SURGERY FOR ACQUIRED HEART DISEASE

RESULTS OF ALLOGRAFT AORTIC VALVE REPLACEMENT FOR COMPLEX ENDOCARDITIS

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Methods: Between November 1985 and July 1995, 36 patients underwent allograft aortic valve replacement for endocarditis. The mean age of the 29 men and seven women was 53 years (range 25 to 79 years). Previous procedures included mechanical ($n = 9$), bioprosthetic ($n = 5$), and allograft ($n = 2$) aortic valve replacement, aortic valvotomy ($n = 1$), and orthotopic heart transplantation ($n = 1$). Infecting organisms were *Staphylococcus* and *Streptococcus* species in 69% of patients and fungi in 6%. Intraoperative findings demonstrated valvular vegetations ($n = 25$), annular abscesses ($n = 25$), and cusp destruction ($n = 13$). Complex reconstruction of the aortic anulus was required in 25 patients, and associated procedures included mitral valve repair ($n = 2$), mitral valve replacement ($n = 3$), coronary artery bypass grafting ($n = 8$), repair of ventricular septal defect ($n = 4$), left ventricular aneurysmectomy ($n = 1$), and repair of atrial septal defect ($n = 1$). Allograft valve insertion was performed by the scalloped technique in seven, intraaortic cylinder technique in 19, and allograft aortic root replacement in 10. **Results:** Follow-up was 100% complete at a mean of 2.6 ± 2.8 years after valve replacement. Operative mortality was 13.8%. Complications included low cardiac output ($n = 10$), bleeding ($n = 2$), myocardial infarction ($n = 1$), stroke ($n = 1$), renal insufficiency ($n = 2$), respiratory insufficiency ($n = 3$), and heart block ($n = 8$). Late echocardiogram (mean 2.6 ± 1.8 years) demonstrated grade III/IV aortic regurgitation in five patients. There were seven late deaths (five cardiac, not valve-related; two noncardiac). No patient has had recurrence of endocarditis. Actuarial survival at 5 years was $53.1\% \pm 11.5\%$. Univariate analysis demonstrated prosthetic valve endocarditis to adversely affect late survival ($p = 0.04$). Cumulative risk of reoperation at 5 years was $8.0\% \pm 5.6\%$. **Conclusion:** Allograft aortic valve replacement facilitated reconstruction of complex aortic valve endocarditis with a low reoperation rate and no recurrent endocarditis in this series. (J Thorac Cardiovasc Surg 1997;113:285-91)

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Despite advances in the ability to diagnose and medically treat both native and prosthetic aortic valve endocarditis, operation is often indicated before complete resolution of active infection. At the same time that the incidence of rheumatic valvular disease is decreasing in the United States, the incidence of infective endocarditis is increasing. This may be due to an aging population with associated prevalence of structural valvular abnormalities, increasing numbers of patients with prosthetic heart valves or indwelling catheter/pacing systems (or both), the enlarging population of immunosuppressed or immunodeficient patients, and the large

Table I. Patient characteristics

	NVE (n = 20)	PVE (n = 16)	p Value
Age (yr)	51 ± 13	57 ± 17	0.2
Age range (yr)	28 to 79	25 to 78	
Male	16 (80%)	13 (81%)	1.0
AR	13 (65%)	14 (88%)*	
AS	1 (5%)	0	0.2
Mixed AS/AR	6 (40%)	2 (13%)	
Preop. EF	0.63 ± 0.06	0.56 ± 0.1	0.03
NYHA class III/IV	14 (70%)	15 (94%)	0.1

Age is presented as mean ± standard deviation and expressed in years. NVE, Native valve endocarditis; PVE, prosthetic valve endocarditis; AR, aortic regurgitation; AS, aortic stenosis; EF, ejection fraction; NYHA, New York Heart Association.

*Aortic regurgitation with prosthetic valve endocarditis refers to perivalvular leak.

Table II. Causative organisms

	NVE (n = 20)	PVE (n = 16)
<i>Staphylococcus</i> *	7 (35%)	11 (69%)
<i>Streptococcus</i> *	10 (50%)	3 (19%)
<i>Corynebacterium</i>	0	1 (6%)
<i>Aspergillus</i>	1 (5%)	0
<i>Candida albicans</i>	0	1 (6%)
<i>Haemophilus influenzae</i>	1 (5%)	0
Culture negative	1 (5%)	0

* *Staphylococcus* and *Streptococcus* species in native versus prosthetic valve endocarditis ($p = 0.07$).

number of intravenous drug abusers. Because operation is frequently required in the presence of active infection for uncontrolled sepsis, congestive heart failure, septic emboli, and prosthetic valve or fungal endocarditis, the surgeon may be confronted with extensive annular destruction and perivalvular ring abscesses that complicate insertion of a standard aortic valve prosthesis. Numerous operative techniques have been reported to manage these challenging problems, including aortic valve replacement (AVR) with an allograft, which is said to have a lower rate of subsequent infection than mechanical prostheses or other bioprostheses.¹⁻¹¹ To determine the early outcome of allograft AVR for complex infections, we reviewed our recent experience with allografts for aortic valve endocarditis.

Patients and methods

Patient characteristics. Between November 1985 and August 1995, 2699 patients underwent AVR at the Mayo Clinic. One hundred seventeen patients underwent AVR for active endocarditis. In 57 of these a mechanical prosthesis was used, in 24 a heterograft bioprosthesis, and in 36 a cryopreserved allograft aortic valve. Valve choice

Table III. Prior aortic valve procedures (n = 17)

	No.
Mechanical AVR*	7
Mechanical AVR (Konno)*	2
Bioprosthetic AVR	5
Allograft AVR	2
Aortic valvotomy	1

AVR, Aortic valve replacement.

*Konno-Rastan aortoventriculoplasty.

Table IV. Operative procedures

	NVE (n = 20)	PVE (n = 16)
Isolated allograft AVR*	9	4
Allograft AVR		
+ CABG†	4	4
+ MV repair	1	1
+ MVR	1	2
+ LV aneurysmectomy	1	0
+ ASD repair	1	0
+ VSD repair	0	4
+ RVOT repair	0	1
+ LV perforation repair	1	0
+ Root enlargement	4	5
Allograft AVR (scallop)‡	5	2
Allograft AVR (cylinder)	15	4
Allograft AVR (root)	0	10

NVE, Native valve endocarditis; PVE, prosthetic valve endocarditis; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; MV, mitral valve; MVR, mitral valve replacement; LV, left ventricular; ASD, atrial septal defect; VSD, ventricular septal defect; RVOT, right ventricular outflow tract.

*Isolated vs associated procedure between NVE and PVE ($p = 0.03$).

†Patients may have had a combination of the above listed associated procedures.

‡Allograft implantation techniques in NVE vs PVE ($p = 0.001$).

was dependent on the local anatomy, the amount of tissue destruction, and the surgeon performing the operation. This review focuses on the patients having allograft AVR.

Patient characteristics are summarized in Table I and causative organisms are listed in Table II. All patients received antibiotic therapy selected on the basis of culture results. The single patient with a "negative" blood culture in the preoperative period had received a renal transplant; he had valvular vegetations and gross evidence of infection at the time of operation despite the inability to culture an organism.

The primary indication for AVR was persistent sepsis in 7 (19%) patients, congestive heart failure in 23 (64%), peripheral embolization in 3 (8%), coronary artery embolization in 1 (3%), and fungal endocarditis in 2 (6%) patients. Heart block was noted before the operation in 4 patients with prosthetic valve endocarditis and 1 patient with native valve endocarditis and necessitated temporary transvenous pacing. Five patients were operated on urgently because of acute hemodynamic collapse and cardiogenic shock.

Previous aortic valve operations ($n = 17$) are shown in Table III. At the time of the current operation, allograft

Fig. 1. Actuarial patient survival after allograft AVR for complex endocarditis. *Expected*, Survival for an age-matched population; *NVE*, native valve endocarditis; *PVE*, prosthetic valve endocarditis. Absolute numbers of patients surviving are indicated at yearly intervals.

AVR was the second AVR in 11 patients, the third AVR in 5 patients, the fourth AVR in 2 patients, and the fifth AVR in 1 patient. An additional patient had undergone previous orthotopic heart transplantation. Operations performed are shown in Table IV.

Echocardiography. Preoperative Doppler echocardiographic examination showed aortic regurgitation in 27, aortic stenosis in 1, and mixed stenosis/regurgitation in 8 patients. Annular abscesses with or without valvular vegetations were noted in 25 patients and cusp perforation or destruction in 13 patients. Preoperative left ventricular ejection fraction by echocardiography ranged from 0.23 to 0.75 (mean 0.61). Since 1988, intraoperative transesophageal echocardiography has been used to assess operative results. All surviving patients underwent echocardiographic assessment of their allograft aortic valve before hospital dismissal. These studies were repeated at approximately 1-year intervals and the most recent echocardiogram available was used for late follow-up.

Operative findings and techniques. Standard cardiopulmonary bypass techniques were used. The duration of cardiopulmonary bypass ranged from 78 to 346 minutes (mean 170 minutes) and the period of aortic occlusion ranged from 52 to 194 minutes (mean 118 minutes). Intermittent periods of circulatory arrest were required in 2 patients. Operative findings demonstrated valvular vegetations in 25 (69%) patients, annular abscesses in 25 (69%), and cusp abnormalities in 13 (36%). Left ventricular-aortic discontinuity was noted in 4 (20%) patients with native valve endocarditis and in 11 (69%) patients with prosthetic valve endocarditis. Allograft AVR insertion facilitated mitral valve reconstruction in 6 (17%) patients and ventricular septal repair in 4 (11%) patients; in these patients the anterior leaflet of the allograft was used to repair defects in the recipient mitral valve or in the septum. Two (6%) other patients required separate mitral

Table V. Early complications of allograft AVR for endocarditis*

	NVE (n = 20)	PVE (n = 16)
Bleeding (exploration)	1 (5%)	1 (6.3%)
Low cardiac output	2 (10%)	8 (50%)
Myocardial infarction	0	1 (6.3%)
Heart block†	0	5 (31.3%)
Stroke	1 (5%)	0
Renal insufficiency	0	2 (12.5%)
Respiratory insufficiency	0	3 (18.8%)

NVE, Native valve endocarditis; PVE, prosthetic valve endocarditis.

*Overall complications in native versus prosthetic valve endocarditis ($p = 0.049$).

†Necessitating placement of a permanent transvenous pacemaker.

valve annuloplasty. Two (6%) patients underwent pericardial repair in addition to the use of the allograft: one patient with a defect in the dome of the left atrium and the other patient with a defect in the right ventricular outflow tract. Seven (19%) patients required intraaortic balloon support after cardiopulmonary bypass.

The techniques of allograft aortic valve implantation were dictated by the pathologic findings at operation. In general, all infected and necrotic tissue was débrided and the anulus was treated locally with phenol. Three allograft insertion methods have been used: the scalloped technique (partial or complete removal of allograft aortic valve sinuses) ($n = 7$; 19%), the cylinder technique (retaining the allograft aortic sinuses) within the native aortic root ($n = 19$; 53%), and allograft aortic root replacement ($n = 10$; 28%). Mean size of the allograft aortic valve was 22 mm (internal diameter)(range 20 to 28 mm). The cryopreserved aortic allografts used in this study were supplied by Cryolife Cardiovascular, Inc.,

Fig. 2. Cumulative risk of reoperation for all patients; the absolute numbers at risk are indicated.

American Red Cross, and United Cryoinstitute. Procurement protocols were performed by each of their respective guidelines.^{9, 12}

Follow-up. The 36 patients who underwent AVR with a cryopreserved allograft between November 1, 1985, and August 1, 1995, constitute the patient cohort. Follow-up data included the most recent clinic or personal physician visit, correspondence by mail questionnaire, or telephone contact. Follow-up (100% complete) ranged from the day of the operation to 9.3 years (mean 2.6 years) and totaled 94 patient-years. All review and patient contacts were coordinated by the first author.

Data analysis. Continuous variables were compared in the two groups with two-sample *t* tests or with Wilcoxon rank sum tests when appropriate. Comparisons of proportions were made with χ^2 tests or Fisher's exact tests. Changes in nominal variables within individuals from early to late follow-up were analyzed with sign tests. Survival and cumulative risk of reoperation were estimated by the Kaplan-Meier method.¹³ Comparisons of survival curves were made with log rank tests. Survival data include all patients, and cumulative risk of reoperation was calculated for those patients who survived for the first 30 postoperative days. Data are expressed as mean $\pm$ standard error of the mean. Values of *p* less than 0.05 were considered to be statistically significant.

Results

Patient survival and morbidity. Overall operative mortality (30-day or hospital mortality) was 13.8%; risk was 10% for patients with native valve endocarditis and 18.8% for patients with prosthetic valve endocarditis. Causes of early mortality (*n* = 5) included sepsis in 2 patients and low cardiac output, myocardial infarction, and stroke in each of the remaining 3 patients. One early death occurred during the operation as a result of sepsis and shock.

There were no early deaths related to the allograft AVR.

There were 7 late deaths. Five were cardiac but not related to the allograft valve, and 2 were non-cardiac deaths. The cardiac causes of death were myocardial infarction (*n* = 3) and congestive heart failure (*n* = 2). One patient died of myelodysplastic syndrome and another of a traumatic subdural hematoma. Actuarial patient survivals 5 years after the operation for native valve endocarditis and prosthetic valve endocarditis were 70.8% $\pm$ 14.5% and 31.9% $\pm$ 14.7%, respectively (*p* = 0.04) (Fig. 1). At late follow-up, 92% of the surviving patients (*n* = 24) were in New York Heart Association class I, 4% in class II, and 4% in class III. Prosthetic valve endocarditis was the only factor that adversely affected long-term survival as determined by univariate analysis (*p* = 0.04).

Nonfatal complications are shown in Table V. No patient had recurrent endocarditis of the allograft aortic valve during the follow-up period.

Aortic valve regurgitation. Early echocardiography performed before hospital dismissal showed no aortic regurgitation in 26 (81%) patients and grade I aortic regurgitation in 6 (19%) patients. Late echocardiography (mean 2.6 $\pm$ 1.8 years) demonstrated no aortic regurgitation in 16 (50%) patients, grade I in 4 (12.5%) patients, grade II in 6 (18%) patients, grade III in 1 (3%) patient, and grade IV aortic regurgitation in 5 (16%) patients (*p* = 0.01; early vs late echocardiography). There was no difference in late aortic regurgitation between the

Fig. 3A. Four-chamber view demonstrating two defects from endocarditis: one annular defect involving the anterior leaflet of the mitral valve and the other a left ventricular outflow tract defect involving the ventricular septum.

patients with native valve endocarditis and prosthetic valve endocarditis. Four patients with grade IV aortic regurgitation have required reoperation (discussed later). At late follow-up there was no evidence of allograft aortic valve stenosis; mean gradient was 17 ± 11 mm Hg and mean valve area was 1.4 ± 0.4 cm².

Reoperation. Five patients required reoperation for allograft failure, 4 because of structural deterioration and resultant severe aortic regurgitation and 1 because of the development of a pseudoaneurysm at the inferior suture line. In the latter patient, the reoperation occurred 2.3 months after the initial operation. The allograft was intact and the dehiscence was presumably caused by residual necrotic native tissue. All patients who underwent reoperation had native valve endocarditis at the time of allograft AVR, and reoperations occurred at a mean of 3.8 years after AVR (range 2.3 months to 6.1 years). The cumulative risk of reoperation 5 years after the operation was $8.0\% \pm 5.6\%$ (Fig. 2).

Discussion

All patients with aortic valve endocarditis, either native valve or prosthetic valve, require appropriate antibiotic treatment. Whereas patients with native valve endocarditis are frequently treated successfully without an operation, patients with prosthetic valve infection usually need operative intervention because of difficulty eradicating infection with antibiotics alone.^{14, 15} In addition, both fungal and staphylococcal endocarditis of the native aortic valve are usually treated with operation because of extensive annular destruction and abscess formation that is unlikely to be adequately treated without annular débridement and excision of all infected tissue.

If operation can be delayed until infection has resolved, the likelihood of successful AVR with either a mechanical or biologic prosthesis is improved; operative mortality is lower and late survival is greater than in those operated on in the setting of active infection.¹⁶⁻¹⁸ When operation is indicated

Fig. 3B. Circumferential reconstruction of the aortic root with the allograft aortic valve being used as an intraaortic cylinder. Note that the allograft anterior mitral leaflet is used to repair the ventricular septal defect and a portion of the allograft aortic wall is attached the recipient anterior mitral leaflet.

with active valve infection, extensive annular destruction and abscess formation make AVR challenging. Small defects may be repaired with direct suture, but larger defects or loss of aortoventricular continuity necessitate patch repair with prosthetic material or autologous pericardium.^{19, 20}

The use of the cryopreserved aortic valve allograft has practical advantages in the setting of AVR with active infection and annular abnormalities. The allograft is a biologic material that appears to be more resistant to infection than prosthetic material such as Dacron fabric.^{17, 18} In addition, because of its contiguous aortic wall and anterior mitral leaflet, complex annular defects are more easily reconstructed after appropriate trimming of the allograft to conform to the residual defect. Figs. 3A and 3B illustrate how this technique can be performed.

In our practice, we have used aortic valve allografts selectively; approximately 5% of all patients undergoing AVR at our institution in the past decade received an allograft, and in this series of

patients with aortic valve endocarditis, the allograft was used in 33% of all patients with aortic valve endocarditis during the same time interval. In a recent follow-up of our patients with allograft aortic valves,²¹ we have noted that the risk of significant aortic regurgitation developing and subsequently necessitating reoperation begins to increase after 5 years of follow-up, whereas others have shown the risk of structural deterioration of the allograft to occur later.²²⁻²⁴ Similar early findings were noted in these patients in whom allografts were used for aortic valve endocarditis; the risk of reoperation was approximately 5% for allograft failure from structural deterioration and 8% overall in the first 5 years after the operation.

Follow-up in this review is not long enough to allow comment on the late results of allograft AVR for endocarditis. However, the overall low operative mortality, low early reoperation rate, and absence of recurrence of endocarditis for this group of patients with complicated infections is quite good when

compared with results in patients receiving a mechanical or bioprosthetic valve under similar circumstances.^{10, 11, 15, 16}

We²¹ and others^{25, 26} have described implantation techniques of allograft aortic valves previously. Although the specific findings at operation are the best guide to the technique of insertion ultimately used, we generally prefer to insert the allograft as an intraaortic cylinder in the setting of endocarditis after complete débridement of infected tissue and to preserve as much noninfected tissue as possible. The anulus and borders of the defect are then treated locally with phenol. We reserve allograft aortic root replacement for situations that necessitate native aortic root excision, for example, prosthetic valve infection with extensive annular destruction and resultant aortoventricular discontinuity.

Although the present series is small and the follow-up period short (mean follow-up 2.6 years), we are encouraged by the acceptably low operative mortality and the absence of reinfection in patients managed with aortic valve allografts. Clearly, late durability of the aortic valve allograft is less than that of a mechanical prosthesis and similar to the bioprosthesis, but the versatility of the allograft aortic valve and its resistance to infection make it our prosthesis of choice when active aortic valve infection is complicated by extensive destruction of contiguous tissue.

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