mitral valve replacement in children with rheumatic heart disease

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SUMMARY We followed 110 children, ages 6–15 years, who had undergone mitral valve replacement for rheumatic heart disease. Group 1 consisted of 74 patients with mechanical prostheses and a mean follow-up of 6.3 years. Group 2 consisted of 13 patients with porcine xenografts followed for 3.3 years. Group 3 included 23 children with dura mater bioprostheses and a mean follow-up of 1.9 years. The clinical evolution of each group was assessed according to the New York Heart Association criteria. The incidence of complications also was determined. Ninety-five percent confidence limits were calculated for all proportions from binomial distribution; lack of superposition was adopted as the criterion of significance.

In group 1, thromboembolic complications occurred in 1.7% per patient/year, infective endocarditis in 0.85% per patient/year, valvular dysfunction in 0.85% per patient/year, and death in 1.3% per patient/year. Group 2 patients had no thromboembolic complications; infective endocarditis occurred in 2.3% per patient/year, dysfunction in 16.3% per patient/year, and death in 14% per patient/year. Seven patients with Hancock porcine xenografts presented valve obstruction, and four cases that were studied anatomically showed fibrocalcific obstruction of the prosthesis. In group 3, thromboembolic episodes occurred in 2.3% per patient/year, dysfunction in 6.8% per patient/year, and death in 2.3% per patient/year. Calcific obstruction of the prosthesis was observed in one patient at necropsy.

We conclude that mechanical prostheses offer the best results in children. With adequate anticoagulation, thromboembolism is of little significance, the incidence of infective endocarditis is comparable to that reported for bioprostheses, dysfunction is less frequent, and the long-term mortality rate is lower.

VALVULAR PROSTHESES have been used to treat congenital or acquired heart defects.1-8 Recently, long-term follow-up studies of bioprostheses in children have shown early dysfunction secondary to severe calcification.9-18 In this report, we present our experience with mitral valve replacement in children with rheumatic heart disease and describe the long-term follow-up of our patients with implanted mechanical or biologic prostheses.

Materials and Methods

From November 1964 to April 1980, 110 children, ages 6–15 years, were followed for at least 1.5 years after implantation of a mitral prosthesis. These patients were divided into three groups according to the type of prosthesis used: mechanical (Starr-Edwards), porcine (Hancock xenograft) and dura mater valves. The latter were preserved in glycerol.

The three groups of patients were comparable before surgery. The criteria of the New York Heart Association (NYHA) were used to evaluate all the patients between the second and the sixth postoperative months. The same criteria were used for complications in all three groups. The incidence of complications such as thromboembolism, infective endocarditis, prosthetic dysfunction and death was determined at the end of the follow-up. A transient or permanent neurologic deficit was considered a thromboembolic episode.

After bioprostheses became available, the selection of the type of valve was done randomly, completely disregarding age, sex, and clinical and hemodynamic features. In seven patients, who were in NYHA functional class III preoperatively, the use of bioprostheses was decided upon because of difficulties anticipated in following anticoagulant therapy.

Since 1964, preoperative and long-term follow-up assessments were carried out by the staff physicians at the outpatient clinic of the Department of Pediatric Cardiology. All patients with an implanted mechanical valve received anticoagulant therapy with aceno-
counadlan; therapeutic levels were 20–30% of our normal standard. In the other two groups, anticoagulant therapy was not administered routinely.

Ninety-five percent confidence limits (CLs) were calculated for all proportions from binomial distribution, and lack of superposition was adopted as criterion of significance. This method is more accurate than the chi-square test for small samples.*

Group 1 consisted of 74 patients (49 females and 25 males) with mechanical prostheses who were followed for a mean of 6.3 years (range 1.8–15.5 years). Ages ranged from 6–15 years (mean 13.2 years). Sixty-seven patients had mitral regurgitation and seven had mitral stenosis.

Group 2 consisted of 13 patients (eight females and five males) who had porcine bioprostheses and were followed for a mean of 3.3 years (range 2.5–4.5 years). The patients were 8–15 years old (mean 12.3 years). Twelve patients had mitral regurgitation and one patient had mitral stenosis.

Group 3 consisted of 23 children (13 females and 10 males) with dura mater bioprostheses who were followed for a mean of 1.9 years (range 1.5–5.3 years). The patients ranged in age from 8–15 years (mean 13.1 years). Twenty-two patients had mitral regurgitation and one patient had mitral stenosis.

**Results**

**Group 1**

Before valvular replacement, 13 (17.6%; 95% CL 9.7–28.7%) of the 74 patients in group 1 were in NYHA functional class II; 56 (75.7%; 95% CL 64.3–84.9%) were in class III, and five (6.7%; 95% CL 2.2–15%) were in class IV. Good clinical improvement was noted after surgery: 11 patients (14.8%; 95% CL 7.6–25%) are asymptomatic, 38 (51.4%; 95% CL 39.4–63.1%) are in functional class I; 19 (25.7%; 95% CL 16.2–37.1%) are in class II and six (8.1%; 95% CL 3–16.8%) are in class III (fig. 1).

Twenty-seven patients underwent cardiac catheterization 1–4 years after surgery, 21 for evaluation of the surgical results and six for determination of the type of dysfunction. The mean pulmonary arterial systolic pressure was 57 mm Hg before operation and decreased to 33 mm Hg after surgery ($p \leq 0.001$). The mean pulmonary arterial wedge pressure decreased from 20.8 to 12.1 mm Hg ($p \leq 0.05$) (fig. 2). Each patient showed reduction in both pressures after surgery.

Long-term follow-up showed the following complications: thromboembolic episodes, 1.7% per patient/year; infective endocarditis, 0.85% per patient/year; and death, 1.3% per patient/year. There was massive thrombosis of the prosthesis in one patient; in the other seven the embolic accidents left no sequelae. All but one of these patients had therapeutic levels of anticoagulant during the episodes of embolization. None of the patients with thromboembolic phenomena was in atrial fibrillation. Four patients had infective endocarditis 9 months to 5 years after surgery. Three of them died, 9, 24 and 60 months after valve replacement; the fourth showed clinical improvement after treatment. Four patients had valve dysfunction. One died with massive thrombotic occlusion of the prosthesis 8 months after surgery; he was not adequately anticoagulated. One patient with moderate dysfunction had a paravalvular leak that

**Figure 1.** Representative curves of the 95% confidence limits for binomial distribution in group 1. The horizontal axis represents New York Heart Association functional classes. Most of the patients were in functional classes III and IV preoperatively. After operation, the majority of patients were asymptomatic or were in functional class I.

**Figure 2.** Pre- and postoperative pulmonary artery systolic pressure (PASP) and pulmonary arterial wedge pressure (PAWP) in group 1. The 95% confidence limits were calculated (corresponding to $p \leq 0.05$ by t test). Statistical differences between the means of the pressures before and after surgery are shown.
was repaired using the same prosthesis. In the other two patients, discrete paravalvular regurgitation was demonstrated by angiography. Both had clinical improvement (from class III to class I) and their pulmonary wedge pressure was normal.

Six patients died: one of massive thrombosis of the prosthesis, three of infective endocarditis and one of progressive heart failure without anatomic evidence of valvular dysfunction or acute rheumatic fever. The cause of death in one patient was unknown.

Group 2

In group 2, 12 (92.7%; 95% CL 63.9–99.8%) of the 13 patients were in NYHA class III and one (7.7%; 95% CL 0.2–36%) was in class IV. Follow-up studies showed that four (30.8%; 95% CL 9.1–61.4%) changed to class I, eight (61.5%; 95% CL 31.5–86.1%) to class II and one (7.7%; 95% CL 0.2–36%) to class III (fig. 3).

There were no thromboembolic episodes. The rates of other complications were: infective endocarditis, 2.3% per patient/year; valvular dysfunction, 16.3% per patient/year; and death, 14% per patient/year.

One patient had infective endocarditis confirmed by postmortem study. Seven patients had valve dysfunc-

![Figure 3](https://example.com/fig3.png)

**Figure 3.** Representative curves of the 95% confidence limits for binomial distribution in group 2. The horizontal axis represents the New York Heart Association functional classes. Before surgery most of the patients were in classes III and IV. The postoperative data show that most of the children are in functional classes I and II. The large values of the confidence limits are due to the small number of patients.

![Figure 4](https://example.com/fig4.png)

**Figure 4.** Representative curves of the 95% confidence limits for binomial distribution in group 3. The horizontal axis represents the New York Heart Association functional classes. In the preoperative period most of the patients were in classes II and III. After surgery most of the children were asymptomatic or in functional class I.

One of these underwent reoperation in which the porcine valve was replaced by a Björk-Shiley prosthesis 31 months after the initial operation. Anatomic study of the resected xenograft revealed fibrocalcific degeneration and severe obstruction. The patient remains in excellent condition. The other six patients were severely ill and died in congestive heart failure with pulmonary venocapillary hypertension. In three of these patients, the postmortem studies also showed extensive fibrocalcific degeneration and stenosis of the porcine prostheses.

Six patients died, five of valvular dysfunction and one of infective endocarditis.

Group 3

Before surgery five (21.7%; 95% CL 7.4–43.7%) of the 23 patients were in class II; 17 (74%; 95% CL 51.5–89.7%) were in class III and one (4.3%; 95% CL 0.1–22%) was in class IV. After operation, one (4.3%; 95% CL 0.1–22%) is asymptomatic; 14 (60.8%; 95% CL 38.5–80.2%) are in class I; seven (30.4%; 95% CL 13.2–53%) are in class II and one (4.3%; 95% CL 0.1–22%) is in class IV (fig. 4).

No patient had infective endocarditis. Systemic thromboembolism occurred in 2.3% per patient/year, valvular dysfunction in 6.8% per patient/year, and death in 2.3% per patient/year.
The only patient who had a thromboembolic accident was in atrial fibrillation and was receiving anticoagulants. Three patients had valvular dysfunction. One was reoperated on 4 months after surgery and the bioprosthesis was replaced by another dura mater valve. The leaflets of the removed prosthesis did not coapt properly. Another patient with valvular regurgitation has been treated medically. The third patient with valvular dysfunction presented with severe heart failure, died in pulmonary edema, and at necropsy was found to have calcific obstruction of the prosthesis. One month before death she was asymptomatic.

The functional class of each patient was assessed clinically 2-6 months postoperatively; functional class did not change during long-term follow-up.

There was no significant difference between the three groups in the incidences of thromboembolism and infective endocarditis, as shown by the wide superposition of CLs. The incidences of dysfunction and mortality did not differ significantly between the mechanical and dura mater groups, or between the dura mater and porcine groups, as shown by the superposition of their respective CLs. In contrast, there were significant differences (p ≤ 0.05) between mechanical and porcine groups for both mortality and dysfunction (fig. 5).

**Discussion**

It is widely accepted that rheumatic mitral valve disease in children can be severe enough to require valvular replacement. Initially, however, there was reluctance to use these surgical procedures in the pediatric age group because of the implications of high operative mortality, elevated rate of infective endocarditis, higher risks due to anticoagulant therapy and the possibility of thromboembolic complications.2, 4, 7, 8, 12, 20

Although anticoagulant therapy was important in reducing the early mortality rate, thromboembolic manifestations can occur despite adequate anticoagulant therapy.2, 7, 21 This has been the major criticism for the use of mechanical prostheses in children. Our long-term results are excellent because only one patient had massive thrombosis of the prosthesis, which occurred in the absence of adequate anticoagulant therapy. The other patients did not have sequelae to thromboembolic manifestations.

The above-mentioned objections to the use of mechanical valves in children were resolved with the advent of bioprostheses. Although there is little experience with bioprostheses in children, immediate results suggest that they may be used with little risk of thromboembolism and do not require anticoagulant therapy.7, 8, 12, 13, 21

The long-term follow-up of children with bioprostheses contrasts with that in adults.9, 13-16, 22 In adult patients who received porcine xenografts and were followed for more than 7 years, a low incidence of calcification has been reported.22-30 Nevertheless, in the pediatric age group the major problem with biologic prostheses is fibrocalcific obstruction that may lead to valvular replacement within a short period of time.12-16 This complication can occur without auscultatory signs of valvular dysfunction and the diagnosis is made on the basis of rapidly progressing pulmonary venocapillary hypertension. These findings can be explained by the presence of decreased flow through the bioprosthesis.18

Seven of our patients with porcine xenografts had sudden onset of severe pulmonary venocapillary hypertension. In four of these children who did not have infective endocarditis or altered calcium metabolism, the anatomic study showed fibrocalcific obstruction. Considering recent reports15-18 and the follow-up of our cases, we concluded that the dysfunction was secondary to fibrocalcific obstruction.

Although the follow-up time of our patients with dura mater bioprostheses is shorter than that of patients with porcine xenografts, similar long-term complications in children are expected in both types of valves. One patient with a dura mater prosthesis died with symptoms of cardiac decompensation in the presence of pulmonary venocapillary hypertension and congestive heart failure. One child who underwent aortic and mitral valves replacement, not included in our series, showed calcification of the dura mater mitral bioprosthesis 20 months after surgery. Gross examination of the aortic dura mater valve during operation did not show alterations (Barragan R: personal communication).

Observations to be published in detail elsewhere showed that gross anatomic, histologic and ultrastructural changes were similar in Hancock valves and glycerol-treated dura mater valves recovered from our patients at necropsy.

These changes were qualitatively similar to those
previously described.14, 15, 31-33 In the present study, both types of valves showed degradation of collagen bundles and calcification close to the annulus on the inflow surface of the valves and along the suture lines to the struts on the outflow side of the cusps. Calcification of the valves was not accompanied by any cellular reaction or thrombus formation but was associated with degenerated tissue, which suggested dystrophic calcification (fig. 6).

These findings contrast with the characteristics of mechanical valve dysfunction in the four patients who had these complications. One of them had dysfunction due to thrombosis of the mechanical valve in the absence of proper anticoagulant therapy; the other three had paravalvular leaks (one of moderate degree that was surgically treated using the same prosthesis), and the other two, without treatment, are in NYHA class I.

Despite a good clinical improvement 2-6 months postoperatively, the long-term follow-up results were different in the three groups.

No statistically significant differences were observed for thromboembolism and infective endocarditis in the three groups. The incidences of dysfunction and death in patients with porcine or with dura mater valves were not significantly different. The absence of statistically significant differences in dysfunction and mortality between patients with mechanical valves and dura mater valves could change with a longer follow-up time for the patients with dura mater valves, because as was reported, fibrocalcific obstruction of the dura mater bioprosthesis was the most important complication in a large series.9 There were significant differences in dysfunction and mortality in patients with mechanical valves and porcine valves.

We conclude from our results that mechanical prostheses offer better long-term results than do bioprostheses in mitral valvular replacement in children with rheumatic heart disease. With adequate anticoagulation, thromboembolism is of little significance, the incidence of infective endocarditis is comparable to that for bioprostheses,24-30 dysfunction is less frequent and the long-term mortality rate is lower.
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