Homograft use in reoperative aortic root and proximal aortic surgery for endocarditis: A 12-year experience in high-risk patients

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Objectives: We examined the early and midterm outcomes of homograft use in reoperative aortic root and proximal aortic surgery for endocarditis and estimated the associated risk of postoperative reinfection.

Methods: From January 2001 to January 2014, 355 consecutive patients underwent reoperation of the proximal thoracic aorta. Thirty-nine patients (10.9%; mean age, 55.4 ± 13.3 years) presented with active endocarditis; 30 (76.9%) had prosthetic aortic root infection with or without concomitant ascending and arch graft infection, and 9 (23.1%) had proximal ascending aortic graft infection with or without aortic valve involvement. Sixteen patients (41.0%) had genetically triggered thoracic aortic disease. Twelve patients (30.8%) had more than 1 prior sternotomy (mean, 2.4 ± 0.6).

Results: Valved homografts were used to replace the aortic root in 29 patients (74.4%); nonvalved homografts were used to replace the ascending aorta in 10 patients (25.6%). Twenty-five patients (64.1%) required concomitant proximal arch replacement with a homograft, and 2 patients (5.1%) required a total arch homograft. Median cardiopulmonary bypass, cardiac ischemia, and circulatory arrest times were 186 (137-253) minutes, 113 (59-151) minutes, and 28 (16-81) minutes. Operative mortality was 10.3% (n = 4). The rate of permanent stroke was 2.6% (n = 1); 3 additional patients had transient neurologic events. One patient (1/35, 2.9%) returned with aortic valve stenosis 10 years after the homograft operation. During the follow-up period (median, 2.5 years; range, 1 month to 12.3 years), no reinfection was reported, and survival was 65.7%.

Conclusions: This is one of the largest North American single-center series of homograft use in reoperations on the proximal thoracic aorta to treat active endocarditis. In this high-risk population, homograft tissue can be used with acceptable early and midterm survival and a low risk of reinfection. When necessary, homograft tissue may be extended into the distal ascending and transverse aortic arch, with excellent results. These patients require long-term surveillance for both infection and implant durability. (J Thorac Cardiovasc Surg 2014;148:989-94)

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Surgery for active infective endocarditis carries significant mortality. Several specific factors, including whether the patient has native or prosthetic valve infection, abscess formation, or root destruction, can significantly affect the outcome. Reoperation for aortic root infection is technically challenging and has been associated with mortality of up to 39%.[1,2] Homograft aortic root replacement for infective native or prosthetic endocarditis has been described with reasonable results in Europe and Japan, including low reinfection rates (5.4%-8%) and 16% to 25% early

mortality.[3-5] From centers in the United States, there is a paucity of reports regarding complex aortic root reconstruction with a homograft for active endocarditis, specifically after previous repair of the root and ascending aorta. Also, there are no extensive data on longer-term outcomes or reinfection rate. Therefore, we report our 12-year experience with these complex, high-risk procedures.

METHODS

Between January 2001 and January 2014, 355 consecutive patients underwent reoperation on the proximal aorta. Data were collected from a prospectively maintained database. Approval of the study was obtained from Baylor College of Medicine's institutional review board. Thirty-nine (10.9%) of these patients (mean age, 55.4 ± 13.3 years; 34 [87.2%] were male) presented with active infection involving their prosthetic aortic root, prior ascending or arch graft, or both. The majority of these patients were referred from outside facilities and had already been treated with antibiotics for an extensive period. While in the hospital, they continued to receive antibiotics as indicated by current or previous cultures.

Patient characteristics and demographics are outlined in Table 1. The postoperative outcomes assessed included early neurologic events, renal insufficiency necessitating hemodialysis, hospital length of stay, early and late reinfection rate, early and midterm survival, and operative mortality.

Operative Details

All patients were treated with surgical implantation of a cryopreserved homograft conduit (Life Net Health Bio-Implants Division, Virginia Beach,

TABLE 1. Preoperative characteristics and demographics of 39 patients who underwent reoperative aortic root and proximal aortic surgery for endocarditis

	All patients (N = 39)	Valved homografts (n = 29)	Nonvalved homografts (n = s10)	P value
Age (y)	55.4 ± 13.3	53.3 ± 13.6	61.6 ± 11.4	.0931
Male gender	34 (87.2)	24 (82.8)	10 (100)	.302
>1 previous sternotomy	12 (30.8)	10 (34.5)	2 (20.0)	.693
Preoperative hypertension	32 (82.0)	24 (82.7)	8 (80.0)	1.00
Prior or current smoker	23 (60.5)	19 (65.5)	4 (44.4)	.436
Congestive heart failure on admission	22 (56.4)	18 (66.7)	4 (40.0)	.258
Genetically triggered thoracic aortic disease	16 (41.0)	13 (44.8)	3 (30.0)	.353
Prior neurologic event (stroke or TIA)	8 (20.5)	7 (24.1)	1 (10.0)	.653
Chronic obstructive pulmonary disease	7 (17.9)	6 (20.7)	1 (10.0)	.653
Preoperative renal insufficiency	7 (17.9)	6 (20.7)	1 (10.0)	.653
Preoperative atrial fibrillation	6 (15.4)	4 (13.8)	2 (20.0)	.636
Previous operations				
Aortic root and ascending aortic replacement	21 (53.8)	20 (69.0)	1 (10.0)	
Ascending aortic replacement only	7 (17.9)	1 (3.5)	6 (10.0)	
Aortic valve replacement only	6 (15.4)	6 (20.7)	—	
Supracoronary ascending graft with aortic valve replacement	5 (12.8)	2 (6.9)	3 (30.0)	

Values are number (percentage) for binary variables and mean (± standard deviation) or median (interquartile range) for continuous variables. Tests performed were the Fisher exact test for binary variables and the Student *t* test or Wilcoxon rank-sum test for continuous variables, as appropriate. *TIA*, Transient ischemic attack.

Va). Twelve patients (30.8%) had more than 1 prior sternotomy. Cardiopulmonary bypass inflow was established by cannulating the right axillary artery in 25 patients (64.1%), the femoral artery in 7 patients (17.9%), the aorta in 5 patients (12.8%), and the innominate artery in 2 patients (5.1%). Twenty-seven patients (69.2%) underwent hypothermic circulatory arrest (temperature 20°C-24°C) for concomitant proximal arch or total arch reconstruction; all except 3 received unilateral or bilateral antegrade cerebral perfusion. The patients who required a valved homograft (n = 29, 73.4%) had aortic root abscesses. The abscess cavity and the aortic annulus were aggressively debrided, and all infected and devitalized tissue was removed. Specific attention was paid to removing all residual prosthetic material, including previously placed pledgets, Dacron graft, and prosthetic valve annular cloth. Any structural cardiac defects resulting from extension of an infected process or from necessary thorough debridement were repaired with bovine pericardium, which was used to patch residual periannular abscess cavities in 2 patients. Perforation of the anterior leaflet of the mitral valve was repaired primarily in 2 patients: 1 who required complete resection of the P2 leaflet for perforation and 1 who required excision of vegetation from the anterior leaflet (Table 2).

In the implantation of valved root homograft conduits, the proximal suture line of the trimmed cryopreserved homograft was constructed with continuous 2-0 or 3-0 Prolene suture and, when necessary, reinforced with pericardial pledgets. In 14 patients (50%), the coronary ostia were reimplanted as buttons with 5-0 or 6-0 running Prolene. In patients in whom the coronary buttons could not be mobilized (n = 31, 79.5%) because of extensive scar tissue, an interposition graft of autologous saphenous vein was placed between the homograft and the coronary artery (left or right) origin. In only 1 patient, an 8-mm Dacron graft was attached to the left main coronary button (Table 2).

For the distal anastomosis and arch repair, nonvalved homografts were used in 10 patients (25.6%) to replace the ascending aorta (Table 2). The distal anastomosis of the homograft conduit to the native aorta was performed with running 3-0 or 4-0 Prolene. If the proximal or the total arch needed replacement, a second additional segment of nonvalved homograft tissue was used when necessary to extend the length of the initial root in cases in which the valved homograft root was not long enough to replace the entire proximal or total arch. With regard to the arch vessels, an island anastomosis was performed with 4-0 or 5-0 Prolene suture. Intraoperative cultures were sent for microbiologic analysis.

Postoperative Care and Follow-up

Intravenous antibiotics were continued for approximately 4 to 6 weeks. The specific regimen depended on the patient's preoperative and intraoperative culture results. Patients were discharged with a peripherally inserted central catheter line for administering the intravenous antibiotics. Late survival and morbidities were determined by clinical follow-up, direct patient inquiry, and survey of the Social Security Death Index. Echocardiographic data were examined to access homograft performance. The median follow-up period was 2.5 years (range, 1 month to 12.3 years).

TABLE 2. Intraoperative data (N = 39)

Cannulation	
Axillary	25 (64.1)
Femoral	7 (18.0)
Direct aortic	5 (12.8)
Innominate	2 (5.1)
Procedures/reoperations	
Valved homografts	29 (74.3)
Cabrol/hemi-Cabrol or SVG to RCA or LAD	21 (72.4)
Nonvalved homografts	10 (25.6)
Proximal arch replacement	25 (64.1)
Total arch replacement	2 (5.1)
Mitral valve repair	2 (5.1)
Need for IABP	4 (10.2)
Need for ECMO	3 (7.7)
Cardiopulmonary bypass time (min)	186 (137-253)
Cardiac ischemia time (min)	113 (59-151)
Circulatory arrest time (min)*	28 (16-81)
Antegrade cerebral perfusion time (min)†	28 (16.5-73)
Hospital stay (d)	20 (13-35)

Values are number (percentage) for binary variables or median (interquartile range) for continuous variables. *ECMO*, Extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump; *LAD*, left anterior descending artery; *RCA*, right coronary artery; *SVG*, saphenous vein graft. *n = 27. †n = 24.

Statistical Analysis

Continuous variables were summarized and presented as mean (± standard deviation) when normally distributed and median (interquartile range) when non-normally distributed. Associations between the use of a valved homograft and the outcomes (in-hospital mortality and postoperative neurologic deficit) were tested with the Student t test or Wilcoxon rank-sum test for normally and non-normally distributed data, respectively. Binary variables were tabulated, and associations were measured with the Pearson chi-square or, when cell sizes were small, the Fisher exact test. Survival functions were estimated by using the Kaplan–Meier method. All analyses were performed with Stata IC 13.1 (Stata Statistical Software: Release 13; StataCorp LP, College Station, Tex).

RESULTS

Operative Mortality

Operative mortality was 10.3% (n = 4). One death (n = 1, 2.6%) was intraoperative in a patient with Marfan syndrome with 2 prior sternotomies for root and ascending graft replacement. Two of the other patients had a complicated postoperative course and required extracorporeal membrane oxygenation for hemodynamic instability and inability to ventilate. These patients developed multiorgan failure, and the families withdrew support on postoperative days 11 and 43. The last patient who died had 2 prior sternotomies for aortic valve replacement, ascending aortic graft placement, and coronary artery bypass grafting. This patient had a prolonged postoperative course that included respiratory failure that necessitated extracorporeal membrane oxygenation and renal failure from which he recovered. The patient received a new dual pacemaker on postoperative day 29 and collapsed a few hours later. Despite cardiopulmonary resuscitation, the patient died.

Neurologic Events

One permanent stroke (n = 1, 2.6%) was observed among the survivors. The stroke occurred in the left middle cerebral artery territory, causing right hemiplegia. The patient was transferred to an extended-care facility and died 4 years later. Transient neurologic events occurred in 3 patients, 2 of whom fully recovered. The third patient recovered successfully from the event but had a prolonged, complicated postoperative course and died 43 days postoperatively.

Long-Term Complications Requiring Operation

Among the postdischarge survivors (n = 34; Figure 1), 1 patient (n = 1, 2.9%), who had Marfan syndrome, returned 10 years later with structural degeneration of the homograft and aortic stenosis. The homograft was removed, and a biologic valve and supracoronary Dacron graft were placed. Table 3 outlines all of the short- and long-term postoperative complications that occurred in our series. In univariate analysis, none of the various preoperative, intraoperative, and postoperative variables we examined was predictive of either operative mortality or postoperative neurologic deficit (Table 4).

TABLE 3. Postoperative complications (N = 38)

Operative mortality*	4 (10.2)
Ventilatory support >48 h	21 (55.3)
Atrial fibrillation	9 (23.7)
Postoperative renal insufficiency (permanent or transient)	9 (23.7)
Tracheostomy	8 (21.0)
Pacemaker	6 (15.4)
Deep vein thrombosis	5 (13.2)
Neurologic events	
Permanent stroke	1 (2.6)
Temporary neurologic deficit	3 (7.9)
Reoperation for bleeding	3 (7.9)
Myocardial infarction	1 (2.6)

Values are number (percentage). *N = 39 (1 intraoperative death).

DISCUSSION

Our study represents a 12-year, single-center experience in a group of high-risk patients with endocarditis whose aortic root or ascending aorta and aortic arch were replaced with cryopreserved homografts. Six of the patients in this series had previously undergone aortic valve replacement only, and all 6 presented with perivalvular abscess or dehiscence. The remainder had undergone ascending graft replacement with or without aortic valve or total aortic root replacement. There is no evidence in the literature that clearly supports any particular choice of aortic root conduit or valve for patients with prosthetic aortic valve or root endocarditis.[5-10] The theoretic advantage of the homograft is resistance to infection because the graft is biologic and contains no artificial material.[11] Experienced centers have chosen to use other prosthetic materials because homografts are not always immediately available and present significant technical challenges when reoperation is necessary for degeneration and calcification.[7]

Meticulous debridement and extirpation of all infected tissues can be even more important than the choice of
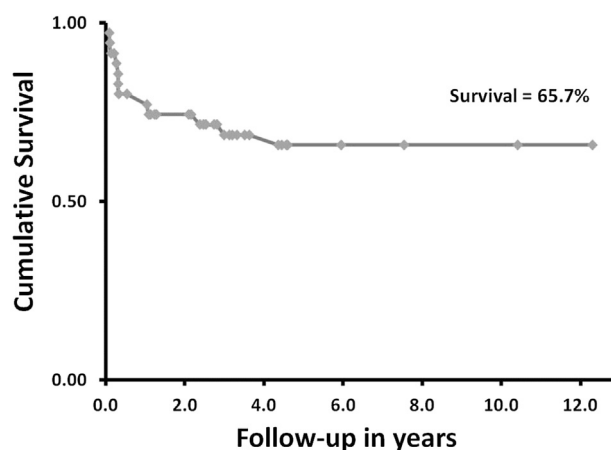

FIGURE 1. Kaplan–Meier survival curve among survivors (n = 35).

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TABLE 4. Univariate analysis and association with in-hospital mortality and postoperative neurologic deficit

	Operative mortality P value	Postoperative neurologic deficit P value
Age (y)	.7506	.306
Gender	1.00	.517
Genetic tissue disorders	1.00	.557
Preoperative hypertension	1.00	1.00
Congestive heart failure on admission	.6	1.00
COPD	.56	1.00
Preoperative stroke	.502	1.00
Preoperative TIA	1.00	1.00
Prior neurologic deficit	1.00	.56
Preoperative renal failure	.563	.147
Valved homograft	1.00	1.00
Nonvalved homograft	1.00	1.00
Proximal or total arch replacement	.292	1.00
Circulatory arrest time (min)*	.1941	.1847
Antegrade cerebral perfusion (min)†	.3134	.2932
Cardiopulmonary bypass time (min)	.4874	.2343
Cardiac ischemia (min)	.8169	.3294
Postoperative neurologic deficit‡	.291	—
Pacemaker‡	1.00	1.00
Reoperation for bleeding‡	1.00	.291
Ventilation >48 h‡	.238	.613
Postoperative atrial fibrillation‡	1.00	.233

Values are number (percentage) for binary variables and mean (± standard deviation) or median (interquartile range) for continuous variables. *COPD*, Chronic obstructive pulmonary disease; *TIA*, transient ischemic attack. *n = 27. †n = 24. ‡n = 38 (1 intraoperative death).

prosthetic valve.[12] In addition to debriding the abscess cavities, it is our practice to use a cryopreserved homograft in patients who present with an infected aortic valve or root. Homograft use is supported by the excellent results— including mortality rates of 3.7% and 3.9%—reported by Lytle and colleagues[8] and Sabik and colleagues[11] more than a decade ago. Since then, there has been a paucity of reports of homograft use in the United States, especially in reoperated infected aortic roots, but it has been advocated extensively in Europe.[4,5] In the largest reported contemporary homograft series, Musci and colleagues[5] described their 20-year experience with 221 patients who underwent homograft aortic root replacement for endocarditis of the native (n = 99) or prosthetic (n = 122) aortic valve. Early (30-day) mortality in the prosthetic valve endocarditis group was 25.4%; 29.1% of the deaths were intraoperative. The investigators noticed that 30-day mortality was substantially lower in their native-valve endocarditis group (16.1%; 6.2% of these deaths were intraoperative).

In our group of 39 patients, all of whom had reoperations, in-hospital mortality was 10.3% (n = 4), including 1 intraoperative death. Our mortality rate is similar to the 11% rate reported by Hagl and colleagues[6] from the Mount

Sinai Group in New York. Only 3 of their 28 patients had homograft placement; the rest received a mechanical composite valve graft. Most other reports that include a mix of prosthetic and biologic valve conduits show higher mortality rates, especially in reoperative patients,[7,12-14] such as those included in our study. Compared with the patients in the Cleveland Clinic series,[8] the patients in the current series had higher mortality. This could be explained by the fact that the percentage of patients who required circulatory arrest for additional proximal arch or total arch replacement was higher in our series (54% vs 15%).[8] In addition, the permanent stroke rate among survivors in our study was 2.6% (n = 1), which is somewhat lower than the rates reported by others.[7,9]

During the median follow-up of 2.4 years (range, 1 month to 12.3 years), our patients, who all received homografts, had 100% freedom from reinfection. In comparison, the University of Pennsylvania group reported that for patients who received mechanical conduits, biological conduits, and homograft roots, freedom from reinfection was 84% ± 7%, 94% ± 4%, and 75% ± 11%, respectively, at 1 year and 74% ± 10%, 89% ± 6%, and 64% ± 14%, respectively, at 5 years.[7] David and coworkers[12] reported that freedom from recurrent infective endocarditis was 91% ± 2% at 5 years for all patients (native and prosthetic valve) and 84% ± 4% and 90% ± 4% at 15 years for patients treated for native and prosthetic endocarditis, respectively. In their study, few patients (18/261 patients [6.9%] with aortic valve replacement) received a homograft; most patients received a mechanical valve or conduit. The authors concluded that the type of valve had no effect on the risk of recurrent endocarditis, and they emphasized the importance of radical debridement and implanting a new valve on healthy and strong tissue.[12] Reinfection rates of 5.4% and 3.7% were observed by Musci and colleagues[5] and Lytle and al,[8] respectively. Leontyev et al[15] reported that their 172 patients (including 76 who had reoperation) had a 5-year freedom from recurrent endocarditis of 80% ± 4%. None of the patients who received a homograft (n = 13, 7.5%) had recurrent endocarditis.[15] The authors stated that they were unable to show a statistically significant effect of implanted valve type on recurrent infection. A review by Perrotta and Lentini[10] found that using a stentless bioprosthesis resulted in the same low reinfection rate as when using cryopreserved homografts. Our series was not intended to compare bioprosthetic valves or homografts with mechanical valves. We encountered no reinfection, which we attribute to aggressive debridement and the use of homograft tissue.

Only 1 patient among the 34 survivors in our series (2.9%) required reoperation for structural deterioration during our follow-up. This patient developed severe aortic stenosis at 10 years, and he required a bioprosthetic valve and a supracoronary aortic graft. Ten-year freedom from

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reoperation was 89% ± 2% as reported by David and colleagues[12] in their series of 383 patients with mechanical (n = 214), bioprosthetic (n = 133), and homograft valves (n = 18). The Stanford group[9] reported that freedom from reoperation in patients with mechanical valves was 74% ± 9% at 10 years and 74% ± 9% at 15 years; they noticed a decline in the freedom from reoperation by the 10th year for patients who had bioprosthetic valves (56% ± 5% at 10 years, 22% ± 6% at 15 years, *P* > .64). In their bioprosthetic group, the indication for reoperation was structural degeneration in 63% of patients. For patients aged more than 60 years, the freedom from reoperation was acceptable after mechanical-valve or bioprosthesis implantation, but for younger patients, the freedom from reoperation after bioprosthesis implantation was low (51% ± 5% at 10 years). In Musci and colleagues'[5] series of homograft operations for native and prosthetic valve endocarditis, the 1-, 5-, and 10-year freedom from reoperation was 91.5% ± 4.7%, 79.8% ± 7.7%, and 79.8% ± 7.7%, respectively, for patients aged less than 40 years (n = 46); 95.6% ± 2.5%, 91.8% ± 3.5%, and 84.4% ± 5.2%, respectively, for patients aged 40 to 60 years (n = 97); and 96.5% ± 2.4%, 92.9% ± 4.2%, and 88.7% ± 5.8%, respectively, for patients aged more than 60 years.

With regard to complete heart block after surgery, 15.4% of our patients required pacemakers. In comparison, the rate of permanent pacemaker implantation among reoperative patients was 37% in Lytle and colleagues'[8] series and 19.7% in Leontyev and colleagues'[15] series. Thus, the need for pacemaker implantation to treat postoperative complete heart block is common among these high-risk patients. It is not specific to the aortic conduit used but is associated with more extensive disease and the need for extensive debridement.

Concerns regarding the technical complexity of the initial operation, the availability of homograft tissue, and the potential need for reoperation on a severely calcified homograft have led several investigators to prefer mechanical or nonhomograft biologic roots.[6,9,12] In contrast, because reinfection can pose complex and challenging problems, we place greater emphasis on reinfection-free survival than on the long-term risk of reoperation; thus, we favor homografts over these other options. It is possible that the risks posed by structural deterioration of the valve in a homograft root will increasingly be ameliorated as the use of transcatheter aortic valve implantation becomes more common.[16-18]

Study Limitations

The limitations of our study include the small number of patients, although, to our knowledge, ours is one of the largest reported studies in North America. Also, the retrospective and nonrandomized design of this study makes it subject to interpretation bias. We did not attempt to make this a comparative study. The availability of the homograft conduit at our institution may have affected our decision to make it our conduit of choice in cases of prosthetic root endocarditis and proximal aortic infection.

CONCLUSIONS

The use of homograft material to replace the aortic root, the ascending aorta, and the arch in patients with reoperative endocarditis can result in acceptable early and midterm survival and a low reinfection rate. Aggressive debridement is important to long-term survival without reinfection. Structural degeneration, which was uncommon in our patients, is even less of a concern today because percutaneous valve technology is now commercially available. Long-term follow-up is important in this high-risk patient population.

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