SURGERY FOR ACQUIRED HEART DISEASE

AORTIC VALVE REPLACEMENT WITH CRYOPRESERVED AORTIC ALLOGRAFT: TEN-YEAR EXPERIENCE

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Objective: Cryopreserved aortic allograft can be used for aortic valve replacement in congenital, rheumatic, degenerative, and infected native valve conditions, as well as failed prosthetic valves. This study was conducted to determine the long-term results of aortic valve replacement with cryopreserved aortic allografts. **Methods:** Aortic valve replacement with cryopreserved aortic allografts was performed in 117 patients from July 1985 until August 1996. All patients requiring aortic valve replacement regardless of valve disease were considered for allograft replacement; the valve was preferentially used in patients under age 55 years and in the setting of bacterial endocarditis. Four operative techniques involving cryopreserved aortic allografts were used: freehand aortic valve replacement with 120-degree rotation, freehand aortic valve replacement with intact noncoronary sinus, aortic root enlargement with intact noncoronary sinus, and total aortic root replacement. Valve function was assessed by echocardiography during the operation in 78 patients (66%) and after the operation in 77 patients (65%). **Results:** One-hundred eighteen aortic valve replacements with cryopreserved aortic allografts were performed on 117 patients; mean age was 45.6 years (range 15 to 83 years) and mean follow-up was 4.6 years (range up to 11 years). Intraoperative echocardiography disclosed no significant aortic valve incompetence. There were four operative deaths (3%) and seven late deaths; freedom from valve-related mortality at 10 years was $9.3\% \pm 4.55\%$. New York Heart Association functional status at latest follow-up was normal in 98 (94%) patients. On postoperative echocardiography, 90% had no or trivial aortic valve incompetence. Freedom from thromboembolism at 10 years was 100% and from endocarditis, $98\% \pm 2.47\%$. Seven (6%) patients required valve explantation, four for structural deterioration. At 10 years, freedom from reoperation for allograft-related causes was $92\% \pm 3.47\%$. **Conclusions:** Aortic valve replacement with cryopreserved aortic allografts can be performed with low perioperative and long-term mortality. Most patients have excellent functional status, and reoperation for valve-related causes is unusual. Aortic valve replacement with cryopreserved aortic allografts demonstrates excellent freedom from thromboembolism, endocarditis, and progressive valve incompetence. (J Thorac Cardiovasc Surg 1998;115:371-80)

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Replacement of the aortic valve with an aortic valve allograft has been shown in several series to have favorable long-term results in hemodynamic performance and freedom from reoperation. The allograft valve is particularly resistant to thromboembolism and is well suited for use in the setting of active valve infection. Late valve failure, an uncommon event, is most commonly the result of progressive valve incompetence.

Operative techniques for aortic valve replacement (AVR) with an aortic valve allograft have evolved since the initial procedures performed independently by Barratt-Boyes,¹ Ross,² and Paneth and O'Brien.³ Current methods now include freehand valve replacement with 120-degree rotation, freehand valve replacement with intact noncoronary sinus, aortic root enlargement, and aortic root replacement by either root inclusion or free-standing root techniques.

Midterm studies of AVR with cryopreserved aortic valve allografts have shown encouraging results.^{4,5} This study was undertaken to examine the long-term results of cryopreserved aortic allograft valves in the aortic position.

Methods

Patient selection. One hundred seventeen patients underwent AVR with a cryopreserved aortic allograft between July 23, 1985, and August 5, 1996, at LDS Hospital, Salt Lake City, Utah. The group comprised 100 male and 17 female patients; mean age was 45.6 years (range 15 to 83 years). Patient demographics stratified according to implant technique are summarized in Table I. One patient required rereplacement with a second allograft for a total of 118 valve replacements. Indications for AVR with a cryopreserved aortic allograft were similar to those for any patient requiring valve replacement for aortic valve disease, so that any patient requiring AVR was considered for inclusion in the study. Cryopreserved valves, however, are a limited resource, and many more prosthetic valves than allografts were used for AVR during the study period. The cryopreserved valve, however, was preferentially used in patients with active bacterial endocarditis, in patients with contraindications for anticoagulation, and in patients less than 55 years of age. No patient was excluded on the basis of age at operation, root deformity, heavy valve calcification, sinus enlargement, or prior aortic valve surgery. Coronary artery bypass, mitral valve repair, or other concomitant procedures were performed as indicated. No form of anticoagulation was used after the operation in any patient. Patients were followed up prospectively and assessed for valve function and clinical status from the time of the operation until the current study closing date of February 1, 1997.

Operative indications. Fifty-one patients (43%) had congenital aortic valve disease, defined as commissural fusion and formation of a bicuspid valve. Thirteen patients

(11%) had rheumatic aortic valve disease, defined as a three-cusp valve with characteristic rolled cusp edges. All other patients with noninfected, three-cusp valves (18 patients, 15%) were considered to have degenerative aortic valve disease. Fifteen patients (13%) had clinical evidence of aortic valve endocarditis. Active bacterial endocarditis, defined as a positive bacterial culture from the operative site or the presence of vegetations or purulence at operation, was identified in 12 patients (10%). Twenty-one patients (18%) had prior AVR; five of these valves were removed for infection.

Allograft valve preservation. Aortic valve allografts were obtained within 12 hours of donor death by means of standard, sterile technique by personnel trained by the transplant organ procurement organization. All allografts underwent processing and cryopreservation by Cryolife, Inc. (Kennesaw, Ga.). The allograft was thawed before implantation, according to protocol.

Operative technique. The methods of allograft valve implantation used in this series are described below. The freehand 120-degree rotation technique was initially used in all patients, but its use was gradually limited to patients with a small, symmetric aortic root and primarily aortic valve stenosis. Valve implantation using the freehand intact noncoronary sinus was later used in most patients and especially in those with a larger aortic root and aortic valve incompetence. The root enlargement technique was used in patients with accompanying subvalvular obstruction or who required a larger valve than the native root would accommodate. The total root replacement technique was used in patients with gross deformity, infection, or complete destruction of the aortic root. A root inclusion ("mini-root") technique was used in only one patient because of our bias against the inclusion of excessive allograft aorta within the native aorta.

Freehand 120-degree rotation AVR. The freehand 120-degree rotation AVR technique was performed in 40 patients (34%). After the institution of cardiopulmonary bypass and aortic occlusion, a transverse aortotomy is made and extended into the noncoronary sinus. The diseased valve is excised and an aortic allograft is selected with an internal diameter approximately 2 mm less than the measured aortic anulus. Septal myocardium and the anterior leaflet are removed from the allograft, leaving a 3 to 4 mm rim below the lowest point of valve cusp attachment. Aortic tissue is removed from all three sinuses to leave a 3 to 4 mm margin for suture placement.

The allograft is rotated 120 degrees counterclockwise, placing the right sinus of the allograft below the left sinus of the recipient. This positions the allograft septal myocardium against the recipient mitral valve. The graft is inverted and the lower edge anastomosed to the outflow tract below the fibrous anulus with continuous 3-0 polypropylene suture. The graft is then returned to its normal configuration and the allograft sinus margins are attached to the recipient sinus aorta with continuous 4-0 polypropylene suture.

Freehand intact noncoronary sinus AVR. The freehand intact noncoronary sinus AVR technique was performed in 52 patients (44%). The diseased aortic valve is removed and the anulus sized as described above. Septal myocardium and the anterior leaflet are trimmed from the

Table I. Patient demographics by implant technique

Group	n	Age (yr)		Gender distribution	Length of follow-up (yr)	
		Mean	Range		Mean	Range
1. 120-degree rotation	40	47.5	(16-75)	33 M/7 F	6.3	(0-10)
2. Intact NC sinus	52	46.3	(17-73)	48 M/4 F	3.5	(0-11)
3. Root enlargement	14	42.0	(16-83)	9 M/5 F	4.4	(0-9)
4. Root replacement	12	41.2	(15-78)	11 M/1 F	3.8	(0-9)
Total	118	45.6	(15-83)	101 M/17 F	4.6	(0-11)

NC, Noncoronary.

allograft in a similar manner. Aortic tissue is removed only from the right and left coronary sinuses, leaving the noncoronary sinus intact. This retains the spatial relationship of two of the commissures and ensures a more reliable valve implantation. The allograft is positioned in the anatomic position without rotation and the lower edge is attached to the outflow tract as previously described. The right and left allograft coronary sinus margins are attached to the recipient aorta, and the aortotomy may be attached to the allograft adventitia or closed over the noncoronary sinus.

Aortic root enlargement. The aortic root enlargement technique was performed in 14 patients (12%). The transverse aortotomy is extended posteriorly and inferiorly into the posterior commissure between the left and noncoronary sinuses, as far as the upper edge of the anterior leaflet of the mitral valve. The incision may be extended into the middle portion of the anterior leaflet to relieve accompanying subvalvular obstruction. Septal myocardium and the right and left coronary sinus tissue is trimmed from the allograft, leaving the noncoronary sinus intact. The allograft mitral anterior leaflet is trimmed appropriately to match the defect in the recipient noncoronary sinus or anterior mitral leaflet.

Interrupted 3-0 braided suture is used to attach the allograft mitral valve tissue to the edge of the recipient anterior leaflet or to the leaflet itself, effectively widening the outflow tract. Hemostasis and support are improved by incorporating a Teflon felt strip into the suture line. The allograft is inverted and the remainder of the lower edge attached to the outflow tract as previously described. The right and left sinuses are reconstructed as noted above, and the aortotomy is closed directly to the edges of the allograft noncoronary sinus. If the roof of the left atrium has been opened, it should be closed with a patch of pericardium or residual allograft aorta.

Aortic root replacement. Aortic root replacement was performed in 12 patients (10%). All diseased aorta and aortic valve tissue is excised, retaining good-sized buttons of sinus aorta around the coronary arteries. Septal myocardium and the anterior leaflet are trimmed, and the allograft is attached to the outflow tract without inversion with interrupted 3-0 polypropylene suture. Hemostasis and support are improved by means of a Teflon felt or pericardial "collar," which is incorporated into the suture line. The allograft coronary arteries are excised to create openings approximately 5 mm in diameter, and the recipient coronary arteries are anastomosed directly with continuous 5-0 polypropylene suture. The distal end of the

allograft is attached in an end-to-end fashion to the recipient ascending aorta with continuous 4-0 polypropylene suture.

Assessment of valve function. Intraoperative allograft valve function was assessed clinically before 1989 by evaluation of closing snap, diastolic thrill, and diastolic arterial pressure. Beginning in 1989, intraoperative allograft valve function was assessed by surface epicardial echocardiography or by transesophageal echocardiography. Valve incompetence was graded on a scale of 0 to 4, 0 representing no incompetence and 4 representing severe incompetence.

Postoperative valve function was assessed clinically in all patients by auscultation and blood pressure measurement. Aortic diastolic murmurs were graded on a scale of 0 to 4, with 0 representing no audible murmur and 4 representing a severe murmur. Patients were questioned regarding functional status and assigned to an appropriate New York Heart Association functional class. Echocardiography for indications of possible valve incompetence was performed at the discretion of the primary physician or cardiologist. Allograft valve incompetence was graded on a scale of 0 to 4, the same as performed during the operation. A valve with no incompetence was graded as 0, trivial incompetence as 1, mild incompetence as 2, moderate incompetence as 3, and severe incompetence as 4. Valve stenosis was graded as present or absent.

Data analysis. Postoperative events for all patients were analyzed by means of Kaplan-Meier methods with 95% confidence intervals (CI). Only four patients had been followed up for more than 10 years; therefore, analysis is presented to the 10-year interval. Outcome data for all patients were then analyzed according to type of operative procedure. The log-rank test was used to compare patient groups for valve-related mortality, valve explantation, and structural deterioration.

Results

Mean length of follow-up for all patients was 4.6 years (range up to 11 years); total follow-up for the series was 515 years. Only seven patients were lost to follow-up at various time intervals from 2 weeks to 6 years. The data for these patients were included in all analyses; each patient was censored from the study at the time of last follow-up.

Fig. 1. Freedom from valve-related mortality at 10 years (Kaplan-Meier methods; 95% CI, 76% to 98%).

Intraoperative findings. Thirty-one (26%) patients had prior cardiac surgery, 21 (18%) for aortic valve disease. Forty-three (36%) patients had a concomitant procedure at the time of AVR with a cryopreserved aortic allograft, which was most commonly coronary artery bypass ($n = 13$, 11%) or mitral valve repair ($n = 13$, 11%). Mean allograft valve size was 22.8 mm (range 18 to 30 mm). Aortic crossclamp time ranged from 66 to 212 minutes with a mean of 122 minutes. Intraoperative echocardiography to assess allograft valve function was performed in 78 (66%) patients; all patients had no or trivial valve incompetence.

Overall outcomes

Mortality. To date, 11 patients have died. Four of these patients (3%; 95% CI, 0.9% to 8.5%) died within 30 days of operation. The remaining deaths occurred at a mean of 5.7 years (range 4 months to 9 years). Overall survival at 10 years was 76% (95% CI, 54% to 89%); the linearized rate for all deaths was 1.4%. Four (3%) deaths were attributable to valve-related causes; three of these were early deaths. Valve-related deaths included sudden death in three patients and death resulting from endocarditis in one patient. Freedom from valve-related death at 10 years was 93% (95% CI, 76% to 98%), as illustrated in Fig. 1; the linearized rate for valve-related death was 0.8%.

Thromboembolism. No patient had a thromboembolic event either in the early postoperative period or during late follow-up. Freedom from thromboembolism at 10 years was therefore 100%.

Endocarditis. *Staphylococcus aureus* endocarditis developed in one patient 6.5 years after he underwent allograft root replacement at age 15 years for congenital bicuspid valve. He was seen at another institution, where the allograft aortic root was found to be extensively calcified and was replaced with a conduit containing a mechanical prosthesis. Freedom from endocarditis at 10 years was 98% (95% CI, 84% to 100%).

Reoperation. Twelve (10%) patients underwent reoperation, seven (6%) for valve-related causes. Other causes included coronary artery bypass in three patients, maze III procedure in one patient, and second-stage thoracoabdominal aneurysm repair in one patient with aortic dissection. Freedom from reoperation for any cause was 69% (95% CI, 36% to 87%).

Seven (6%) patients underwent reoperation and valve explantation, as summarized in Table II. Mean time to explantation was 5.2 years (range 5 months to 10 years). The indication for reoperation was allograft valve incompetence in four patients, endocarditis in one patient, technical error in one patient, and perivalvular leak in one patient. The last

Fig. 2. Freedom from valve explantation for any cause at 10 years (Kaplan-Meier methods; 95% CI, 82% to 97%).

Table II. Allograft valve explants

Age (yr)	Gender	Years to explant	Procedure	Cause
16	F	10.3	Freehand 120-degree rotation	Structural deterioration
31	M	10.2	Freehand 120-degree rotation	Structural deterioration
36	M	4.3	Freehand 120-degree rotation	Structural deterioration
48	M	2.8	Freehand 120-degree rotation	Structural deterioration
27	M	0.4	Freehand 120-degree rotation	Technical error
15	M	4.7	Root replacement	Endocarditis
46	M	3.9	Root replacement	Perivalvular leak

patient had a second cryopreserved aortic allograft implanted and is doing well 4 years later. Freedom from reoperation for valve-related causes requiring explantation was 92% (95% CI, 82% to 97%), as illustrated in Fig. 2; the linearized rate for explantation was 1.4%.

Four (3%) patients had explantation for allograft valve incompetence resulting from structural deterioration. This occurred at a mean of 6.9 years from operation (range 2.8 to 10.3 years). Freedom from valve explantation for structural deterioration was 97% (95% CI, 89% to 99%), as illustrated in Fig. 3; the linearized rate for structural deterioration was 0.8%.

Functional status. Functional status was normal at last follow-up in 98 (94%) of 104 surviving patients. Four (4%) patients were in New York Heart Asso-

ciation class II, two (2%) patients were in class III, and no patients were in class IV. Functional class for all patients requiring reoperation was assessed at the time of the operation.

Allograft valve incompetence. Postoperative clinical assessment of the allografts for evidence of diastolic murmur was performed in all patients. Eighty-four (71%) patients had no diastolic murmur, 20 (17%) had grade 1, eight (7%) had grade 2, and six (5%) had grade 3 murmurs. Three of the patients with grade 3 murmur and one with grade 2 murmur have undergone allograft valve explantation. The remaining patients with grade 2 or 3 murmur are clinically doing well.

Postoperative echocardiography was performed in 77 (65%) patients. Sixty-nine (90%) patients evaluated had no or grade 1 incompetence, five

Fig. 3. Freedom from allograft valve incompetence caused by structural deterioration at 10 years (Kaplan-Meier methods; 95% CI, 89% to 99%).

Table III. Outcomes at 10 years by implant technique

Group	n	Freedom from valve-related mortality (%)	Freedom from explantation (%)	Freedom from structural deterioration (%)
1. 120-degree rotation	40	100	92	94
2. Intact NC sinus	52	98	100	100
3. Root enlargement	14	62	100	100
4. Root replacement	12	92	57	100
Total	118	93	92	97

Data represent Kaplan-Meier 10-year survival or freedom from event. NC, Noncoronary.

(6%) had grade 2, two (3%) had grade 3, and one (1%) had grade 4. One patient with grade 3 and the single patient with grade 4 incompetence have undergone valve explantation. The remaining patient with grade 3 and all patients with grade 2 incompetence are clinically well. Six (8%) patients also had allograft valve stenosis on echocardiography; four patients had associated grade 1 incompetence, one patient had grade 2 incompetence, and one patient had no valve incompetence.

Subgroup analysis. Kaplan-Meier curves for valve-related mortality, valve explantation, and structural deterioration were compared by means of the log-rank test by operative procedure type. Table III lists the freedom from valve-related mortality, freedom from explantation, and freedom from structural deterioration at 10 years for each group.

Valve-related mortality. Group 1 (120-degree rotation) had the best survival and group 3 (root

enlargement) had the worst survival at 10 years. This difference was statistically significant ($p = 0.01$); comparisons between the remaining groups were not statistically significant.

Valve explant. Groups 1 (120-degree rotation) and 4 (root replacement) contained the only patients requiring allograft explantation. In group 1, four patients had explantation for structural deterioration and one for technical error. In group 4, one patient had explantation for endocarditis and one for perivalvular leak. No patient in either group 2 or 3, where the noncoronary sinus remains intact, required allograft explantation. The difference between groups 1 and 2 was statistically significant ($p = 0.05$), as was the difference between groups 2 and 4 ($p = 0.01$).

Structural deterioration. All four allograft explantations for structural deterioration were performed in group 1 patients, but this difference was not

statistically significant when compared with the other groups.

Comment

AVR with cryopreserved aortic allograft has produced favorable long-term results at 10 years in this series of patients. The technique has a low operative mortality (3%) and late valve-related mortality (also 3%). Overall survival at 10 years was 74%, similar to the 70% survival at 10 years demonstrated by O'Brien and associates⁶ and the 85% survival at 8 years reported by Kirklin and associates.⁷ The 93% freedom from valve-related mortality at 10 years was particularly good in this series.

The cryopreserved aortic allograft continues to demonstrate excellent freedom from thromboembolism and endocarditis. There were no thromboembolic events even though no anticoagulants were used. Allograft endocarditis developed in only one patient in this series, and all 15 patients with active or inactive endocarditis at operation were cured. O'Brien and associates⁶ noted four embolic events and four cases of endocarditis in their series of 184 patients followed up for 11 years. Kirklin and associates⁷ reported a single incident of thromboembolism and three cases of endocarditis in 178 patients followed up for 9 years.

Cryopreserved allografts have been shown to have excellent resistance from structural deterioration, particularly when compared with fresh refrigerated valves.⁸⁻¹¹ Varying amounts of viable endothelium and fibroblasts have been found on cellular analysis.¹²⁻¹⁵ The mechanical properties of cryopreserved allografts are superior to those of xenograft or fresh allograft tissue, although inferior to those of native valve tissue.^{16,17} This series of patients provides clinical follow-up at 10 years with cryopreserved aortic allografts in which uniform cryopreservation techniques by a single processor (Cryolife) were used.

Freedom from reoperation and valve explantation remains a central issue in assessing the long-term durability of the cryopreserved aortic allograft. A total of seven allograft valves were explanted in this series, four for structural deterioration, one for perivalvular leak, one for endocarditis, and one for technical reasons. Freedom from valve explantation was 92% at 10 years, identical to the 92% 10-year freedom from reoperation reported by O'Brien and associates⁶ and similar to the 86% freedom at 8 years demonstrated by Kirklin and associates.⁷ Reoperation for structural deterioration occurs infrequently, with a 97% freedom at 10 years in this

series, suggesting excellent performance of cryopreserved aortic tissues for at least 10 years. Valve explants appear to have occurred randomly during the first 10 years. No accelerated phase of valve explantation has been encountered at this point of follow-up.

Durability of the cryopreserved aortic allograft past 10 years remains to be demonstrated conclusively. Valve implantation in young patients is of particular concern, because xenografts and fresh allografts have shown accelerated degeneration in this patient population. O'Brien and associates¹⁸ have the only series with follow-up to 15 years; freedom from structural deterioration with cryopreserved aortic allograft was 80%. Two of the patients in this series have had valve explantation just over 10 years after the initial operation, both for structural deterioration. Both patients were young (16 and 31 years) at the time of allograft implantation.

Use of the cryopreserved aortic allograft in younger patients is desirable, because no anticoagulation is required, and its excellent hemodynamic characteristics favor a more vigorous functional status.¹⁹ Analysis of patients under the age of 50 years in this series was done; the mean age of these younger patients was 33.8 years and mean follow-up was 4.7 years (range up to 11 years). Only one valve-related death occurred in this group, but all four explants for structural deterioration occurred in this group of younger patients.

Considerable debate continues over the preferred operative technique for replacement of the aortic valve with a cryopreserved aortic allograft. Clearly, no single technique is applicable to all types of aortic root disease, as reviewed by O'Brien and associates.²⁰ Some authors favor aortic root replacement over subcoronary implantation to more consistently maintain allograft geometry as a means of reducing valve insufficiency.²¹⁻²³ Others recommend careful subcoronary implantation to achieve optimal results.^{24,25} Still other series have demonstrated no conclusive evidence to favor one technique over another.²⁶⁻²⁹ Nevertheless, in today's practice, intraoperative echocardiography should assure that a competent aortic valve is achieved at operation and perhaps should allow meaningful comparison of late results related to operative technique.

Root replacement with cryopreserved aortic allograft retains the allograft valve in its native position, which helps avoid valvular distortion during implantation. The operation may be technically easier and avoids long-term changes in the native aortic root, such as dilatation, which could affect the function of

Table IV. Selected events by implant technique

Group	n	Valve-related deaths	Explants	Structural deterioration
1. 120-degree rotation	40	0	5	4
2. Intact NC sinus	52	1	0	0
3. Root enlargement	14	2	0	0
4. Root replacement	12	1	2	0
Total	118	4	7	4

NC, Noncoronary.

a freehand implanted allograft. The allograft aorta, however, always undergoes calcification as time passes, with progressive shrinkage and hardening. This places undue stress on the allograft valve, which may also distort the otherwise intact valve leaflet tissue. Mini-root or intraluminal (inclusion) cylinder techniques retain the patient's native aortic tissue, but the space between the graft and the natural aortic root may be redundant or too small, resulting in kinking or distortion of the graft when the aorta is closed. Conversely, freehand techniques are technically more demanding and require precise positioning of the valve commissures to prevent distortion of the leaflets. Reimplantation of the coronary arteries, however, is not necessary, and the patient's aortic tissue is retained, providing more flexible support for the graft and less leaflet stress. Removal of most of the graft aorta should reduce the degree of long-term calcification in the root.

This series used four separate techniques for AVR: freehand 120-degree rotation, freehand intact noncoronary sinus, root enlargement, and root replacement. The freehand 120-degree rotation technique was used initially but has been largely abandoned in favor of the freehand intact noncoronary sinus technique developed by Ross.³⁰ Leaving the noncoronary sinus intact retains the anatomic relationship of two of the three commissures, making valve implantation more consistent, reproducible, and reliable. Both operations had low valve-related mortality in this series, with no deaths in group 1 and one valve-related death in group 2 (Table IV). However, all explantations for structural deterioration occurred in the 120-degree rotation group. The intact noncoronary sinus technique was therefore clinically superior to the 120-degree rotation technique for freedom from valve explantation.

Root enlargement with cryopreserved aortic allograft also retains the noncoronary sinus and resulted in no explants among 14 patients. No statistically significant difference was observed between this

group and the intact noncoronary sinus group for either outcome. Although the number of patients was considerably smaller than in the intact noncoronary sinus group (52 patients), the techniques have the same long-term results and for practical purposes may be considered equivalent.

In this series, valve-related mortality was not significantly different between the intact noncoronary sinus group and the root replacement group, with one death in each group (Table IV). There was also no significant difference in structural deterioration between the groups, because no valves required reoperation for this event in either group. Two valves in the root replacement group required explantation for other causes, one for endocarditis and one for perivalvular leak. In the latter patient, the allograft had been implanted as an inclusion root. Although the allograft valve cusps were structurally intact, the graft had pulled away from the aorta, which was much larger. The allograft was excised and a second cryopreserved aortic allograft was implanted by means of the intact noncoronary sinus technique after the natural aortic root was remodeled; the patient is clinically well at 4 years' follow-up. The intact noncoronary sinus technique was statistically superior when compared with the root replacement technique for freedom from valve explantation. Importantly, this difference was evident despite the smaller number of patients and shorter follow-up in the root replacement group. In addition, when patients receiving allografts with an intact noncoronary sinus (combined groups 2 and 3) were compared with patients in the root replacement group for freedom from explantation, the difference was highly statistically significant ($p = 0.005$).

In summary, this series demonstrates that the intact noncoronary sinus technique has favorable results for valve-related mortality, freedom from valve explantation, and freedom from structural deterioration. AVR with the cryopreserved aortic allograft demonstrated excellent freedom from valve-related mortality and reoperation for all techniques, and the incidence of endocarditis was negligible. Thromboembolism was nonexistent and patients did not require anticoagulation of any type. The cryopreserved aortic allograft also demonstrated excellent freedom from structural deterioration and, when required, all explants for structural deterioration occurred in the freehand 120-degree rotation group. AVR with cryopreserved aortic allograft results in a well-functioning valve in more

than 90% of patients at 10 years without need for anticoagulation and no evidence for accelerated valve degeneration.

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Discussion

Dr. R. Scott Mitchell (*Stanford, Calif.*). Dr. Doty, we are indebted to you and your colleagues for reporting United States data with a standardized cryopreservation technique that begin to approach the results of Mr. O'Brien. Many of these issues have now been resolved: Valve performance is excellent, including resistance to infection and freedom from thromboembolism. Data are fairly good out to 10 years, although the numbers become somewhat small in those last 2- or 3-year intervals. Unfortunately, inasmuch as four implantation techniques were used, it is difficult to rigorously establish differences

between these various techniques. Questions regarding valve durability remain, especially for the younger patients less than 50 years old. However, it is encouraging that no trends have yet become apparent in your data; such trends were certainly obvious with the pig valves by 8 or 9 years. The favored techniques seemed to be the freehand technique with intact coronary sinus and root replacements, both of which minimize the potential for distortion of the valve apparatus. This leads to my first question. Do you think that this preservation of the relationships with the intact sinotubular ridge and the valve commissures is important for maximal prolongation of leaflet function?

Dr. Doty. Yes, we do. We prefer the intact noncoronary sinus technique for a couple of reasons. First, this method reduces the amount of allograft aorta that is actually implanted into the patient; we know that the allograft calcifies with time, and eventually the tube becomes rigid. There has been some evidence from the literature that exact allograft sizing using a root replacement technique may result, over time, in a small loss of coaptation of the valve leaflets at 8 to 10 years. With the intact noncoronary sinus technique, a small amount of redundant leaflet tissue is implanted; therefore, because the allograft may shrink with time, we have extended coaptation of the leaflets.

Dr. Mitchell. That is an important point. Obviously, sizing is critical. We have noticed that few homografts greater than 23 mm are available. Can you offer some advice on how much annular size can be reduced to implant an available homograft?

Dr. Doty. We try not to reduce the size of the anulus; typically 2 or 3 mm can be obtained by simply stitching the commissure. That has been a problem with allografts all along—first, availability of the allografts and, second, the size restriction—which is the reason we have had to reserve our valve selection for patients.

Dr. Mitchell. My third question stems from our own experience. Dr. Shumway, in the early days, had a significant number of patients in whom fresh allograft from transplant recipients and unsuitable donor hearts was implanted. I did not implant any of those allografts, but I have removed some, and they are extensively calcified. Very little aorta remains. What do you do in terms of trying to reconstruct the aortic tissues?

Dr. Doty. If we need to reoperate on a patient who has undergone root replacement, we prefer to open the allograft and insert a prosthetic valve. As you have mentioned, the options are rather limited if primary root replacement has been done; that is why we prefer the intact noncoronary sinus technique. It is purely valve implantation, and options at reoperation may then include prosthetic implantation, implantation of additional homograft or allograft, Ross procedure, or implantation of a xenograft.

Dr. Mitchell. One of your indications for reoperation was the appearance of coronary disease. Was any of this

coronary ostial disease, maybe attributable to the reimplanted coronary button?

Dr. Doty. I do not have that information; I cannot comment on that, Dr. Mitchell.

Dr. Mitchell. Last, how do you account for the greater fallibility of grafts in which you had to do anulus enlargements?

Dr. Doty. We have not been able to account for that. The root enlargement group comprised only 14 patients, and two of those required explantation. At this point, we have no explanation for that.

Dr. Vaughn A. Starnes (*Los Angeles, Calif.*). Did you see any age-related differences in your implants? Your data look very good, but we all know that homografts deteriorate in the very young.

Dr. Doty. Yes, we did, Dr. Starnes. Of the seven grafts that were explanted, five were from patients who were younger than 40 years old. One of our patients was 15 years old, and that patient had explantation, so we did notice more of the explants in the younger age group.

Dr. Starnes. Can you offer some recommendations about homograft replacement in terms of age-related factors?

Dr. Doty. Yes. As a result of this study, we have altered our indications for use of the homograft; in particular, we try to avoid using homografts in the younger age group and have now begun using the autograft procedure instead. We now typically use the homografts in the following situations: for endocarditis, because all of our patients were cured of endocarditis when treated with an allograft; for extensive root destruction whether it be from endocarditis or other processes; for patients who are older and do not have an expected life span of more than 10 or 15 years; and also in contraindications for anticoagulation.

Dr. Starnes. Would you say younger is less than 50, less than 45, less than 40?

Dr. Doty. We are saying less than 45.

Dr. Starnes. In that group, less than 45, would you use the Ross procedure?

Dr. Doty. That is correct.

Dr. Fareed Khouqeer (*Houston, Tex.*). Dr. David Clarke was experimenting with the use of cyclosporine (INN: ciclosporin) in 1987 or 1986. Are any of your patients using immunosuppressive drugs?

Dr. Doty. No, we have not used steroids, cyclosporine, azathioprine, or ibuprofen, as has been recommended by others. According to the current literature, endothelium seems to be the most immunogenic portion of the allograft, and the cryopreservation technique probably destroys the vast majority of the endothelium. In addition, when the allograft is being implanted, it is placed over the index finger of the surgeon. During manipulation, most of the remaining endothelium is probably rubbed off, so we have not used any form of immunosuppression on our patients.