Long-term Hemodynamic Assessment of the Porcine Heterograft in the Mitral Position

Late Development of Valvular Stenosis

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SUMMARY  We undertook a study of patients who had porcine mitral valves in place for more than 5 years and who had no clinical signs or symptoms suggestive of valve dysfunction. Of the first 54 patients who had porcine valves implanted in the mitral position, 18 were available for catheterization; all had a routine hemodynamic study postoperatively (mean 7 months) for comparison. Mean follow-up was 85 months (range 61–111 months). Compared with the early postoperative data, there was a significant increase in mean mitral valve gradient, from 5.9 ± 0.7 to 8.6 ± 0.7 mm Hg (p < 0.01), and a significant decrease in calculated mitral valve area, from 2.2 ± 0.2 to 1.7 ± 0.2 cm² (p < 0.01). Moreover, seven patients showed a decrease in valve area greater than 1.0 cm², five with valves in place for more than 80 months and only two of 11 patients with valves in place for 80 months or less (p < 0.05). We conclude that there is a significant incidence of hemodynamic deterioration of porcine heterografts in the mitral position for greater than 5 years, even in patients who are clinically stable.

THE GLUTARALDEHYDE-STABILIZED porcine heterograft is the valve of choice for mitral valve replacement in many centers. Numerous investigators have found acceptable hemodynamic performance of porcine heterografts in the mitral position when studied shortly after implantation.

However, there has been concern that the porcine heterograft would undergo the same fate as other bioprostheses: late deterioration. Pathologic studies have revealed extensive degenerative changes in porcine heterografts excised as early as 3 months. Lakier and co-workers reported a 7.8% late clinical failure rate of porcine mitral prostheses.

The present study was undertaken to investigate the incidence and mechanism of late deterioration of porcine heterografts in the mitral position. Specifically, we sought evidence of hemodynamic deterioration in patients whose porcine heterograft had been in position for at least 5 years and who were not felt by clinical criteria to have manifestations of prosthetic valve dysfunction. Determination of late deterioration was possible because almost all patients operated upon at the National Institutes of Health (NIH) have routine hemodynamic evaluation 6 months postoperatively, to which late hemodynamic data may be compared.

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Methods

Patients

Before October 1973, 54 patients had Hancock gluteraldehyde-stabilized porcine heterografts implanted in the mitral position, either alone or in combination with another prosthesis implanted in the tricuspid or aortic position (fig. 1). Minimum follow-up was, therefore, 5 years at the time of initiation of this study in October 1978. Seven patients died peroperatively, 14 died late postoperatively (including one due to documented valve failure), and three patients have been lost to follow-up. Four patients had their initial porcine heterograft removed because of valve failure at a mean of 74 months and one had it removed because of a perivalvular leak at 7 months. Six other patients either could not travel to the NIH or refused to participate in the study, and one patient had not had an early postoperative catheterization for comparison, so was eliminated from analysis. The remaining 18 patients form the basis of this study.

The study population consisted of 13 women and five men, ages 18–70 years (mean 53 years). The average duration from the time of operation to the late postoperative catheterization was 85 months (range 61–111 months). Seven patients had isolated mitral valve replacement, two had associated tricuspid valve replacement (both porcine), three had associated aortic valve replacement (all mechanical), two had triple-valve replacements (one porcine aortic and porcine tricuspid, and one mechanical aortic and porcine tricuspid valve), three had tricuspid annuloplasties, and one had an aortic annuloplasty. Of the porcine mitral valves, there were four 25-mm valves, one 27-mm valve, nine 29-mm valves and four 31-mm valves (table 1).
FIGURE 1. Breakdown of the 54 patients receiving porcine mitral valve replacements before October 1973. Of survivors, one patient is counted both as a valve failure and a late death.

TABLE 1. Hemodynamic Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Valve size (mm)</th>
<th>NYHA functional class</th>
<th>Follow-up (months)</th>
<th>PAW (mm Hg)</th>
<th>MVG (mm Hg)</th>
<th>CI (l/min)</th>
<th>MVA (cm²)</th>
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<tr>
<td>Mean ± SEM</td>
<td>85</td>
<td>18 ± 4</td>
<td>20 ± 5</td>
<td>5.9 ± 0.7</td>
<td>8.6 ± 0.7</td>
<td>2.8 ± 0.2</td>
<td>25 ± 0.2</td>
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Abbreviations: NYHA = New York Heart Association; PAW = pulmonary artery wedge pressure; MVG = mitral valve gradient; CI = cardiac index; MVA = mitral valve area.

All patients were believed by their referring physicians to be clinically stable; any patient who was catheterized because of clinical deterioration or suspicion of valve dysfunction was eliminated from this study. Thus, all 18 patients underwent totally elective catheterization after they gave informed consent.
Catheterization

All patients were studied in the postabsorptive state under mild sedation with either pentobarbital or diazepam. Digitalis and diuretics were continued up to the time of catheterization if clinically indicated. All patients had routine right-heart catheterization and either retrograde left-heart catheterization or a transthoracic left ventricular puncture with a #20-gauge needle. Pressures were measured with Statham transducers and recorded on an Electronics for Medicine recorder. Mean mitral valve gradient was determined by planimetry of simultaneously obtained pulmonary artery wedge and left ventricular pressure tracings. Cardiac output was measured by dye dilution using indocyanine green. Mitral valve area was computed according to the Gorlin formula.21 Thirteen patients undergoing retrograde left-heart catheterization had left ventriculogram cineangiograms in the right anterior oblique position using 0.5–1.0 ml/kg Renografin 76 (meglumine diatrizoate) after all pressure measurements had been made; mitral regurgitation was graded on a scale of 0 to 4. Results were compared with those of the early catheterization, which was obtained at a mean of 7 months postoperatively (range 4–17 months).

Statistics

Statistical analysis was performed using Wilcoxon’s rank-sum test and linear regression, where appropriate.

Results

Functional Status

Figure 2 shows the New York Heart Association functional class of the patients preoperatively and at the time of their early and late postoperative catheterizations. All but two were in either functional class I or II at the late catheterization. The two patients in functional class III had a gradual symptomatic deterioration since the early catheterization, but had stable symptoms for 2–3 years before the late study.

Hemodynamics

Hemodynamic data from the early and late postoperative catheterizations are shown in table 1. Mean changes of mitral valve gradient and mitral valve area for the total group were small but statistically significant. Mean mitral valve gradient increased from 5.9 ± 0.7 to 8.6 ± 0.7 mm Hg (p < 0.01) and mitral valve area fell from 2.2 ± 0.2 to 1.7 ± 0.2 cm² (p < 0.01) (figs. 3 and 4). More important, several patients demonstrated substantial hemodynamic deterioration. Thus, four of 18 patients (22%) had an increase in mean mitral valve gradient of at least 5 mm Hg and 39% (seven of 18) had a decrease in calculated valve area of at least 1.0 cm². Six of the seven patients with valve deterioration had 29-mm heterografts and one had a 31-mm heterograft. In the

11 patients with valves in place for 80 months or less, mitral valve gradient was unchanged, 8.4 ± 2.6 mm Hg early vs 8.4 ± 1.0 mm Hg late, as was mitral valve area, 2.0 ± 0.2 cm² early vs 2.0 ± 0.3 cm² late; however, in the seven patients with valves in place for more than 80 months, mitral valve gradient rose significantly, from 5.8 ± 0.5 mm Hg to 9.7 ± 0.9 mm Hg (p < 0.01), and mitral valve area fell from 2.4 ± 0.2 cm² to 1.3 ± 0.2 cm² (p < 0.05). The relationship between the change in mitral valve area and the time since the valve had been implanted is shown in figure 5. Although the correlation coefficient does not achieve statistical significance (r = −0.442, 0.05 < p < 0.10), five of seven patients with valves in place for longer than 80 months had a decrease in valve area of 1.0 cm² or more, compared with only two of 11 patients with valves in place for 80 months or less (p < 0.05 by rank-sum analysis). Of 13 patients who had left ventricular cineangiograms, nine had no mitral regurgitation and three had, at most, 1+. Patient 9, who had 2+ mitral regurgitation, had a similar degree at the early postoperative catheterization. None of the other five patients had a murmur suggestive of mitral regurgitation. Patient 17 had developed severe aortic regurgitation, which had been only mild at the early postoperative study.

Discussion

Over the past 10 years the glutaldehyde-stabilized porcine heterograft has become widely used for mitral valve replacement. The central flow characteristics
and low thrombogenicity of the porcine heterograft provide theoretical advantages over existing mechanical prostheses. However, the poor performance of previous tissue valves, coupled with reports of porcine valve failure due to degeneration of the valve leaflets have raised doubts about the long-term durability of the porcine prosthesis.

The present investigation was undertaken to assess changes in the hemodynamic characteristics of the porcine heterograft over a prolonged period of time. Our study is unique not only because it provides the longest hemodynamic follow-up reported to date, but also because we could compare these late hemodynamic findings to those obtained in the same patients shortly after implantation of the valve. Moreover, the patients studied were not selected because of any suspicion of valve dysfunction.

In a mean interval of 77 months between the early and late postoperative catheterizations, the transvalvular gradient increased significantly and the calculated orifice size decreased significantly. More than one-third of the patients had a marked decrease (> 1.0 cm) in valve area. This progressive prosthetic valve stenosis was not accompanied by evidence of valvular insufficiency in any patient.

Several factors may contribute to progressive prosthetic valve stenosis. Patient 18 has since come to operation. The valve removed had thin, delicate leaflets; the stenosis was caused by "creep" of the valve struts, narrowing the secondary valve orifice. Other investigators have shown pathologic evidence of alterations in the collagen architecture of the valve leaflets, focal calcification of the valve leaflets, and immobilization of the valve by thrombus; these factors could also explain our hemodynamic findings.

Although only 54 patients were followed for over 5 years, and only eight were studied late postoper-
Atively, there was a relationship between the time the valve was in place and the tendency to develop valve stenosis. Thus, all valves in place for longer than 98 months, and five of seven valves in place for longer than 80 months, had decreases in valve area of 1.0 cm² or more (fig. 5). A similar decrease in valve area was observed in only two of 11 valves in place for 60–80 months. These differences could be due either to a time threshold required for stenosis to develop or to difficulties with valve manufacture or surgical technique used at the time of the initial experience with this valve; our data do not allow us to distinguish between these possibilities.

The present study concentrates on hemodynamic changes in patients with stable symptoms. We have no way of knowing if the changes we have found will become clinically meaningful, and if so, when. Furthermore, our data focus on the hemodynamic performance of the porcine heterograft and are not intended to address the frequently discussed advantages of the porcine heterograft, namely the relative freedom from thromboembolic and infectious complications.¹ ² ³ ⁴ ⁵ ⁶ ⁷ ⁸ ⁹ ¹⁰ ¹¹ ¹² ¹³ ¹⁴ ¹⁵ ¹⁶ ¹⁷ ¹⁸ ¹⁹ ²⁰ ²¹ ²² ²³ ²⁴ ²⁵ ²⁶ ²⁷ ²⁸ ²⁹ ³⁰ ³¹ ³² ³³ ³⁴ ³⁵ ³⁶ ³⁷ ³⁸ ³⁹ ⁴⁰ ⁴¹ ⁴² ⁴³ ⁴⁴ ⁴⁵ ⁴⁶ ⁴⁷ ⁴⁸ ⁴⁹ ⁵⁰ ⁵¹ ⁵² ⁵³ ⁵⁴ ⁵⁵ ⁵⁶ ⁵⁷ ⁵⁸ ⁵⁹ ⁶⁰ ⁶¹ ⁶² ⁶³ ⁶⁴ ⁶⁵ ⁶⁶ ⁶⁷ ⁶⁸ ⁶⁹ ⁷⁰ ⁷¹ ⁷² ⁷³ ⁷⁴ ⁷⁵ ⁷⁶ ⁷⁷ ⁷⁸ ⁷⁹ ⁸⁰ ⁸¹ ⁸² ⁸³ ⁸⁴ ⁸⁵ ⁸⁶ ⁸⁷ ⁸⁸ ⁸⁹ ⁹⁰ ⁹¹ ⁹² ⁹³ ⁹⁴ ⁹⁵ ⁹⁶ ⁹⁷ ⁹⁸ ⁹⁹ ¹⁰⁰ ¹⁰¹ ¹⁰² ¹⁰³

In conclusion, we have shown that a considerable percentage of porcine mitral valves develop progressive stenosis before patients become symptomatic. Whether this is caused by initial problems with valve manufacture or implantation or is an intrinsic feature of the valve itself has not been determined. In either case, if a patient with a porcine prosthesis does become increasingly symptomatic, he or she should be investigated for the possibility of valve dysfunction as a cause. Finally, this potential drawback of the porcine heterograft must be weighed carefully against its potential advantages when selecting a prosthetic valve.

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Atrial Septal Defect in Patients Ages 60 Years or Older: Operative Results and Long-term Postoperative Follow-up

MARTIN G. ST. JOHN SUTTON, M.B., ABDUL J. TAJIK, M.D., AND DWIGHT C. McGOON, M.D.

SUMMARY Between 1955 and 1977, 66 patients ages 60 years or older underwent operative closure of secundum atrial septal defect. Of these, 56 (85%) were catheterized preoperatively. The 56 patients were divided into three groups to assess the effects of pulmonary hypertension on operative mortality, symptoms and longevity. The 17 group 1 patients had peak systolic pulmonary artery pressures (PAPs) of less than 40 mm Hg; the 21 group 2 patients had PAPs of 40–60 mm Hg; and the 18 group 3 patients had PAPs of more than 60 mm Hg. Among the three groups, there was no significant difference in OP/Qs, right or left atrial pressures, right or left ventricular end-diastolic pressures and Qs, although pulmonary vascular resistance was significantly higher (p < 0.01) in group 3 than in group 1. Four patients died, yielding an operative mortality of 6%. All four patients had undergone additional operative procedures. Operative mortality was unrelated to preoperative symptom class, PAP or pulmonary vascular resistance. Forty-seven patients were followed up for 2–20 years (mean 6.6 years), and of these, 41 (87%) improved by at least one functional class. Symptomatic benefit occurred in all groups, regardless of preoperative PAP, pulmonary vascular resistance or functional class. Actuarial survival curves showed that longevity at 5 and 10 years postoperatively was significantly increased (p < 0.01) for patients with atrial septal defect treated surgically compared with that predicted for age-matched patients treated medically.

ATRIAL SEPTAL DEFECT is one of the most common forms of congenital heart disease in adults.1 The few long-term survival studies of patients with atrial septal defect treated medically have indicated that the average age at death is 39–49 years.2,4 Although survival into the eighth and ninth decades has been documented,5,6 there is a yearly attrition rate of 5–10% in patients more than 40 years old who are treated medically.7,10 Surgical closure of atrial septal defects in children and young adults with large left-to-right shunts can be recommended with confidence because surgical mortality is low,11 the frequent debilitating symptoms that develop in the third to fifth decades of life may be obviated,11–14 and life expectancy may return to normal. In contrast, the efficacy of surgical as opposed to medical treatment in elderly patients (60 years of age or older) is still debated. Surgical experience is limited and mortality figures vary and are increased by the higher incidence of pulmonary hypertension and heart failure15–18 and by the necessity of associated atrioventricular valve and coronary artery operations. In addition, the likelihood of long-term symptomatic improvement and the effect on life expectancy after surgery in this age group are unknown.

We reviewed a large series of patients with atrial septal defect who were 60 years of age or older. We investigated the effects of preoperative symptom class, preoperative hemodynamics, associated disease, and atrial fibrillation on surgical mortality, postoperative symptom class and longevity.

Materials and Methods

Between January 1955 and December 1977, 72 patients who were 60 years of age or older had the diagnosis of atrial septal defect established at the Mayo Clinic. The oldest patient was 83 years old. Of the 72 patients, 37 (51%) had the condition diagnosed between 1971 and 1977. The diagnosis of atrial septal defect was established by cardiac catheterization in 62 patients (82%) and by operation in 66 patients (92%).

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