Homograft aortic root replacement in native or prosthetic active infective endocarditis: Twenty-year single-center experience

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Objective: We compared early and long-term results of cryopreserved homograft aortic root replacement in native valve endocarditis or prosthetic valve endocarditis associated with periannular abscess.

Methods: Between May 1986 and December 2007, 1163 patients with endocarditis were operated upon. Of these, 221 patients (n = 185 men, median age 55 years) had homograft aortic root replacement due to 99 cases of native valve endocarditis (45%) and 122 of prosthetic valve endocarditis (55%). Perinannular abscess developed in 189 patients (86%), and aortoventricular dehiscence in 120 (63.5%) of them. Perioperative characteristics, probability of survival, freedom from recurrence, and reoperation were analyzed. Follow-up (mean 5.2 ± 0.4 years, maximum 18.4 years) was completed in 96.8% with a total of 1127 patient-years.

Results: Overall native valve endocarditis survival at 30 days and 1, 5, and 10 years was $83.8\% \pm 3.7\%$, $76.6\% \pm 4.3\%$, $66.5\% \pm 4.9\%$, and $47.3\% \pm 5.6\%$, respectively, significantly better than for patients with prosthetic valve endocarditis, who had a greater tendency toward abscess formation ($P = .029$). Thirty-one patients (14.0%) required reoperation either for structural valve deterioration (n = 19, 8.6%), with a greater tendency in patients aged <40 years, or for recurrent endocarditis of the homograft (n = 12, 5.4%). One-year reoperation mortality rate was 16.1% (n = 5).

Conclusions: Homograft aortic root replacement in active infective endocarditis with periannular abscess formation shows satisfactory early and long-term results with significantly better survival in native valve endocarditis than prosthetic valve endocarditis. It is associated with a low recurrence rate, although the risk of structural valve deterioration increases over time, especially in young patients, and reoperation remains a challenge. In our institution, the homograft remains the preferred valve substitute in active infective endocarditis with periannular abscess formation. (J Thorac Cardiovasc Surg 2010;139:665-73)

Despite improvements in medical therapy, the incidence of active infective endocarditis (AIE) and also the proportion of approximately one-third of patients with endocarditis requiring surgery because medical therapy has failed remain unchanged.¹ Surgical treatment for AIE still carries a high mortality risk, and results of surgery depend on many variables, especially on whether the patients have native valve endocarditis (NVE) or prosthetic valve endocarditis (PVE),² which is a very severe complication of valve replacement and frequently associated with paravalvular abscess formation,³⁻⁵ a destructive process that can progressively and very rapidly lead to total aortic root destruction.

It has been our surgical strategy to treat active infective aortic root endocarditis by radical excision of all infected

tissue, drainage and exclusion of myocardial abscesses from the blood stream, repair with homologous material of any cardiac defects caused by infection, and reconstruction of the aortic root with a cryopreserved aortic homograft.⁶

This study was undertaken to review the 20-year experience of homograft aortic root replacement (ARR) at the Deutsches Herzzentrum Berlin and to reevaluate that strategy. The goals of this retrospective study were: (1) to characterize the demographic and clinical differences between patients with NVE and patients with PVE and the nature of their endocarditic disease; (2) to compare early and long-term results of cryopreserved homograft ARR in these patients, especially with regard to the survival in relation to periannular abscess formation; (3) to determine the rates of reoperation due to homograft endocarditis recurrence; and finally (4) to analyze the freedom from reoperation due to structural valve deterioration (SVD) especially with regard to patient age at initial operation.

PATIENTS AND METHODS

Patient Population

An overview of the patient population is given in Table 1. Between May 1986 and December 2007, a total of 1258 operations in 1163 patients with AIE were performed at the Deutsches Herzzentrum Berlin, 925 (73.5%) of them for NVE and 333 (26.5%) for PVE. Of these patients, 221 (n = 185 men, median age 55, range 2–81 years) who had ARR with cryopreserved

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Abbreviations and Acronyms

AIE = active infective endocarditis
 ARR = aortic root replacement
 NVE = native valve endocarditis
 PVE = prosthetic valve endocarditis
 SVD = structural valve deterioration

homograft due to 99 cases of NVE (45%) and 122 cases of PVE (55%) were enrolled in the study. To exclude the effects of other endocarditic cardiac pathologies on the outcome after homograft ARR, such as mitral valve endocarditis, jet lesions, ventricular septal defects, or right-sided endocarditis, only patients with isolated aortic valve and root endocarditis were enrolled.

An overview of the microbiologic epidemiology and the differences between the patients with NVE and patients with PVE is given in Table 2. Of the other patients ($n = 951$), 426 were operated on due to isolated aortic valve endocarditis; 280 due to mitral valve endocarditis, with 219 cases of mitral valve replacement and 61 of mitral valve repair; 157 due to double valve endocarditis; and 88 due to isolated ($n = 59$) or combined ($n = 29$) right- and left-sided endocarditis.

Indications for Surgery

Table 3 presents an overview of the main operative indications during the acute phase of AIE. In general, patients had several indications for surgery during antibiotic treatment for AIE. The majority had to be operated on due to progressive heart failure, suspected vegetations, recurrent septic embolism, or therapy-resistant infections. In the NVE group, 67 (67.7%) patients additionally showed aortic valve destruction. Early prosthetic infection (<30 days) was found in 31 (25.4%) patients from the PVE group.

Surgical Technique of ARR

ARR is performed during standard cardiopulmonary bypass. Until 1999, antegrade cold crystalloid cardioplegia with topical ice slush and with mild systemic hypothermia (32 °C) was used; later this was replaced by normothermic blood cardioplegia.

After extensive debridement and complete removal of all macroscopically involved tissue of the diseased aortic root, the coronary ostia are excised with a small rim of surrounding aortic tissue. This is followed by intensive irrigation of the infected area with polyvidone-iodine solution. If the aortic annulus is not destroyed by abscess, the proximal suture line of the trimmed cryopreserved homograft conduit is placed using interrupted 4-0 polypropylene sutures preserved in polyvidone-iodine solution and reinforced with glutaraldehyde-fixed equine pericardial pledgets from the ventricle to the aorta at the aortic ventricular junction. In the presence of severe aortic root endocarditis with extensive annular and subannular destruction by abscess formation, proximal homograft anastomosis is performed with the lower margin of the abscess cavity in the left ventricular outflow tract in the area of intact endocardial tissue. In the case of abscess aortoventricular dehiscence, restoration of the structure and anchoring of the mitral valve can be achieved by making use of the anterior mitral leaflet adhering to the aortic homograft. The coronary ostia are reimplanted into the homograft conduit using the button technique with 5-0 or 6-0 running monofilament sutures. Finally, the distal anastomosis of the ascending aortic segment of the homograft conduit, which is used for replacing the native ascending aorta, is performed with 4-0 running polypropylene sutures.

Follow-up

Follow-up was completed by telephone contact with the patient, by analyzing standardized mail questionnaires sent to the patients, by consulting

the population registry, and by contacting peripheral hospitals. In the NVE group, 3 patients were lost to follow-up; follow-up was completed in 96.9% of all cases with a median follow-up time of 6.5 years (range 0–17.7 years) and 654.9 patient-years. In the PVE group, 4 patients were lost to follow-up; follow-up was completed in 96.7% of all cases with a median follow-up time of 2 years (range 0–18.4 years) and 471.5 patient-years. The significantly shorter duration of median follow-up for the PVE group is due to the fact that many patients from this group were operated on in recent years.

Statistical Analysis

Statistical analysis was performed using SPSS 12.0.1 for Windows. For quantitative data, medians and ranges or means and standard error of the mean were calculated. Qualitative data are reported as relative frequencies and percentages. For comparison of different patient groups, Pearson's χ^2 test or Student t test was used. Analysis of survival and freedom from end points was performed according to the method of Kaplan-Meier. Standard errors of the mean for Kaplan-Meier estimates were calculated by the Greenwood formula. Comparison of survival in different patient groups was performed using weighted log-rank tests. All the statistical analyses were performed by an independent statistician.

RESULTS**Demographic and Clinical Differences Between Patients With NVE and Patients With PVE**

Patients with PVE were significantly older ($P \leq .001$); preoperatively, they showed renal insufficiency significantly more often ($P = .024$) and they more often developed abscess formation ($P = .003$) than patients with NVE. By analyzing the extent of the abscess formation, it was found that patients with PVE more often showed severe aortic root destruction with aortic-ventricular dehiscence compared with patients with NVE ($P \leq .001$), in whom predominantly well-circumscribed and localized abscess formation was found (Table 1). Patients with PVE showed significantly more infection caused by *Staphylococci* ($P = .016$) compared with the patients with NVE, in whom streptococcal infection was the main finding ($P \leq .001$; Table 2).

In the quantity of preoperative septic embolization, there was no difference between the groups, but analyzing the localization, the incidence of skin embolism was higher in patients with PVE ($P = .016$).

By analyzing the preoperative status, it was found that a large proportion of patients were referred to our department with advanced endocarditis and in a condition of cardiac and pulmonary decompensation. No significant differences were found in the degree of fever ($P = .955$) and septic shock ($P = .402$), cardiac decompensation ($P = .258$) leading to high-dose catecholamines ($P = .711$), or pulmonary edema ($P = .143$) with the need of intubation ($P = .359$) between the 2 groups. In terms of the urgency of operation, both groups showed a high percentage of patients having an emergency or urgent procedure ($P = .412$) with similar numbers of days from diagnosis until operation ($P = .891$).

Gender ($P = .680$), diabetes ($P = .198$), chronic obstructive pulmonary disease ($P = .144$), and intravenous drug

TABLE 1. Demographic and clinical differences between patients with NVE and patients with PVE (May 1986–December 2007)

	NVE	PVE	P value
Patients with AIE			.680
Men	84 (84.8%)	101 (82.8%)	
Women	15 (15.2%)	21 (17.2%)	
Total	99	122	
Age (y)			<.001
Median	50.0	60.0	
Mean age	47.4 ± 14.8	57.3 ± 14.8	
Range	2–76	18–81	
Age groups (y)			<.001
< 40	27	19	
40–60	54	43	
> 60	18	60	
Preoperative status			
Cardiac shock	5 (5.1%)	11 (9.0%)	.258
High-dose catecholamines	24 (24.2%)	27 (22.1%)	.711
Pulmonary edema	25 (25.2%)	21 (17.2%)	.143
Intubation	21 (21.2%)	20 (16.4%)	.359
Septic shock	8 (8.1%)	14 (11.5%)	.402
Renal insufficiency	24 (24.2%)	47 (38.5%)	.024
Dialysis	4 (4.0%)	11 (9.0%)	.144
Persistent fever	46 (46.4%)	57 (46.7%)	.955
Diabetes	18 (18.2%)	31 (25.4%)	.198
COPD	4 (4.0%)	11 (9.0%)	.144
Hypertension	17 (17.2%)	54 (44.3%)	<.001
Intravenous drug abuse	5 (5.1%)	5 (4.0%)	.217
Alcohol abuse	21 (21.2%)	7 (5.7%)	<.001
Septic embolization			
Quantity			.348
One	22 (22.2%)	23 (18.9%)	
Multiple	12 (12.1%)	9 (7.4%)	
Localization			
Cerebral	14 (14.1%)	20 (16.4%)	.644
Lung	3 (3.0%)	1 (0.8%)	.220
Spleen	10 (8.2%)	9 (9.1%)	.814
Kidney	7 (7.1%)	4 (3.3%)	.197
Eye	3 (3.0%)	1 (0.8%)	.220
Skin	3 (2.5%)	10 (10.1%)	.016
Aortic root abscess formation			.003
No	22 (22.2%)	10 (8.2%)	
Yes	77 (77.8%)	112 (91.8%)	
Extent of abscess formation			<.001
Localized abscess formation	42 (42.4%)	27 (22.1%)	
Aortic-ventricular dehiscence	35 (35.4%)	85 (69.7%)	
Operation performed as			.412
Elective	6 (6.1%)	11 (9.0%)	
Urgent	69 (69.7%)	91 (74.6%)	
Emergency	24 (24.2%)	20 (16.4%)	
Days until operation			.891
Median (range)	25 (2–161)	29.5 (2–133)	
Mean	40.0 ± 3.5	38.0 ± 2.7	
Follow-up (y)			.029
Completed	96.9%	96.7%	
Median	6.5	2	
Mean	6.6 ± 0.5	3.8 ± 0.4	

TABLE 1. Continued

	NVE	PVE	P value
Range	0–17.7	0–18.4	
Patient-years	654.9	471.5	

NVE, Native valve endocarditis; PVE, prosthetic valve endocarditis; AIE, active infective endocarditis; COPD, chronic obstructive pulmonary disease. Significant differences are in italic.

abuse ($P = .217$) were nonsignificant variables in the comparison, whereas hypertension ($P \leq .001$) was significantly higher in the PVE group and alcohol abuse in the patients with NVE ($P \leq .001$).

Overall Survival, Early (≤ 30 Days) and Late Mortality

The overall survival curves after homograft ARR in patients with NVE and patients with PVE are given in Figure 1. We found a highly significant better survival for the NVE compared with the PVE group. The 30-day and 1-, 5-, and 10-year survivals for the NVE group were $83.8\% \pm 3.7\%$, $76.6\% \pm 4.3\%$, $66.5\% \pm 4.9\%$, and $47.3\% \pm 5.6\%$, compared with $74.6\% \pm 3.9\%$, $67.1\% \pm 4.2\%$, $48.1\% \pm 4.9\%$, and $35.0\% \pm 5.4\%$ for the PVE group, respectively ($P = .029$).

Analysis of the survival curve showed a particularly clear difference between the 2 groups in the first 30 days. In the NVE group ($n = 99$), there were 16 early deaths (≤ 30 days) resulting in an early mortality rate of 16.1%. Of these, 1 was an intraoperative death due to myocardial failure (6.2%), 1 patient died of hemorrhagic shock in the first postoperative week (6.2%), 9 patients died of septic multiorgan failure (56.3%), 4 patients died of myocardial failure (25.0%), and 1 other died of other causes (6.2%).

In comparison, in the PVE group ($n = 122$) there were 31 early deaths (≤ 30 days) resulting in an early mortality rate of 25.4%. There were 9 (29.1%) intraoperative deaths: 6 patients died of myocardial failure and 3 patients died of septic multiorgan failure operated on as a last resort treatment. The causes of the other 22 early deaths in this group were septic multiorgan failure in 14 (45.2%), myocardial failure in 6 (19.3%), cerebral abscess formation in 1 (3.2%), and excessive esophageal bleeding in 1 other case (3.2%).

Analysis of early mortality in various subgroups of patients showed that patients with persistent fever despite antibiotic treatment (31.4%), patients requiring high doses of catecholamines (47.1%), patients on ventilation (53.7%), and those who arrived at our hospital in septic shock (72.7%) were highly exposed.

Comparison of late mortality (30 days to 1 year) showed similar rates in both groups. In the NVE group, the late mortality rate was 7.0%, with 7 late deaths due to septic multiorgan failure in 3, myocardial failure in 2, and other causes in 2 patients, compared with late mortality rate of

TABLE 2. Microbiologic epidemiology: Differences between patients with native valve endocarditis and patients with prosthetic valve endocarditis (May 1986–December 2007)

	NVE	PVE	<i>P</i> value
Staphylococci	26 (26.2%)	51 (41.8%)	.016
<i>S aureus</i>	19 (19.2%)	27 (22.1%)	.593
<i>S coagulase-negative</i>	4 (4.0%)	8 (6.6%)	—
<i>S epidermidis</i>	2 (2.0%)	8 (6.6%)	—
MRSA	—	4 (3.3%)	—
<i>S general</i>	1 (1.0%)	4 (3.3%)	—
Streptococci	41 (41.4%)	21 (17.2%)	<.001
<i>S general</i>	21 (21.2%)	12 (9.8%)	
<i>S viridans</i>	17 (17.2%)	6 (4.9%)	
<i>S B-hemolysis</i>	2 (2.0%)	2 (1.6%)	
<i>S epidermidis</i>	1 (1.0%)	1 (0.8%)	
Enterococcus	9 (9.1%)	16 (13.1%)	.348
Culture-negative	17 (17.1%)	21 (17.2%)	.994
Candida	1 (1.0%)	1 (0.8%)	—
Pseudomonas	—	1 (0.8%)	—
Others	2 (2.0%)	4 (3.3%)	—
Unknown	3 (3.0%)	7 (5.7%)	—

NVE, Native valve endocarditis; PVE, prosthetic valve endocarditis; MRSA, methicillin-resistant *Staphylococcus aureus*.

7.3% in the PVE group, with 9 late deaths due to septic multiorgan failure in 6, myocardial failure in 1, and other causes in 2 patients.

In addition, the comparison of the 426 patients who were operated on without homograft implantation due to isolated aortic valve endocarditis (NVE = 358 patients, PVE = 68 patients) showed the following survival rates: 81.2% $\pm$ 2.1%, 70.0% $\pm$ 2.4%, 57.7% $\pm$ 2.8%, 44.7% $\pm$ 3.2%, and 24.4% $\pm$ 4.1% for 30-day and 1-, 5-, 10-, and 15-year survivals in the NVE group compared with 80.9% $\pm$ 4.8%, 69.1% $\pm$ 5.6%, 52.5% $\pm$ 6.8% for 30-day and 1- and 5-year survivals in the PVE group, respectively (P = .626).

Survival in Relation to Abscess Formation

The comparison of the patient subgroups having abscess formation revealed a highly significant better survival of the NVE compared with the PVE group: the 30-day and 1-, 5-, 10-, and 15-year survivals for the NVE group were 83.0% $\pm$ 4.3%, 73.8% $\pm$ 5.0%, 65.0% $\pm$ 5.6%, 47.7% $\pm$ 6.5%, and 29.8% $\pm$ 8.7%, respectively, compared with 74.1% $\pm$ 4.1%, 66.8% $\pm$ 4.5%, 48.5% $\pm$ 5.1%, 36.7% $\pm$ 5.5%, and 31.0% $\pm$ 6.5% in the PVE group (P = .042).

Analyzing survival after homograft ARR in relation to the extent of abscess formation, there was a nonsignificant trend toward better survival in patients with localized abscess (n = 69) compared with those with severe aortic root destruction leading to aortoventricular dehiscence (n = 120): the 30-day and 1-, 5-, and 10-year survivals for patients with localized abscess were 84.0% $\pm$ 4.4%, 73.8% $\pm$ 5.3%, 61.9% $\pm$ 6.1%, and 44.8% $\pm$ 7.2%, respectively, in comparison

TABLE 3. Main indications for surgery

Indication	NVE	PVE
Progressive heart failure	80 (80.8%)	86 (70.5%)
+ vegetations	66 (66.6%)	35 (28.7%)
+ recurrent septic embolisms	24 (24.2%)	21 (17.2%)
+ therapy-resistant septic infections	16 (16.1%)	11 (9.1%)
Vegetations	81 (81.8%)	52 (42.6%)
Recurrent septic embolism	34 (34.3%)	32 (26.2%)
Therapy-resistant septic infection	25 (25.2%)	39 (31.9%)
Aortic valve destruction	67 (67.7%)	20 (16.4%)
Early prosthetic infection (<30 d)	—	31 (25.4%)

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

with 74.1% $\pm$ 4.0%, 67.3% $\pm$ 4.3%, 51.8% $\pm$ 4.8%, and 39.4% $\pm$ 0.5% in patients with aortoventricular dehiscence (P = .091; Figure 2).

Freedom From Reoperation Due to All Events

A total of 31 of 221 patients (14.0%) had either reinfection (n = 12, 6 patients with NVE and 6 patients with PVE) or SVD (n = 19, 11 patients with NVE and 8 patients with PVE) leading to reoperation following homograft ARR.

Analysis of the freedom from reoperation due to all events after homograft ARR in patients with NVE and patients with PVE showed no significant differences between the 2 groups: the 30-day and 1-, 5-, 10-, and 15-year freedom from reoperation was 97.6% $\pm$ 1.2%, 91.3% $\pm$ 3.2%, 83.7% $\pm$ 4.4%, 77.6% $\pm$ 5.3%, and 73.9% $\pm$ 6.2% for the patients with NVE in comparison to 98.0% $\pm$ 1.4%, 89.7% $\pm$ 3.3%, 84.2% $\pm$ 4.4%, and 79.3% $\pm$ 5.8% for 10 years for patients with PVE (P = .957).

Freedom From Reoperation Due to Reinfection

A total of 12 of 221 patients (5.4%) had reinfection leading to reoperation following homograft ARR in patients with NVE (n = 6) and patients with PVE (n = 6), resulting in 10-year freedom from reoperation of 92.9% $\pm$ 3.2% and 92.1% $\pm$ 2.5%, respectively (P = .913; Figure 3). Preoperatively, all 12 patients showed aortic root abscess formation.

Of the 6 cases of reinfection in the NVE group (6.0%), there were 2 early reinfections ($\leq$ 60 days, 2.0%), 2 late reinfections (60 days to 1 year, 2.0%), and 2 de novo infections 6.7 and 16.8 years after the first operation (2.0%). On reoperation, 1 patient received a mechanical valve, 2 a bioprosthesis, and 3 an aortic homograft. There was no intraoperative or cardiac-related death. One patient died on postoperative day 130, resulting in a 1-year reoperation mortality rate of 16.6% (1/6) for the NVE group.

The 6 reinfections of the PVE group (4.9%) were 3 early reinfections ($\leq$ 60 days, 2.5%), 2 late reinfections (1.6%), and 1 de novo infection 2.8 years after the first operation (0.8%). On reoperation, 2 patients received mechanical valves, 1 received a bioprosthesis, and 3 patients received

FIGURE 1. Survival after homograft aortic root replacement in native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE).

an aortic homograft. There was no intraoperative or cardiac-related death, and all patients survived the first year.

In summary, of the 12 patients reoperated upon due to reinfection, there was no intraoperative or cardiac-related death and 1 patient from the NVE group died on postoperative day 130, resulting in 1-year reoperation survival of 91.6% for this collective (11/12).

Freedom From Reoperation Due to SVD

SVD developed in 19 of 221 patients (8.6%), leading to reoperation following homograft ARR: 11 patients with NVE and 8 patients with PVE. Figure 4, A shows the freedom from reoperation due to SVD with no significant differences between the 2 groups: the 30-day and 1-, 5-,

and 10-year freedom from reoperation was 98.8% ± 1.2%, 96.3% ± 2.1%, 88.8% ± 3.8%, and 85.0% ± 4.5% for patients with NVE in comparison with 99.1% ± 0.9%, 94.4% ± 2.5%, 92.0% ± 3.3%, and 86.0% ± 5.2% for patients with PVE (P = .910).

In the NVE group, of the 11 of 99 patients (1.68%/patient-year), 3 had to be reoperated on due to early homograft valve insufficiency (3.0%) at a mean of 78 days (30–140 days) after the first operation. Four patients had homograft degeneration leading to severe aortic insufficiency (4.0%) and were reoperated on after a mean of 3.3 years (1.5–6.2 years). Another 4 patients had homograft calcification with severe aortic stenosis (4%) leading to reoperation after a mean of 5.9 years (1.8–10.9 years). On reoperation, 9

FIGURE 2. Survival after homograft aortic root replacement. Aortoventricular dehiscence versus localized abscess formation.

FIGURE 3. Freedom from reoperation due to reinfection after homograft aortic root replacement. *NVE*, Native valve endocarditis; *PVE*, prosthetic valve endocarditis.

patients received mechanical valves, 1 a bioprosthesis, and in 1, a 2-year-old child, a Ross operation was performed. There was no intraoperative or cardiac-related death. Two patients died, 1 on postoperative day 14 due to septic multi-organ failure and the other on postoperative day 64 due to pulmonary failure, resulting in a 1-year reoperation mortality rate of 18.1% (2/11) for the NVE group.

In the PVE group, of the 8 of 122 patients (1.7%/patient-year), 5 had to be reoperated upon within 1 year due to early homograft valve insufficiency or paravalvular leakage (4.1%) at a mean of 122 days (1–345 days) after the first operation.

Three patients had homograft degeneration (2.4%) leading to severe aortic insufficiency in 1 and severe aortic stenosis in 2 and were reoperated on at a mean of 5.4 years (4.2–6.8 years). On reoperation, 3 patients were given mechanical valves, 3 received a bioprosthesis, and 2 received an aortic homograft. Two patients died from cardiac failure (on the postoperative days 1 and 209), and the 1-year reoperation mortality rate was 25.0% for this group.

In summary, of the 19 patients reoperated upon due to SVD, 4 patients died within 1 year (mean 72 days, range 1–209 days), resulting in a 1-year reoperation survival rate of 78.9% for this collective (15/19).

FIGURE 4. A, Freedom from reoperation due to structural valve deterioration after homograft aortic root replacement in native valve endocarditis (*NVE*) and prosthetic valve endocarditis (*PVE*). B, Freedom from reoperation due to structural valve deterioration after homograft aortic root replacement. Age at operation.

Freedom From Reoperation Due to SVD According to Patient Age at Initial Operation

Figure 4, B shows the freedom from reoperation due to SVD in 3 patient age groups (<40 years, 40–60 years, >60 years) at the time of initial operation: the 30-day and 1-, 5-, and 10-year freedom from reoperation for the <40 years group (n = 46 patients) was 97.7% ± 2.3%, 91.5% ± 4.7%, 79.8% ± 7.7%, and 79.8% ± 7.7%. In comparison, the rates for the 40- to 60-year group (n = 97 patients) were 98.6% ± 1.4%, 95.6% ± 2.5%, 91.8% ± 3.5%, and 84.4% ± 5.2% and for the >60-year group (n = 78 patients), 100%, 96.5% ± 2.4%, 92.9% ± 4.2%, and 88.7% ± 5.8%.

The comparison showed no significant difference between the <40-year group and the 40- to 60-year group ($P = .141$) or between the 40- to 60-year and the >60-year groups ($P = .711$). Comparing the <40-year group and the >60-year groups, there was a higher tendency toward reoperation for the younger group ($P = .088$), which did not reach statistical significance, likely due to the low number of patients at risk for the period of 10 to 15 years postoperatively.

DISCUSSION

Our study presents 20-year single-center results in a group of high-risk patients with active infective NVE and PVE having ARR with cryopreserved homografts and compares the outcome of these patients. The results of our study confirm previous reports that documented worse outcomes of patients with PVE compared with patients with NVE in regard to higher operative mortality and poorer long-term survival.⁷⁻⁹

In our study, analysis of the survival curve shows a particularly clear difference between the 2 groups in the first 30 days. The argument can be forwarded that the better results in the NVE group are related to the fact that the patients with PVE in general had more advanced endocarditis and were more critically ill. As shown in our series, patients with PVE were not only significantly older but preoperatively they had a significantly higher prevalence of renal insufficiency and infection caused by *Staphylococci*. They more often had abscess formation with severe aortic root destruction leading to a higher rate of aortic-ventricular dehiscence than the patients with NVE (69.7% vs 35.4%). Each of these factors increases the clinical variability and complexity of AIE and may represent an additional possible explanation for much of the morbidity and mortality in the PVE group.^{3,5} Our study confirms previous reports that documented the association of periannular abscess complications with increased mortality and the need of surgery in almost all patients,^{2,5} underlined by recently published data by David and colleagues.¹⁰ They demonstrated that surgery for active endocarditis with paravalvular abscess was associated with high operative mortality, particularly in patients in shock and with abscess formation on both mitral and aortic annuli.

Despite high operative mortality and morbidity, the long-term survival was satisfactory considering how sick the patients were prior to surgery and the complexity of the operative procedures, similar to published data from Toronto and Stanford University.^{7,11} For the risk stratification and survival in our study, it has to be taken into consideration that our hospital is a referral surgical center receiving patients who have already been treated medically elsewhere and we had no input regarding the medical management. They were referred for surgery only after medical therapy failed.

The low early reinfection rate and the excellent long-term freedom from reinfection without any significant differences between the NVE and PVE groups reported in this study document the outstanding role of the homograft in the treatment and eradication of AIE and confirm the findings of previous publications.^{10,12} Additionally, in severe destructive endocarditis with aortoventricular dehiscence, restoration of the structure can be achieved by making use of the muscular cuff of the soft annulus and of the anterior mitral leaflet adhering to the aortic homograft.

However, several additional aspects have to be emphasized in this analysis. The goals of aggressive surgical treatment for acute aortic root endocarditis are radical excision of all infected tissue, drainage and exclusion of myocardial abscesses from the bloodstream, repair of any cardiac defects caused by infection, and reconstruction of the aortic root with the aim of placing a competent valve and preventing recurrent infection. We believe our lower risk was due both to these surgical principles and to the use of homografts, which by their natural biocompatibility are resistant to infection.¹³ In the evaluation of results of homograft series, one must clearly identify the incidence of AIE and abscess reported in the study population and the surgical techniques used. Kaya and associates¹⁴ reported only 4 cases of homograft endocarditis in 213 patients (1.9%) having ARR with a cryopreserved aortic homograft, but in their series only 125 patients (58.7%) had clinical evidence of AIE. O'Brien and colleagues¹² reported only 2 cases of early endocarditis in 1022 patients (0.19%) and freedom from late infection (34 patients) at 20 years was 89%, but endocarditis was reported as the preoperative indication in only 92 patients (9.0%) in their series compared with our study with 221 patients with endocarditis, 189 of them (85.5%) with abscess formation. David and coworkers¹⁰ reported on 135 patients with AIE (n = 69 NVE, 66 PVE) and paravalvular abscess. In their study, there were 16 episodes of recurrent endocarditis in 15 patients (11.1%) and the freedom from recurrent endocarditis was 82.4% at 15 years, but only 14 patients received an aortic homograft at the primary operation. Excellent results are reported by Sabik and colleagues¹³ from Cleveland Clinic, who analyzed their experience of homograft ARR in 103 consecutive patients with prosthetic aortic valve endocarditis presenting with an aortic root abscess in 78% of the cases. Four patients (3.8%) had recurrent endocarditis.

Their instantaneous risk of recurrent endocarditis differed from that found in other studies and peaked at 9 months after operation; freedom from recurrent endocarditis at 5 and 10 years was 95%.

Reinfection may be caused not only by virulent organisms but also by surgical factors such as inadequate debridement of necrotic tissues and the abscess cavity prior to exclusion from the circulation. In our study, all 5 patients in whom early recurrent endocarditis developed had deeply invasive and destructive infections, and the offending microorganisms were the same as in the first infection. Because of its complexity, homograft reoperation remains a challenge. In our study, 1 of 12 patients reoperated upon due to homograft endocarditis died on postoperative day 130, resulting in a low hospital mortality, which varies greatly in the literature.^{14,15}

The influence of the age of the recipient on the long-term durability of the homograft has been reported previously by numerous studies showing that younger patient age is the most important predictor of SVD.⁹ In our study, the comparison between the <40-year group and the >60-year group showed a greater tendency for reoperation due to SVD for the younger group, which did not reach statistical significance because of the low number of patients at risk in the long-term period ($P = .088$). Using the Weibull model to calculate long-term freedom from reoperation, which is based on the assumption that the risk of SVD increases with time and therefore that the estimates are still hypothetical, Takkenberg and colleagues¹⁶ demonstrated that median time to reoperation for SVD varies from 23 years in a 65-year-old patient down to approximately 12 years in a 25-year-old patient.¹⁶

Because of these data, the complexity of the operation, and the controversial discussion of the risk of recurrent endocarditis for mechanical and bioprosthesis reported in the literature, the superiority of the homograft in the treatment of AIE has been questioned. The best type of prosthesis for implantation in patients with native and prosthetic AIE is a matter of controversial discussion in the literature. However, the few studies that compare mechanical and biological prostheses are limited in terms of the numbers of patients, and the study populations are mostly not comparable with each other. In the study by Moon and colleagues¹¹ of patients with native and prosthetic endocarditis, the operative mortality, the survival rate, and the rate of freedom from reoperation were independent of whether a mechanical or a biological valve was implanted. Leyh and associates¹⁷ published a study that found the 1- and 5-year survival rates in patients with acute aortic valve prosthetic endocarditis who received an ARR to be independent of whether a homograft or a composite prosthesis was used. None of these patients ($n = 24$) had to be reoperated on because of reinfection. Many have treated this problem with prosthetic root replacement, using either mechanical or tissue valves. Additionally, excellent results have been reported in patients with AIE by using the Ross procedure, although the number of patients is still low.^{11,18,19}

Study Limitations

The present study is retrospective. Clinical end points such as exercise capacity and echocardiographic hemodynamic control could not be assessed. There is a natural bias in the clinical assessment of the 2 patient groups.

CONCLUSIONS

Homograft ARR in AIE with periannular abscess formation shows satisfactory early and long-term results with significantly better survival in NVE than PVE. It enables complete eradication of the infection by radical excision, replacement of all infected tissue of the aortic annulus and aortic root, and reconstruction of the left ventricular outflow tract, especially in severe destructive endocarditis with aortoventricular dehiscence. Homograft ARR is associated with a low endocarditis recurrence rate. The risk of SVD increases over time, especially in young patients, and reoperation remains a challenge. Even more than 45 years after its clinical introduction,²⁰ homograft ARR remains the preferred valve substitute in AIE with periannular abscess formation in our institution.

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