy or superimposed myocardial infarction.6 Postoperative improvement of ventricular performance in patients with severely diminished ejection fractions would indicate that systolic function is recoverable in these patients due to the unloading conferred by valve replacement. Such recovery in function should be curtailed by prior myocardial infarction. Previously, only small numbers of patients with severe left ventricular dysfunction who have undergone aortic valve replacement have been described,6,7 without defining the prevalence of previous infarction.8

The purpose of this study was to evaluate the outcome of aortic valve replacement for severe aortic stenosis in patients with profoundly impaired left ventricular systolic function, both with and without prior myocardial infarction.

RESULTS

PATIENT POPULATION

Patient characteristics are presented in Table 1. The average age of the 55 patients (17 women) with severe aortic stenosis and severe left ventricular dysfunction who underwent aortic valve re-
PATIENTS AND METHODS

From our echocardiography database, we identified all patients with severe left ventricular systolic dysfunction (ejection fraction ≤ 30%) and severe aortic stenosis (aortic valve area ≤ 0.75 cm²). There were 74 such patients seen between April 1989 and December 1996. Of these, 55 patients had had subsequent aortic valve replacement, and all of their echocardiograms performed less than 10 days before surgery were reviewed by us. All echocardiograms were technically adequate for interpretation and none were incomplete. Ejection fraction determinations were made by the area length method. The aortic valve area (AVA) was calculated by means of the continuity formula using flow velocity integrals (FVI) of the aorta and left ventricular outflow tract (LVOT) as follows:

\[ \text{AVA} = \frac{(\text{Area}_{\text{LVOT}})(\text{FVI}_{\text{LVOT}})}{\text{FVI}_{\text{aorta}}} \]

In the setting of atrial fibrillation, calculations from 3 to 5 cardiac cycles were averaged. Technically adequate 2-dimensional and Doppler echocardiographic studies documenting the above criteria for severe aortic stenosis and profoundly reduced left ventricular systolic function were available for a study group of 55 patients.

For each patient, the presence of significant regional wall motion abnormalities (defined as akinesis or dyskinesia) was recorded. The mean aortic pressure gradient was calculated by Doppler echocardiography using the optimal window (apical, suprasternal, or right parasternal) for the aortic valve envelope. The degree of mitral regurgitation was determined by Doppler color flow mapping.

All medical records of these patients were reviewed, including preoperative clinical information, cardiac catheterization hemodynamic data and coronary anatomy, and operative data. Preoperative coronary angiography had been performed in all patients. A history of prior myocardial infarction required confirmation by (1) electrocardiographic Q waves or (2) total or subtotal occlusion of a coronary artery with akinesis or dyskinesia of the corresponding myocardial segment. Q waves had to be more than 0.04 seconds in duration (patients with left ventricular hypertrophy and narrower Q waves were not considered to have prior infarction). In the case of left bundle branch block, the angiographic (and not the electrocardiographic) criteria would be used to define infarction. Coronary artery stenosis was defined as 70% or greater stenosis of a major epicardial coronary artery.

Postoperative echocardiograms performed without concomitant intravenous inotropic support were analyzed, including quantification of ejection fractions.

Postoperative follow-up included review of all subsequent hospital charts, questionnaires sent to referring physicians, and, when necessary, direct contact with the patients. The most recent assessment of each surviving patient’s New York Heart Association functional class was ascertained. Otherwise, the time and cause of death were established.

Statistical analysis was done with SPSS (PC-90) (SPSS Inc, Chicago, Ill) and Microsoft Excel (Macintosh v. 5.0a) (Microsoft, Redmond, Wash) software. Univariate analysis of categorical variables was done using the χ² test. Continuous variables were analyzed with a 2-tailed t test. For multivariate analysis, variables significantly associated with perioperative death on univariate analysis were entered into a model for logistic regression. Odds ratios with 95% confidence intervals were calculated for the multivariate analysis. The changes in postoperative ejection fractions in survivors and nonsurvivors were compared using a between-groups and a repeated-measures analysis of variance. P ≤ .05 was considered significant. Data are presented as mean ± SD.

PERIOPERATIVE MORTALITY AND PRIOR MYOCARDIAL INFARCTION

There were 10 perioperative deaths, for an overall operative mortality rate of 18%. However, in the 35 patients (64% of the entire group) who did not have a history of prior myocardial infarction, there was only 1 death (3%). In contrast, 9 of 20 patients with prior myocardial infarction died, for a perioperative mortality rate of 45% (P ≤ .001) (Table 2). The patients can also be subdivided into 3 groups (those without coronary artery disease or prior infarction, those with coronary disease but no prior myocardial infarction, and those with coronary disease and prior myocardial infarction). None of the 21 patients with coronary disease but no prior infarction died. There was only 1 death in the group without coronary disease and no prior infarction; all the remaining patients who died (9 patients) had prior infarction.

Those who died are compared with the surviving patients in Table 3. On univariate analysis, those who died had a significantly higher (worse) New York Heart Association functional class (3.8 ± 0.4 vs 3.3 ± 0.9; P = .006). They also had a significantly lower mean aortic gradient (32 ± 13 vs 43 ± 13 mm Hg; P = .01), although their ejec-
tion fractions and aortic valve areas were not significantly different from those of the survivors. Patient age and sex and the performance of concomitant coronary bypass and mitral valve surgery were not significantly associated with perioperative death. There was also no significant difference in the prevalence of mitral regurgitation in the group that did not survive surgery.

Atherosclerotic coronary artery disease as defined by coronary angiography (single-, double-, or triple-vessel disease) was not significantly associated with perioperative mortality. However, 9 (90%) of 10 patients who died had had a previous myocardial infarction, which was a significantly higher prevalence than that in those who did not die perioperatively (11 [24%] of 45 patients; P < .001). The ejection fractions and valve areas were similar in those with and without prior infarction (mean valve area and ejection fraction in patients with infarction were 0.47 ± 0.2 cm² and 24% ± 6%, vs 0.49 ± 0.2 cm² and 21% ± 6% in those without infarction, respectively). The mean aortic gradient was lower in patients with prior infarction (35 ± 13 mm Hg vs 44 ± 13 mm Hg; P = .01).

The factors significantly associated with perioperative death on univariate analysis (functional class, mean aortic gradient, and prior myocardial infarction) were entered into a model for stepwise logistic regression. This multivariate analysis showed that only prior myocardial infarction was independently associated with perioperative death, with an odds ratio of 14.9 (95% confidence interval, 2.4-92.1; P = .004). More infarctions involved the anterior wall in those who died (8 of 9; 89%) than in those who survived (5 of 10; 50%), although this trend did not reach statistical significance (P = .07).

**CLINICAL FOLLOW-UP**

The 45 surviving patients were followed up for 2 to 96 months (mean, 29 months). Those with previous myocardial infarction were compared with those without infarction (Table 2). There was no significant difference in age, ejection fraction, or aortic valve area. The 11 patients with prior infarction who survived the operation were followed up for an average of 24 months, and 3 patients (27%) had cardiac death (at 3, 6, and 70 months). Despite a longer mean follow-up of 31 months, there were no cardiac deaths among the 34 survivors of surgery without prior infarction, and this difference was highly significant (P = .002). There was a similar incidence of noncardiac death in both groups (18% vs 21%; P = .86). The total (perioperative plus follow-up, cardiac and noncardiac) mortality rate was significantly higher for the group with prior infarction (70%) than for the patients without prior infarction (23%) (P < .001) (Figure).

**ECHOCARDIOGRAPHIC FOLLOW-UP**

Postoperative echocardiograms were available for 38 (84%) of 45 survivors of surgery, and for 5 (50%) of 10 patients who had perioperative death. The follow-up time for the survivors ranged from 1 to 47 months (mean, 5.6 months). For those who had perioperative death, the postoperative ejection fraction increased compared with the preoperative ejection fraction in only 1 patient (20%); it did not
The natural history of nonsurgically treated severe aortic stenosis may be characterized by a long asymptomatic period. However, in one series the 5-year mortality rate in medically treated patients was 36%, and in another it was 60%. The average survival of patients once angina or syncope occurs is only 2 to 3 years, and if congestive heart failure supervenes, the survival time averages only 1.5 years. Therefore, the current standard of care is to replace the aortic valve once symptoms occur.

At our institution, a tertiary referral center, the operative mortality for aortic valve replacement for aortic stenosis was 5.2% of 363 patients who had surgery from 1993 to 1996. The general operative mortality for aortic valve replacement is reported to range from 2% to 8%. If overt left ventricular failure or a reduced ejection fraction is present, the mortality rate increases to 10% to 25%, and depends on the severity of cardiac dysfunction and the experience of the surgical team. Despite this high operative mortality, the average survival of patients who undergo aortic valve replacement for severe aortic stenosis associated with significant left ventricu-

The present study describes a severely symptomatic group of patients with severe aortic stenosis and profoundly abnormal left ventricular systolic function who have undergone aortic valve replacement. The mortality rate of 18% for the whole group is similar to that previously reported.

However, there is a striking dichotomy between those whose left ventricular dysfunction was associated with a previous myocardial infarction and those with no previous infarction. Although their ejection fractions were similar, their operative mortality was significantly different: 45% in the 20 patients with prior infarction and only 3% in the 35 patients with no prior infarction. In fact, the 3% mortality rate for aortic valve replacement in this group with an average ejection fraction of only 21% is half that of the entire group of 4377 patients who underwent cardiac surgery at our institution (both coronary bypass and valve surgery) from 1993 to 1996, which was 6%.

In a previous study, the presence of coronary artery disease was significantly associated with a reduced survival rate following aortic valve replacement. However, in the present study, coronary obstructive disease per se is not significantly related to operative risk. Prior myocardial infarction confers the markedly worse prognosis with operation. Perhaps the reason for this seeming discrepancy is that patients with and without prior infarction were grouped together in the previous study. In the present study, the patients with prior infarction had approximately the same valve areas and ejection fractions as those without infarction; however, the mean gradients were lower on average in those with prior infarction. This indicates a lower stroke volume in those with prior infarction, and lower cardiac output is known to decrease overall survival.

Although patients with anterior myocardial infarction are known to have a worse prognosis than those with inferior infarction, in our group there was no significant difference in the location of the myocardial infarction between those who survived (70% of infarctions were anterior) and those who did not (62% of infarctions were anterior).

Even in the absence of coronary artery disease, it is well known that left ventricular hypertrophy may result in subendocardial (non-Q wave) infarction; however, we have analyzed the impact of transmural (Q wave) infarction on survival. In the patients without Q wave infarction, who may well have had subendocardial damage, all but 1 survived surgery. They also had a significant recovery of left ventricular function. This was manifested by a doubling of the mean preoperative ejection fraction. In the group with prior transmural infarction, nearly half of whom did not survive the operation, the ejection fraction improved in only 1 of 5 in whom it was measurable. This was predictable, as the systolic dysfunction in these patients was at least in part due to permanent scarring rather than just reversible afterload mismatch.

In the follow-up period, the only cardiac deaths occurred in those with prior infarction. The cardiac mortality in this group was 27% vs 0% in those without prior infarction. This significantly higher cardiac mortality rate

![Graph showing survival rates for patients with prior myocardial infarction (MI) and patients without prior MI.](https://example.com/graph.png)
occurred despite the fact that those with infarction were followed up for a shorter period. However, the sample size is small, and the follow-up period was not prolonged.

These results confirm that it is possible to replace the aortic valve with an acceptably low mortality rate, and with recovery of left ventricular function, in some patients with severe aortic stenosis and severe left ventricular dysfunction. However, the results also identify a group of patients, those with prior myocardial infarction, whose operative risk is in the same order of magnitude as the mortality rate of patients who do not undergo surgery, whose long-term prognosis is poor. Screening for atherosclerotic heart disease appears to be appropriate in patients with aortic stenosis.

It is striking that of the 20 patients with severe aortic stenosis, severe left ventricular systolic dysfunction, and a prior infarction who underwent aortic valve replacement, only 6 (30%) were alive 2 years after surgery.

LIMITATIONS

This was a retrospective study, and as such was subject to the effects of selection bias. However, patients who have aortic valve replacement at our institution routinely undergo echocardiography before and after surgery. Furthermore, all echocardiograms were analyzed by us specifically for this study, with calculations of valve area, gradients, and ejection fractions performed in a masked fashion.

In this study, concomitant coronary bypass, preoperative mitral regurgitation, and mitral valve surgery were not significantly associated with perioperative death. However, the groups may not have been large enough to judge the impact of these factors.

The comparison of outcomes for the present patient group with those in patients treated medically is based solely on historical results (this was not a prospective trial of surgery vs medical management). Although the 2-year mortality of 70% in those with prior infarction is similar to or worse than the unoperated mortality in patients with severe aortic stenosis and heart failure, it is possible that the present study included patients with worse left ventricular dysfunction on average than did other reported groups. However, the strikingly low operative mortality (3%) in the group without prior infarction but with a mean ejection fraction of only 21% would seem to indicate that this particular selection bias (worse systolic function than was reported in previous studies) did not apply.

The severity of aortic stenosis was derived from the Doppler measurements and continuity equation. It is known that this may underestimate the valve area (overestimate the severity of stenosis) in patients with a low ejection fraction and low cardiac output, as such patients may not have fully opened valves due to a low stroke volume. The administration of dobutamine may increase the valve area in patients with this set of circumstances although in patients with truly fixed small valve areas, the valve area will not increase significantly with dobutamine (rather the gradient will increase). However, the valve areas of the patients in our study were very small (mean, 0.48 cm²; range, 0.17-0.73 cm²). No dobutamine was administered to our patients, although an increase in valve area on the order of magnitude reported with dobutamine in the literature (0.2 cm²) would still leave a severely reduced valve area in our cohort of patients. It is therefore likely that these patients had truly severe stenosis.

CONCLUSIONS AND CLINICAL IMPLICATIONS

The risk of aortic valve replacement in patients with severe aortic stenosis and severely reduced left ventricular systolic function is extremely high if the patients have had a prior myocardial infarction. This information should be factored into the risk-benefit analysis that is done preoperatively for these patients, and it may preclude operation for some.

Accepted for publication June 13, 1999.

Presented in part at the 70th Scientific Sessions of the American Heart Association, Orlando, Fla, November 11, 1997.

Reprints: Paul A. Tunick, MD, Noninvasive Cardiology Laboratory, NYU School of Medicine, 560 First Ave, New York, NY 10016 (e-mail: Paul.Tunick@med.nyu.edu).

REFERENCES


