OUTCOME OF PULMONARY AND AORTIC HOMOGRAFTS FOR RIGHT VENTRICULAR OUTFLOW TRACT RECONSTRUCTION

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To determine late patient outcome and homograft durability, we reviewed 326 patients who received aortic ($n = 230$) or pulmonary ($n = 118$) cryopreserved homografts for right ventricular outflow reconstruction between January 1985 and October 1993. Patient survival, including operative mortality, 5 years after the operation was similar between the two groups (pulmonary homograft 86%, aortic homograft 80%; $p =$ not significant by log-rank test). However, 5-year freedom from homograft failure was significantly better for pulmonary homografts (94% versus 70%, $p < 0.01$ by log-rank test). Late calcification was evaluated by chest roentgenography and echocardiography. Overall, 20% of aortic homografts became moderately or severely calcified compared with 4% of pulmonary homografts ($p < 0.01$). Twenty-six percent of aortic homografts in children 4 years old or younger had moderate or severe obstruction associated with calcification, whereas only 11% of aortic homografts in patients over 4 years of age had calcific obstruction ($p < 0.01$). No late deaths among patients receiving pulmonary homografts were related to graft failure; two late deaths in the aortic homograft group were homograft related. Risk factors for patient mortality and homograft failure (defined as either need for homograft replacement because of homograft failure or as homograft-related death) were identified by the Cox multivariate analysis. Aortic type of homograft was a significant risk factor for homograft failure ($p < 0.0001$), but type of homograft was not correlated with patient mortality. Age 4 years or younger was a significant risk factor for both mortality ($p < 0.01$) and homograft failure ($p = 0.03$) in aortic homograft recipients but not in pulmonary homograft recipients. These results indicate that both aortic and pulmonary homografts provided excellent intermediate-term patient survival after right ventricular outflow tract reconstruction, but pulmonary homografts are more durable than aortic homografts with less calcification and obstruction, especially among children 4 years old or younger. (*J THORAC CARDIOVASC SURG* 1995;109:509-18)

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Use of an extracardiac conduit between the right ventricle and the pulmonary arteries has made possible the routine repair of pulmonary atresia,^{1,2} complex tetralogy of Fallot,³ truncus arteriosus,⁴ transposition of the great arteries with ventricular septal defect and pulmonary stenosis,⁵ and other complex forms of congenital heart disease.⁶⁻¹¹ Although techniques of reconstruction of the right ventricular outflow tract (RVOT) have been refined during the past 30 years, the search continues for an ideal conduit to establish right ventricle-pulmonary artery continuity.^{12,13}

Homografts are among the many varieties of prosthetic materials that have been used for RVOT reconstruction. At our institution, aortic valve homografts were first used in September 1967. Late calcification and obstruction occurred in many patients in our series and elsewhere; these complica-

tions appeared to be due in part to early methods of sterilization and preservation.¹⁴⁻¹⁷ Recent promising results with fresh aortic homografts sterilized with antibiotics and preserved with freezing have resulted in a resurgence of use of homografts.¹⁸

Pulmonary homografts have a thinner wall than aortic homografts and may be less susceptible to calcification. However, few comparative data are available on aortic versus pulmonary homografts.^{19,20} Accordingly, we reviewed the results of cryopreserved aortic versus pulmonary homografts for reconstruction of the RVOT to determine risk factors for patient mortality and homograft failure.

Patients and methods

Between January 1, 1985, and October 30, 1993, 326 consecutive patients received cryopreserved aortic ($n = 230$) or pulmonary ($n = 118$) homografts for RVOT

Table I. Clinical data on 326 patients

	Initial homograft implantation	
	Aortic	Pulmonary
Number	212	114
Age		
Range	10 days–61 yr	3 days–48 yr
Mean	11.4 yr	14.4 yr
Median	9 yr	12 yr
≤4 yr	52 (24%)	22 (19%)
Sex (male/female)	112/100	62/52
Primary diagnosis		
Complex tetralogy of Fallot/pulmonary atresia with VSD	117 (55%)	75 (66%)
Truncus arteriosus	32 (15%)	10 (9%)
Transposition of great arteries	32 (15%)	9 (8%)
Double-outlet right ventricle	26 (12%)	9 (8%)
Others	5 (2%)	11 (10%)
Prior palliative procedures	112 (53%)	58 (51%)

VSD, Ventricular septal defect.

Table II. Primary indication for homograft implantation after previous RVOT reconstruction

Indication	Aortic homograft	Pulmonary homograft
Failure of prosthetic valved conduit	60	28
Failure of aortic homograft	17	3
Failure of pulmonary homograft	3	4
Pulmonary insufficiency	20	20
Other	23	12
Total	123	67

reconstruction at the Mayo Clinic. Postoperative patient status was determined by evaluation of the patient or by letters from referring physicians. If recent (<6 months) follow-up had not been accomplished, the patients were contacted directly by telephone or letter during the months of January, February, and March 1994. Late homograft status was evaluated by one or more of the following: echocardiography, chest roentgenography, or cardiac catheterization. Clinical data are shown in Table I. One hundred twenty-one patients had received a nonhomograft extracardiac conduit during a prior cardiac repair. Primary indications for 190 homograft implantations after prior RVOT reconstruction are shown in Table II.

Most of the patients in whom a previous conduit had been placed underwent successful resternotomy and cannulation of the ascending aorta. In some patients, particularly those with prosthetic conduits that had eroded into the sternum or calcified homografts that lay beneath the sternum, the femoral artery and vein were cannulated before or during sternotomy. The operation was done with the use of standard cardiopulmonary bypass. In some patients who did not require associated intracardiac pro-

Table III. Homograft anastomosis augmentation techniques

Procedure	Aortic homograft	Pulmonary homograft
Proximal anastomosis		
Hemashield graft patch	61	14
Bovine pericardium	51	25
Autologous pericardium	13	12
Remaining homograft	9	5
Previous graft	5	3
Other prosthetic material	5	7
None or unknown*	86	52
Distal anastomosis		
Hemashield graft patch	9	5
Remaining homograft	7	0
Bovine pericardium	7	1
Autologous pericardium	6	5
Previous graft	3	3
Other prosthetic material	12	8
None	186	96

*Includes aortic homografts in which the anterior leaflet of the mitral valve was used.

cedures, the patient was cooled to 32° to 34° C, an aortic tack vent was placed, the heart was kept beating, and conduit replacement was done without crossclamping the aorta. In other patients and in those requiring an associated intracardiac procedure, moderate hypothermia (20° to 28° C), aortic crossclamping, and myocardial protection with cold blood or crystalloid potassium cardioplegic solution were used. Exposure for the distal anastomosis was often facilitated with short periods of low flow (0.5 L/min per square meter) or, rarely, circulatory arrest.

Cryopreserved homografts were obtained from Cryo-Life Inc., Marietta, Georgia, Red Cross Transplantation Services, St. Paul, Minnesota, and United Cryo Institute, Chicago, Illinois. The techniques for preparation of cryopreserved homografts and storage in liquid nitrogen have been described previously.^{21, 22} Choice of conduit size was based on the patient size, pulmonary artery size, anticipated somatic growth, and physical limitations of the sternum and mediastinal structures (Appendix 1). Except in some infants under 1 year of age, an effort was made to insert a homograft larger than the size predicted from tables of normal pulmonary valve sizes.^{23, 24} Homografts were thawed and trimmed in standard fashion after intraoperative assessment of the anatomy. The distal anastomoses were performed first; the distal ends of the homografts were tailored to provide a maximal size of anastomosis and, where applicable, to enlarge proximal right and left pulmonary artery stenoses. A bifurcated reconstruction with a pulmonary homograft was used in 27 patients. In some patients, other prosthetic material was used to extend the homograft, enlarge the pulmonary arteries, or provide continuity between the pulmonary arteries (Table III). Proximal anastomoses were made to vertical right ventriculotomies directed toward the site of the distal anastomosis, as permitted by the coronary artery

anatomy. The anterior leaflet of the mitral valve, often extended with other material, was usually used in the proximal anastomoses of the aortic homografts. Most of the pulmonary homografts required prosthetic extension (Table III). Whenever possible, the conduits were positioned away from the sternum to avoid compression.

Selection of the homograft type was not random; surgeon preference was the primary selection factor. In general, aortic homografts were used for patients who were expected to have pulmonary hypertension after the operation, and the majority of infants with truncus arteriosus received aortic homografts. Pulmonary homografts were often used for patients requiring an anastomosis to branch pulmonary arteries, or when augmentation of the pulmonary arteries was required. Pulmonary homografts were more frequently used for complex tetralogy of Fallot and for pulmonary atresia with ventricular septal defect and pulmonary stenosis. Because of the scarcity of aortic homografts, pulmonary homografts were often implanted when the appropriate size of aortic homograft was not available, especially in the larger sizes. No attempt was made to achieve ABO blood type compatibility before June 1991; since then, ABO blood type compatible homografts were implanted whenever possible.

Early mortality was defined as death within 30 days. Data were entered into a computerized database and analyzed with Statistica software, Statsoft, Inc. Tulsa, Oklahoma. The cumulative survival estimates of patients and homografts were made by the actuarial (life-table) method and the 95% confidence intervals for the estimates were determined by the Greenwood formula.²⁵ Homograft failure was defined as the need for homograft replacement because of homograft failure or as death related to failure of the homograft. Homograft failure was defined as conduit stenosis with or without calcification severe enough to warrant homograft replacement and conduit valve insufficiency severe enough to warrant homograft replacement. Conduit compression between the heart and the sternum, proximal or distal homograft anastomotic stenosis, and development of a false aneurysm at the proximal or distal anastomosis were not considered homograft failures. The Cox proportional hazard model was used to identify the independent contribution of potential risk factors for patient mortality in the total cohort of 326 patients. The Cox model was also used to identify the independent risk factors for homograft failure in the entire group of 348 implanted homografts, as well as in the subgroups with aortic ($n = 230$) and pulmonary ($n = 118$) homografts. The variables entered into the risk factor analysis are summarized in Table IV. The selection of independent variables in the models was a forward stepwise method with a critical p value for variable inclusion and exclusion of 0.15. A p value of less than 0.05 was considered significant.

Results

There were 22 early (6%) deaths related to the initial homograft implantation. Early mortality for reoperation for conduit replacement was lower (6/171, 3.5%) than early mortality for patients in whom homografts were implanted during the initial car-

Table IV. Potential risk factors for patient mortality and homograft failure

Preoperative risk factors	
Age	
Sex	
Date of procedure	
Blood ABO patient - homograft mismatch	
Ratio of homograft size to body weight	
Cardiac diagnosis	
Previous palliative procedure	
Previous repair or conduit	
Mean pulmonary artery pressure ≥ 45 mm Hg	
Operative risk factors	
Surgeon	
Technique of homograft extension	
Type of homograft	
Postrepair mean pulmonary artery pressure ≥ 45 mm Hg	
Postrepair right ventricular/left ventricular pressure ratio	

Table V. Primary cause of early death

Cause	Initial homograft recipients	
	Aortic homograft ($n = 212$)	Pulmonary homograft ($n = 114$)
Acute ventricular failure	6	4
Multisystem organ failure	3	0
Pulmonary hypertensive crisis	2	1
Neurologic deficit	2	1
Sepsis	1	0
Arrhythmia	1	0
Myocardial infarction	1	0
Total deaths	16 (7.5%)	6 (5.3%)

diac repair (16/155, 10.3%). Early mortality was similar in patients who received aortic homografts and in those who received pulmonary homografts (16/212, 7.5%, versus 6/114, 5.3%). Primary causes of early death are shown in Table V.

One patient in the aortic homograft group was lost to follow-up. Follow-up in the remaining patients ranged from 6 months to 8.8 years with a mean of 2.7 years for aortic homografts and 3.2 years for pulmonary homografts. There were 24 (7.4%) late deaths. Sixteen of the 212 (7.5%) initial recipients of aortic homografts died late; two of the deaths were homograft related (one death at reoperation and one death from an arrhythmia associated with a high RVOT gradient) (Table VI). Eight late deaths (7.0%) were observed in the initial 114 recipients of pulmonary homografts, but none were considered to be homograft related (Table VI).

Overall survival, including early deaths, was 87% at 3 years after the operation and 83% at 5 years.

Fig. 1. Patient survival including early mortality. Vertical bars enclose a 95% confidence interval. NS, Not significant.

Table VI. Primary cause of late mortality

Cause	Initial homograft recipients	
	Aortic homograft (n = 212)	Pulmonary homograft (n = 114)
Arrhythmia	6	3
Heart failure	2	0
Sepsis	2	1
Multisystem organ failure	2	2
Reoperation	1	1
Pneumonia	1	1
Others	2	0
Total deaths	16 (7.5%)	8 (7.0%)

Survival was similar for patients with aortic and pulmonary homografts (5-year survival 80% and 86%, respectively) (Fig. 1). Survival in children 4 years of age or younger with aortic homografts was significantly less than in older patients with aortic homografts ($p < 0.01$) (Fig. 2, A), but age did not influence survival of patients receiving pulmonary homografts (Fig. 2, C). Five-year survival of patients receiving homografts at the time of initial cardiac repair (78%) was significantly less than survival of patients receiving homografts after previous repair (87%) ($p = 0.01$ by the log-rank test). However, this difference was due entirely to early mortality, because later survival was similar in both groups.

In the multivariate analysis of overall patient survival, homograft type was entered as a variable. Multivariate analysis was also applied separately to the patients who received aortic and pulmonary homografts. Overall patient survival was adversely affected by age of 4 years or younger at operation, initial repair with homograft, and smaller homograft

size/body weight ratio (Table VII, A). These same factors were predictive of late death in the subgroup of patients receiving aortic homografts, but only smaller homograft size relative to body weight was predictive of late death in patients receiving pulmonary homografts.

Late cardiac catheterization was performed in 40 of 212 aortic homograft recipients and 23 of 114 pulmonary homograft recipients. Follow-up data from one or more of the following, echocardiogram, chest x-ray film, or cardiac catheterization, were available for 197 aortic homografts and 104 pulmonary homografts. Moderate or severe graft calcification was identified in 20% of aortic homografts and 4% of pulmonary homografts (Fig. 3).

Twenty-three percent (53/230) of aortic homografts became moderately or severely stenotic. Twenty-seven aortic homografts required reoperation because of stenosis; in 20 of these, obstruction was associated with calcification of the homograft (Table VIII). Two pulmonary homografts necessitated reoperation because of stenosis (both without calcification) and three pulmonary homografts necessitated reoperation because of homograft valve insufficiency. Reoperation for indications other than homograft failure are also listed in Table VIII. Three of the 75 patients who received Hemashield graft patches (Meadox Medicals, Inc., Oakland, N.J.) for augmentation of the proximal anastomosis required reoperation for anastomotic stenosis.

Twenty-six percent (14/53) of aortic homografts implanted in patients 4 years of age or younger became moderately or severely obstructed with calcification, whereas only 11% (20/177) of aortic homografts implanted in patients older than 4 years became obstructed with calcification ($p < 0.01$). Only 4% (5/118) of pulmonary homografts became moderately stenotic with calcification; all but one had been implanted in patients older than 4 years.

Thirty-two reoperations were required for conduit failure in 28 patients. Twenty-five patients had one reoperation, two had two reoperations, and one patient had three reoperations for conduit failure. Twenty-seven reoperations were for aortic homograft failure and five were for pulmonary homograft failure ($p = 0.02$) (see Table VIII). However, if false aneurysms, all three of which occurred in the pulmonary homografts, are included in the definition of homograft failure, the differences were not significant ($p = 0.14$). If all causes of reoperation are considered, the reoperation rate for pulmonary compared with aortic homografts was also not

Fig. 2. A and B, Aortic homograft recipients: A, Patient survival including early mortality stratified according to age at operation. B, Freedom from homograft failure stratified according to patient age at operation. C and D, Pulmonary homograft recipients: C, Patient survival including early mortality according to age at operation. D, Freedom from homograft failure stratified according to patient age at operation. Vertical bars enclose a 95% confidence interval.

Table VII. Results of multivariate analysis of risk factors for late patient mortality and homograft failure

Risk factor	Overall	Homograft	
		Aortic	Pulmonary
A. Patient mortality			
Age ≤4 years old	<i>p</i> < 0.001	<i>p</i> < 0.001	NS
Initial repair with homograft	<i>p</i> < 0.01	<i>p</i> < 0.01	NS
Smaller homograft size/body weight	<i>p</i> < 0.001	<i>p</i> < 0.001	<i>p</i> = 0.02
B. Homograft failure			
Aortic homograft	<i>p</i> < 0.0001	—	—
Age ≤4 years old	<i>p</i> = 0.01	<i>p</i> = 0.03	NS
Cardiac diagnosis (TA, TGA, DORV, and others)	<i>p</i> = 0.03	<i>p</i> = 0.04	NS

TA, Truncus arteriosus; TGA, transposition of great arteries; DORV, double-outlet right ventricle; NS, not significant.

significant ($p = 0.25$). Replacement conduits were as follows: aortic homograft ($n = 21$), pulmonary homograft ($n = 4$), Hancock conduit ($n = 4$), porcine valve with pericardial roof reconstruction ($n = 2$), and nonvalved pericardial roof reconstruction ($n = 1$).

Actuarial freedom from failure of pulmonary homografts was significantly higher than that of

aortic homografts (5-year freedom from failure 94% versus 70%, Fig. 4). Freedom from failure of aortic homografts in patients 4 years of age or younger was significantly lower than for older patients (Fig. 2, B), but age had little effect on freedom from failure for pulmonary homografts (Fig. 2, D).

By Cox multivariate analysis, type of homograft (aortic versus pulmonary) was the strongest predic-

Fig. 3. Radiographic and/or echocardiographic evaluation of late homograft calcification.

Fig. 4. Freedom from homograft failure. Vertical bars enclose a 95% confidence interval.

Table VIII. Indication for reoperation

Indication	Homograft	
	Aortic	Pulmonary
Homograft failure	27	5
Homograft stenosis	27	2
With calcification	20	0
Without calcification	7	2
Homograft valve insufficiency	0	3
Homograft compression	1	3
False aneurysm, distal anastomosis	0	2
False aneurysm, proximal anastomosis	0	1
Stenosis proximal anastomosis	3	0
Total	31	11

tor of homograft failure (Table VII, B). Age 4 years or younger and cardiac diagnosis group of truncus arteriosus, transposition of the great arteries, double-outlet right ventricle, and others were also predictive of late homograft failure for the entire group and for the aortic homograft group. The cardiac diagnosis group of tetralogy of Fallot and pulmo-

Fig. 5. A, Patient survival including early mortality for all homografts stratified according to diagnostic groups. B, Freedom from homograft failure stratified according to diagnostic groups. Complex tetralogy of Fallot (TOF) and pulmonary atresia with ventricular septal defect (PA + VSD) represent one group and truncus arteriosus (TA), transposition of great arteries (TGA), double-outlet right ventricle (DORV), and others represent the other group. Vertical bars enclose a 95% confidence interval. NS, Not significant.

nary atresia with ventricular septal defect had a higher freedom from homograft failure (Fig. 5, B) ($p = 0.01$).

By multivariate analysis, preoperative pulmonary hypertension was not a significant risk factor for patient mortality, which was 18% in those with pulmonary hypertension and 11% in those without pulmonary hypertension ($p = \text{not significant}$). Pulmonary hypertension was also not a significant risk factor for homograft failure, which occurred in 8% of patients with pulmonary hypertension compared with 11% of patients without pulmonary hypertension ($p = \text{not significant}$). There were no significant differences in preoperative systolic pulmonary pressure between nonsurvivors (41.4 ± 21.4 mm Hg) and survivors (37.8 ± 19.4 mm Hg) or between patients with homograft failure (36.3 ± 19.8 mm Hg) and those without homograft failure ($38.6 \pm$

19.7 mm Hg). Homograft survival was not significantly influenced by the type of material used for augmentation of the homograft anastomoses, date of procedure, ABO blood type matching of the homograft and patient, or other factors mentioned in Table IV.

The percentages of late survivors who were in New York Heart Association class I or II were 94% (170/180) in the aortic homograft group and 92% (92/100) in the pulmonary homograft group.

Discussion

The use of homografts for RVOT reconstruction was first reported for pulmonary atresia in 1966,² for truncus arteriosus in 1968,⁴ and for transposition of the great arteries with ventricular septal defect and pulmonary stenosis in 1969⁵; by the 1970s, homografts had become widely used for RVOT reconstruction in many types of complex congenital heart disease.⁶⁻¹¹ However, because of problems with late calcification and obstruction, many centers discontinued the use of homografts and changed to prosthetic grafts with porcine valves.^{26, 27} Subsequent experience with those conduits showed late obstruction by calcification of the porcine valve and by peel formation.²⁸ Recent reports of encouraging late results with antibiotic-sterilized homografts²⁹ and especially with fresh aortic homografts sterilized with antibiotics and preserved with freezing¹⁸ have resulted in a resurgence of interest in homografts. Our experience with sterile, fresh cryopreserved homografts began in 1985.

This study and others¹⁹ have demonstrated excellent patient survival after RVOT reconstruction with cryopreserved homografts and low risk of mortality for reoperation for conduit replacement.³⁰ However, aortic homograft failure in this series was more than expected. Other investigators have also expressed concerns about the durability of cryopreserved aortic homografts.¹⁹ In addition, both calcification and conduit stenosis were greater in the aortic homografts in this series. A higher rate of calcification in aortic homografts compared with pulmonary homografts may be related to a greater content of elastic tissue and a greater amount of total calcium in the wall of the aortic homograft.³¹

Accelerated degeneration of aortic homografts in young patients has been observed by others³² and was a statistically significant risk factor in this series. Accelerated degeneration may be related to a host immunologic response, although this theory remains unproved.³³

A few of our homografts failed without calcification. The homografts were contracted and edematous, and thrombus was sometimes seen in the retracted cusps. Some of these homograft failures occurred within 2 years of implantation and had the appearance of an immunologic response. ABO incompatibility and immunologic response as risk factors for homograft durability have been debated extensively.³³⁻³⁵ In this series, we could not demonstrate a relationship of ABO incompatibility with homograft survival, but the number of patients may be too small to demonstrate a difference. The role of viable cells in cryopreserved homografts is another issue of uncertain significance, but this may actually be detrimental compared with survival of refrigerator-stored antibiotic-preserved homografts, in which most cells, especially endothelial cells, are no longer viable after 48 hours.

Although the type of material used for augmentation of the homograft anastomoses was not a statistically significant risk factor, there were three instances of proximal stenosis resulting from failure of a Hemashield patch; this material has also been reported by others to contribute to anastomotic stenosis.^{36, 37}

Small size of the homograft compared with body weight was a significant risk factor for patient mortality and also for late overall homograft and aortic homograft failure in this series. Other reports have not found the size of the homograft to be a risk factor for late failure.^{38, 39}

In summary, for RVOT reconstruction, pulmonary homografts were more durable than aortic homografts, especially among young children. Small homograft size relative to patient body weight and the diagnostic group of truncus arteriosus, transposition of the great arteries, double-outlet right ventricle, and others were significant risk factors for subsequent homograft failure. Pulmonary homografts appear to be the preferred conduits for most cases of RVOT reconstruction, especially in patients 4 years of age or younger.

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Discussion

Dr. David R. Clarke (*Denver, Colo.*). The data presented parallel our experience in Denver for homograft reconstruction of the RVOT. We have a mean of 4 years of clinical follow-up of 200 patients; 29 received aortic homografts and 171 received pulmonary homografts to reconstruct the RVOT over a comparable time interval. In the Denver series, conduit failure that necessitated replacement was more prevalent with aortic homografts (24% failure) than with pulmonary homografts (4.7% failure). Recipient age at implantation also significantly affected failure rate.

My first question relates to diagnosis and patient age at the time of homograft implantation. In our experience that is similar to yours, 47% of homografts that required replacement had been implanted in children with truncus arteriosus. Because this anomaly usually mandates surgical repair at an early age in your series, can you clearly separate diagnosis and age at operation as independent risk factors, and can you comment on this phenomenon please?

Dr. Bando. Diagnosis and age at operation are interrelated in part by the associations you mentioned. However, on multivariate analysis of our data, both age and the diagnostic group of truncus, double-outlet right ventricle, and transposition of the great arteries were found to be independent risk factors for homograft failure.

Dr. Clarke. Our current policy regarding implantation of aortic valve homografts in the RVOT differs from yours

because you intentionally selected aortic conduits for specific patients. The majority of Denver's aortic homografts represent our early experience; since 1988 we have implanted aortic homografts only when the appropriate pulmonary homograft is unavailable. After having evaluated and reported your current series, will you reassess your future use of aortic homografts in the RVOT?

Dr. Bando. This is the first analysis of our late homograft experience. We have confirmed that the failure rate of the aortic homograft is higher than that of the pulmonary homograft, so we now prefer to implant pulmonary homografts whenever feasible.

Dr. Clarke. In your paper you cited three organizations as sources for the tissue that was implanted. Inasmuch as minor variations may exist in the preservation processes among these organizations and these variations might account for some differences in viability that could be important, did you evaluate tissue source as a risk factor? Do you have any subjective feeling about differences that exist there?

Dr. Bando. Tissue source was not evaluated as a risk factor.

Dr. Clarke. Allograft degeneration in younger patients has been a problem in both our series. Denver data reveal a higher prevalence of allograft fibrocalcification and regurgitation in young patients. Of the 15 patients who underwent reoperation to replace an aortic or pulmonary allograft in our series, 13 (87%) were less than 4 years of age at the initial allograft operation. We have been unable to pinpoint a mechanism for early conduit failure, but like you we have considered the possibility of an immunologic reaction. My question is a monumental one and concerns the immune response that might occur in younger children. From the data you have so thoroughly researched, can you and your colleagues shed any light on the presence and/or nature of this phenomenon?

Dr. Bando. A few of our homografts failed very early, without calcification. Edema and thrombus were found around the cusp area. We believe that in those particular cases the patients clearly had rejection. The role of the immune response in graft failure is controversial. However, in at least some cases, it appears that viable cells in the cryopreserved homograft may be detrimental. We have not used any form of immunosuppression.

Dr. Ronald Elkins (*Oklahoma City, Okla.*). I have two questions: What would you recommend for the older patient with known pulmonary hypertension requiring conduit reconstruction of the RVOT? It is fairly well known that the pulmonary homograft will fail fairly early from pulmonary insufficiency in this setting.

Dr. Bando. For initial operation in a patient with pulmonary hypertension, we prefer an aortic homograft or a porcine-valved Dacron conduit. For reoperation, we prefer an autologous tissue reconstruction employing a pericardial roof patch over a porcine valve.

Dr. Elkins. My second question relates to our experience primarily with the pulmonary autograft procedure. We have approximately 170 patients now. Among them were two patients in whom a discrete narrowing of the pulmonary homograft developed distal to the pulmonary valve within the first year after the operation. In talking to

other surgeons with similar experience across the country, we learned that most of them have had one or two similar cases. Have you seen similar lesions in those patients in whom reconstruction was done primarily for congenital lesions rather than for movement of the normal pulmonary valve from the RVOT? Do you have any thoughts as to the etiology of this other than perhaps an unusual rejection phenomenon?

Dr. Bando. We are aware of stenosis of pulmonary homografts employed both in congenital lesions and as replacement of a native pulmonary valve in the autograft operation. We have no explanation for these occurrences but suspect early pulmonary homograft stenosis, especially without calcification, is a rejection phenomenon.

Dr. Edward Verrier (Seattle, Wash.). I have two relatively straightforward questions. A greater percentage of aortic conduits were used in patients with pulmonary hypertension. Although the numbers did not achieve significance, I am interested in the relationship, because clearly biomechanical factors and stress/strain relationships across the valve or conduit have been shown both experimentally and in the valve literature to potentiate the calcification issue. Could you further comment on the relationship between pulmonary hypertension and the early development of calcification in the aortic conduits?

Dr. Bando. We specifically looked at that matter and compared survivors and nonsurvivors. Preoperative pulmonary artery pressure was not different. Furthermore, we found no significant difference between patients whose homografts failed and those whose homografts did not fail, so I have no good explanation for that. The only thing I can say is that from these data preoperative pulmonary hypertension did not appear to be a significant risk factor.

Dr. Verrier. In explanted conduits, have you looked at the endothelium for the development of intimal hyperplasia or vascular adhesion molecules or procollagen expression? Such factors may potentiate the proliferative obstructive process that frequently is associated with the calcification.

Dr. Bando. That is a very good point. We have not yet done special studies on the explanted homografts, so we cannot comment further regarding endothelial mechanisms for homograft failure.

Dr. Davis Drinkwater (Los Angeles, Calif.). We recently evaluated our experience in this area at the University of California at Los Angeles. Like you and the Toronto group, we found that the best long-term results may be

achieved with a large-sized allograft in the orthotopic position. We did not, however, find a difference between the aortic and pulmonary homografts, as you did. Indeed, we found that the use of an oversized orthotopic xenograft in the form of a bioprosthetic valve had excellent longevity. I am wondering whether you can clarify several issues. You said that the extension material did not appear to be a factor. Was the material placed as a circumferential extension, which was a commonly practiced technique in making right ventricle-pulmonary artery connections, or were they just patch overlays? Early on, we also used this technique for extending the homograft away from the sternum, and we found that the circumferential configuration was at greater risk for future obstruction because of intimal proliferation.

Dr. Bando. We use it as a patch overlay.

Dr. Drinkwater. Was the difference in age groups between the aortic and the pulmonary homograft (I think it was 11 versus almost 15 years) a significant one in terms of the outcome data? Does this difference reflect a differing time period and, therefore, have bearing on the outcome data resulting from improved preservation and handling techniques in the more modern era?

Dr. Bando. I do not think so. We looked at both the anastomosis material and the anastomosis technique, and there was no difference.

Dr. El-Gamel (Manchester, United Kingdom). Have you looked at the donor age of the aortic homografts and correlated that with the degree of calcification? Do you think that is possibly a risk factor?

Dr. Bando. We tried to obtain the donor age but were successful in only about 80%. Thus we could not include the data in the multivariate analysis.

Appendix 1. Patient weight and homograft size

	Homograft	
	Aortic	Pulmonary
Weight at operation (kg)		
Range	2.3-91.2	3.0-131.0
Mean	33.7	40.9
Median	28.0	42.6
Conduit anulus diameter (mm)		
Range	7-28.5	15-32
Mean	20.5	23.4
Median	21.0	23.0