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ORIGINAL ARTICLE

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Cryopreserved aortic homografts for complex aortic valve or root endocarditis: a 28-year experience

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Key question

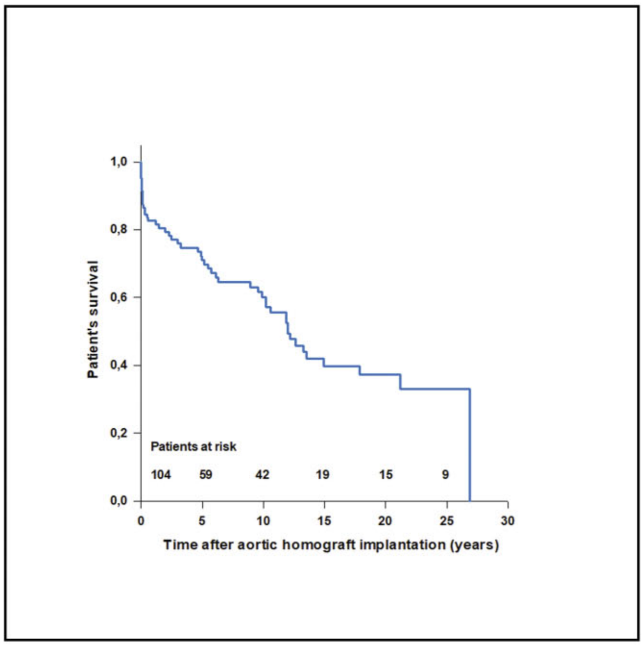
Which is the optimal surgical strategy in patients with complex aortic valve endocarditis?

Key finding(s)

Use of aortic homograft for complex infective endocarditis is associated with good early and long-term results.

Take-home message

Patients with infective endocarditis complicated by annular abscess may benefit from aortic valve or root replacement with aortic homograft.



Abstract

OBJECTIVES: The aim of this study was to evaluate early- and long-term outcomes of cryopreserved aortic homograft (CAH) implantation for aortic valve replacement (AVR) or aortic root replacement (ARR) in patients with or without complex infective endocarditis.

METHODS: All adult patients undergoing AVR or ARR with CAH at our institution between January 1993 and July 2021 were included in the study.

RESULTS: One hundred four patients, 75 males and 29 females, aged 59 ± 17 years, underwent AVR or ARR with CAH for infective endocarditis (*n* = 94, 90%) or aortic valve disease (*n* = 10, 10%). There were 33 (35%) native valve endocarditis and 61 (65%) prosthetic valve endocarditis, which were complicated by annular abscess in 77 (82%) patients, mitral valve endocarditis in 13 (14%) and tricuspid valve endocarditis in 13 (14%). The mean cardiopulmonary bypass time was 214 ± 80 min and the mean aortic cross-clamping time was

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164 ± 56 min. There were 12 (12%) hospital deaths and 7 (7%) postoperative low cardiac output syndrome requiring extracorporeal membrane oxygenation in 4 patients and intra-aortic balloon pump in 3. Thirty-nine (42%) patients died during the follow-up (94% complete). The mean survival time was 13.9 ± 1.2 years. Twenty-five patients (26%) underwent late reoperation for aortic homograft degeneration (*n* = 17, 18%), homograft endocarditis (*n* = 6, 7%), homograft dehiscence (*n* = 1, 1%) and mitral valve regurgitation (*n* = 1, 1%). The mean survival free from reintervention was 15.7 ± 1.2 years.

CONCLUSIONS: AVR or ARR with a CAH for complex endocarditis is associated with satisfactory hospital survival, considering the critical patient presentation at surgery, and excellent survival free from recurrent infection. Need for reoperation late after surgery is similar to other biological prostheses.

Keywords: Aortic homograft • Infective endocarditis • Prosthetic valve endocarditis • Annular abscess

ABBREVIATIONS

ARR	Aortic root replacement
AVD	Aortic valve disease
AVR	Aortic valve replacement
CAH	Cryopreserved aortic homograft
CPB	Cardiopulmonary bypass
ECMO	Extracorporeal membrane oxygenation
IE	Infective endocarditis
MV	Mitral valve
NSVD	Non-structural valve deterioration
NVE	Native valve endocarditis
PVE	Prosthetic valve endocarditis
SVD	Structural valve deterioration
VARC-3	Valve Academic Research Consortium 3

INTRODUCTION

Infective endocarditis (IE) is a relatively rare but still challenging disease with an estimated incidence of 3–10 cases per 100 000 people per year [1]. Despite diagnostic and therapeutic advances, prognosis remains poor with 14–22% in-hospital mortality rates and up to 50% mortality at 10 years [2]. Surgery is required in 25–50% of cases in the acute phase, and in 20% to 40% during convalescence. IE of the aortic valve complicated by extensive destruction of the aortic annulus due to annular abscess or pseudoaneurysm, resulting in left ventricular-aortic discontinuity, particularly in patients with prosthetic valve endocarditis (PVE), complicates the surgical procedures and causes worsening of short and long-term outcomes. Although technically demanding, cryopreserved aortic homograft (CAH) has been used in the context of complex IE due to its intrinsic resistance to infection and great versatility and flexibility for the reconstruction of the aortic annulus and aorto-mitral continuity allowing for more aggressive wide debridement of all infected and necrotic structures [3]. However, concern remains about its durability and the risk of structural valve deterioration (SVD) requiring reoperation. The aim of the present study was to evaluate the early- and long-term outcomes of CAH implantation for aortic valve replacement (AVR) or aortic root replacement (ARR) in patients with complex IE.

PATIENTS AND METHODS

Ethical statement

This study was approved by the Ethics Committee of our institution (ID Verona: 2020/64927); written patient informed consent was waived by the Ethics Committee.

Study population

All adult patients who underwent AVR or ARR with a CAH at our institution between January 1993 and July 2021 were included in the study. Patients' characteristics, perioperative data, laboratory test results, echocardiographic reports and in-hospital outcomes were extracted from patients' paper-based and electronic medical records. The diagnosis of IE was based on clinical, echocardiographic and biological findings according to the revised Duke's criteria [4]. During the study period (1993–2021), isolate native aortic valve endocarditis (NVE) or PVE was managed by standard prosthetic AVR. Complex infective endocarditis, defined as NVE or PVE associated with aortic root abscess, fistulae and/or with multiple valve involvement, was typically managed using CAH. Patients undergoing elective CAH implantation for aortic valve disease (AVD), other than endocarditis, were also analysed in the present work to assess the impact of preoperative endocarditis on CAH degeneration.

Operative techniques

All operations were performed through a median full sternotomy, standard cardiopulmonary bypass (CPB) and cold blood or crystalloid cardioplegia. CAH was implanted using the following techniques: full-root, free-hand sub-coronary with intact non-coronary sinus or cylinder inclusion technique according to the anatomical findings and surgeon's individual choice. In case of an extensive annular abscess, discontinuity of the mitro-aortic curtain and fistulae, the anterior mitral leaflet of the CAH or a bovine pericardial patch was used to repair the defect. In the case of left ventricle to right atrium or to the right ventricular outflow tract fistulae, extensive debridement was carried out simultaneously via the aortic root and via the right atrium or infundibulum, as requested. Thereafter, the residual defect was patch repaired with bovine pericardium on the right side and using the anterior mitral leaflet on the left side. Aortic homografts were all cryopreserved and provided by the Treviso Tissue Bank Foundation (Treviso, Italy).

Follow-up

Follow-up data were collected between January and August 2021, via phone contact with physicians, cardiologists or patients themselves. Subsequent hospitalization and routine visit data were collected from hospital records and cardiologists' reports. The follow-up time was calculated either to death or to the last verified contact with the patient. Clinical outcomes of interest included mortality and reintervention for bioprosthetic valve

Table 1: Pre- and perioperative characteristics as a whole and according to surgical indication

	Total (*n* = 104)	NVE (*n* = 33)	PVE (*n* = 61)	AVD (*n* = 10)	*P*-Value
Preoperative characteristics					
Male sex, *n* (%)	75 (72)	23 (70)	46 (75)	6 (60)	0.6
Age (years), median [IQR]	64 [45–73]	52 [36–66]	70 [62–75]	31 [29–49]	<0.001
BMI, median [IQR]	25 [23–28]	25 [22–28]	26 [23–28]	23 [22–24]	0.8
BSA, median [IQR]	1.9 [1.7–2]	1.9 [1.8–2]	1.9 [1.7–2]	1.8 [1.7–2]	0.9
BAV, *n* (%)	22 (21)	4 (12)	14 (23)	4 (40)	0.1
Previous neoplasia, *n* (%)	14 (13)	2 (6)	12 (20)	0	0.1
Hepatic cirrhosis, *n* (%)	11 (11)	4 (12)	7 (11)	0	0.9
Chronic kidney disease, *n* (%)	9 (9)	4 (12)	5 (8)	0	0.7
IV drug abuse, *n* (%)	7 (7)	4 (12)	3 (5)	0	0.2
Active IE, *n* (%)	85 (90)	30 (91)	55 (90)	–	0.9
Septic shock, *n* (%)	12 (13)	6 (18)	6 (10)	–	0.3
Operative characteristics					
Vegetations, *n* (%)	53 (56)	26 (79)	27 (44)	–	0.003
Annular abscess, *n* (%)	77 (82)	17 (52)	60 (98)	–	<0.001
Aorto-mitral discontinuity, *n* (%)	33 (35)	9 (27)	27 (44)	–	0.1
Mitral valve endocarditis, *n* (%)	13 (14)	5 (15)	8 (13)	–	0.8
Tricuspid valve endocarditis, *n* (%)	13 (14)	2 (6)	11 (18)	–	0.1
Gerbode defect, *n* (%)	9 (10)	0	9 (15)	–	–
Surgical technique, *n* (%)					
Full root replacement	45 (43)	10 (30)	30 (45)	5 (50)	0.9
Free-hand sub-coronary technique	45 (43)	13 (39)	27 (41)	5 (50)	0.9
Cylinder inclusion technique	14 (13)	10 (30)	4 (7)	0	0.005
Concomitant procedure, *n* (%)					
Ascending aorta replacement	4 (4)	0	4 (7)	0	–
Mitral valve replacement	6 (6)	3 (9)	3 (5)	0	0.8
Mitral valve repair	10 (10)	3 (9)	6 (9)	1 (10)	0.9
Tricuspid valve repair	7 (7)	0	7 (10)	0	–
CABG	1 (1)	1 (3)	0	0	–
CPB time (min), median [IQR]	193 [165–235]	180 [144–200]	217 [182–284]	139 [122–174]	<0.001
Aortic cross-clamping time (min), median [IQR]	152 [123–194]	135 [118–173]	168 [139–206]	107 [99–121]	0.001
IABP, *n* (%)	3 (3)	0	3 (5)	0	–
ECMO, *n* (%)	4 (4)	1 (3)	3 (5)	0	0.9
Re-exploration for bleeding, *n* (%)	9 (9)	2 (6)	7 (11)	0	0.7
Pace-maker implantation, *n* (%)	20 (20)	1 (3)	19 (29)	0	0.006
Mediastinitis, *n* (%)	3 (3)	0	3 (5)	0	–
Periprocedural mortality, *n* (%)	12 (12)	5 (15)	7 (11)	0	0.1

AVD: aortic valve disease; BAV: bicuspid aortic valve; BMI: body mass index; BSA: body surface area; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic ballon pump; IE: infective endocarditis; IQR: interquartile range; IV: intra-venous; MVR: mitral valve replacement; NVE: native valve endocarditis; PVE: prosthetic valve endocarditis.

dysfunction. Mortality was defined according to Valve Academic Research Consortium 3 (VARC-3) as periprocedural mortality was defined as any death occurring ≤30 days after the index procedure or >30 days but during the index hospitalization (including transfer to another hospital or rehabilitation facility for continuity of acute care); early mortality was defined as any death occurring >30 days but ≤1 year the index hospitalization; late mortality was defined as any death >1 year the index hospitalization [5]. Bioprosthetic valve dysfunction was defined according to VARC-3 as the presence of SVD, non-SVD (NSVD), endocarditis and thrombosis [5].

Statistical analysis

Categorical variables are expressed as numbers and percentages and compared with χ^2 test. Continuous variables are expressed as the mean ± 1 standard deviation and compared using the Student's *t*-test; continuous variables with a skewed distribution are presented as median and interquartile range and compared with Mann–Whitney *U*-test. The Kaplan–Meier method was used to draw survival curves; the log-rank test was used to compare survival among groups. Hazard ratios for mortality were determined by univariate and multivariate Cox proportional hazards regression analyses with data presented as hazard ratios with 95% confidence intervals. Univariate analysis was performed with pre- and perioperative variables; significant variables at univariate analysis were entered in the Cox multivariate regression. A two-tailed *P*-value of <0.05 was taken to indicate statistical significance. Statistical analysis was performed using Sigmaplot version 12.0 (Systat Software Inc, San Jose, CA, USA).

RESULTS

Demography

One hundred four patients, 75 males and 29 females, aged 59 ± 17 years (median age: 64 [45–73]) years, underwent AVR or ARR with CAH at our institution during the study period. The main indication for AVR or ARR was IE (*n* = 94, 90%) or, more rarely, AVD other than IE such as aortic regurgitation (*n* = 9, 9%) and aortic stenosis (*n* = 1, 1%). Twenty-two (21%) patients had bicuspid aortic valve, 14 (13%) a previous history of neoplasia, 11 (11%), hepatic cirrhosis, 9 (9%) chronic kidney disease and 7 (7%)

Table 2: Aetiology of endocarditis

Isolated microorganism	N = 94, n (%)
Staphylococcus aureus	15 (16)
Staphylococcus epidermidis	12 (13)
Staphylococcus coagulase negative	9 (10)
Streptococcus species	12 (13)
Enterococcus	12 (13)
Other GRAM+	3 (3)
GRAM-	4 (4)
Fungi	4 (4)
Negative blood tests	9 (10)
Unknown	14 (15)

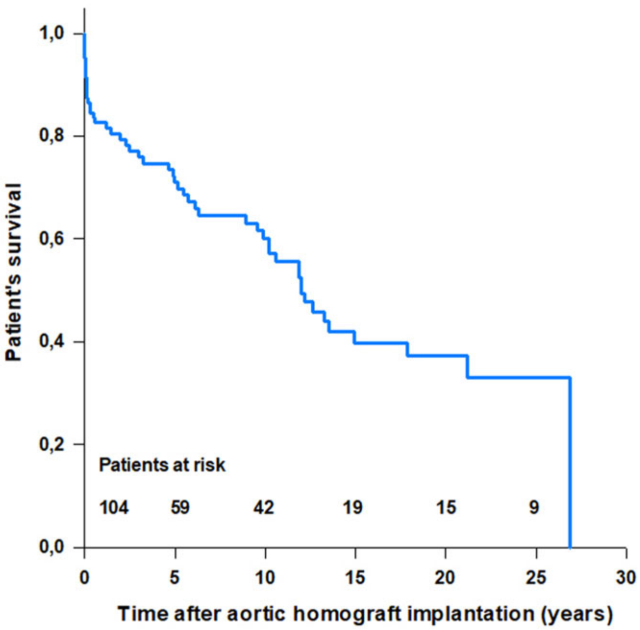


Figure 1: Survival after aortic homograft implantation.

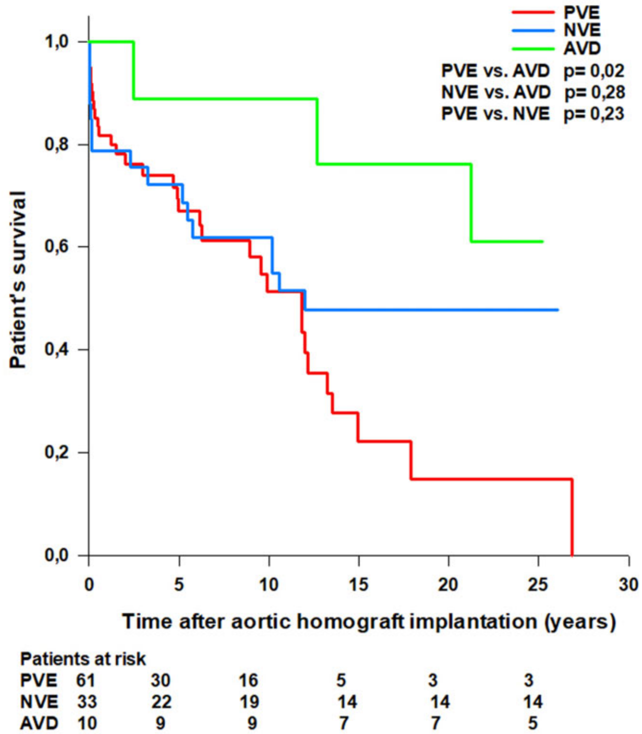


Figure 2: Survival stratified for surgical indication. AVD: aortic valve disease; NVE: native valve endocarditis; PVE: prosthetic valve endocarditis.

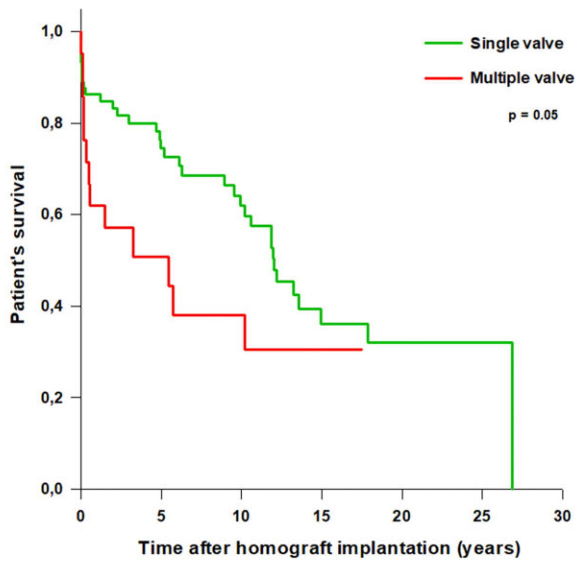
a history of IV drug abuse. There were 85 (90%) active IE, 9 (10%) healed IE, 33 (35%) NVE and 61 (65%) PVE, which were complicated by aortic root abscess in 77 (82%) patients, mitral valve (MV) endocarditis in 13 (14%), tricuspid valve endocarditis in 13 (14%) and Gerbode defect in 9 (10%). Sixty-five (63%) patients had previous cardiac surgery, 27 (42%) of whom developed early (<1 year from prior cardiac operation) IE. The mean time from the prior cardiac surgery was 3.1 ± 3.6 years (median time: 1.4 [0.4–5] years). The main indication for prior cardiac surgery was AS in 36 (55%), AR in 6 (9%), ascending aorta aneurysm in 14 (22%) an IE in 9 (14%). Seven (7%) patients had 2 previous cardiac operations. Baseline characteristics as a whole and according to preoperative diagnosis are listed in Table 1; of note patients with PVE were significantly older (median age 70 [62–75] years) (Table 1). Isolated microorganisms from blood and valve/prosthesis cultures are listed in Table 2.

Operative and perioperative course

The mean aortic homograft size was 22.7 ± 1.7 mm (median size 23 [21–24] mm); the median age of the aortic homografts donors was 31 (26–42) years old. The CAH was implanted using the full root replacement (*n* = 45, 43%), the free-hand sub-coronary technique with intact non-coronary sinus (*n* = 45, 43%) or the intraluminal cylinder technique (*n* = 14, 13%). Concomitant procedures were MV replacement (*n* = 6, 6%) or repair (*n* = 10, 10%), tricuspid valve repair (*n* = 7, 7%) ascending aorta replacement (*n* = 5, 5%) and coronary artery bypass (*n* = 1, 1%). The mean CPB time was 214 ± 80 min (median: 193 [165–235] min) and the mean aortic cross-clamping time was 164 ± 56 min (median: 152 [123–194] min). Postoperative low cardiac output syndrome was recorded in 7 (7%) patients (1 NVE and 6 PVE), requiring extracorporeal membrane oxygenation (ECMO) in 4 and intra-aortic balloon pump in 3. Re-exploration for bleeding was necessary for 9 (9%) patients and permanent pacing for the third-degree atrioventricular block in 20 (19%). Mediastinitis requiring surgical treatment occurred in 3 (3%) patients, 1 with NVE and 2 with PVE, the latter 2 having already had mediastinitis at the time of the prior surgery. Intra- and perioperative characteristics as a whole and according to preoperative diagnosis are listed in Table 1; of note, patients with PVE had significantly more extensive IE with annulus abscess, longer CPB and aortic cross-clamping times, and PM implantation.

Survival

According to the VARC-3 definition [5], 12 (12%) periprocedural deaths (5 patients with NVE and 7 patients with PVE), 6 (6%) early deaths (2 patients with NVE and 4 patients with PVE) and 33 (32%) late deaths were recorded. Three patients (1 with NVE and 2 with AVD) were lost at follow-up; completeness of the follow-up was 94% according to Clark's formula [6]. The overall mean follow-up duration was 8.1 ± 7.6 (median 5.8 [1.5–12.6]) years and the cumulative follow-up was 864.9 patient-years. Overall patient's mean survival time was 13.9 ± 1.2 years (median 12 [3.3–26.9] years); overall long-term survival rates were 91.3%, 82.6%, 71.1%, 60.1%, 39.8% and 37.2% at 30, 1, 5, 10, 15 and 20 days, respectively (Fig. 1). Patient's mean survival time stratified for preoperative diagnosis was 20.5 ± 3.2 years in patients with AVD, 14.9 ± 2.1 years in patients with NVE and 10.9 ± 1.5 years in patients with PVE (PVE versus AVD $P = 0.02$; NVE versus AVD $P = 0.28$; PVE versus NVE $P = 0.23$) (Fig. 2). Patient's mean survival time in patients with single valve IE was better than in patients with multiple valve IE even if the difference was not statistically significant (13.9 ± 1.4 vs 7.2 ± 1.8, respectively; $P = 0.05$) (Fig. 3). No difference was found in patients' mean survival time between early and late PVE (11.3 ± 2.2 vs 10.1 ± 1.5 years, respectively; $P = 0.84$). We also found no difference in patients' mean survival between patients operated with the full root replacement technique ($n = 45$) and patients operated with the free-hand sub-coronary with intact non-coronary sinus technique ($n = 45$) (14.5 ± 1.7 vs 12.8 ± 1.9; $P = 0.58$); patients operated with the cylinder inclusion technique ($n = 14$) were excluded from the analysis because of the small number of patients. We also considered complex valve endocarditis ($n = 77$) versus non-complex valve endocarditis ($n = 17$) as subgroups and found a greater survival in patients with non-complex IE compared to patients with complex IE (18.6 ± 2.7 vs 11 ± 1.4 $P = 0.02$). Univariate analysis was performed with pre- and perioperative variables; significant variables at univariate analysis are presented in Table 3 and were entered in the Cox multivariate regression. Multivariate analysis showed that patients' age >65 years, annular abscess and heart failure requiring postoperative ECMO were independent predictors of mortality (Table 3).



Patients at risk

Single valve	73	43	29	12	9	9
Multiple valve	21	9	7	5		

Figure 3: Survival stratified for single or multiple valve infection.

Reoperation

Four (4%) patients with PVE required early reoperation within 30 days from CAH implantation for NSVD due to para-prosthetic regurgitation for homograft dehiscence ($n = 2$), SVD due to flail leaflet with aortic regurgitation ($n = 1$) and congestive heart failure ($n = 1$) and underwent re-suturing of the previous implanted CAH, prosthetic ARR, prosthetic AVR and cardiac transplantation, respectively, with 1 hospital death. During the follow-up period, 7 (7%) patients had recurrent IE, 1 patient died before surgery and 6 underwent reoperation; survival free from endocarditis was 97% at 1 year, 94.7% at 5 years, 93% at 15 years and 46.5% at 25 years. Twenty-five patients (26%), 10 (36%) with NVE, 7 (12%) with PVE and 8 (80%) with AVD, underwent late reoperation for SVD ($n = 17$, 18%), homograft endocarditis ($n = 6$, 6%), NSVD due to para-prosthetic regurgitation for homograft dehiscence ($n = 1$, 1%), MV regurgitation ($n = 1$, 1%), respectively, at a median time of 11.6 [3.8–15.9] years after CAH implantation (Table 4). Echocardiographic data of patients who underwent late reoperation for SVD ($n = 17$) and patients who did not undergo reintervention during the follow-up ($n = 36$) are illustrated in Table 5. SVD and the need for reoperation were more frequent in patients with NVE and AVD compared to patients with PVE. Four (16%) patients, 2 with SVD (1 first operated for NVE and 1 for PVE both with the full root technique) and 2 with IE (both first operated for PVE with the full root technique and the subcoronary technique respectively), died within 30 days from reoperation (Table 4).

Overall mean survival time free from reoperation was 15.7 ± 1.2 years (median 16.5 [11.6–21.6] years); freedom from reoperation was 93%, 87.2%, 79.1%, 57.3%, 33.8%, and 11.3% at 1, 5, 10, 15, 20 and 25 years, respectively (Fig. 4). Twenty-three CAHs were replaced with a prosthetic aortic valve ($n = 20$) or a new aortic homograft ($n = 3$,) while 1 was re-sutured. Expected valve durability estimated from median survival time without SVD (18 patients, 1 with early SVD and 17 with late SVD) was 17.6 (13.7–21.5) years (Fig. 5). We found no difference in mean survival time free from SVD between patients aged <40 years and patients aged > 40 years (17.4 ± 1.5 vs 19.6 ± 2.6 years; $P = 0.5$). Aortic homograft donor's age did not differ between patients who underwent reintervention for SVD and patients who did not

Table 3: Predictors of mortality at univariate at multivariate analysis

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P*-Value	Hazard ratio (95% CI)	*P*-Value
Patient's age >65 years	2.435 (1.338–4.432)	0.004	2.06 (1.018–4.168)	0.04
Annular abscess	3.268 (1.543–6.92)	0.002	2.946 (1.438–6.025)	0.004
Tricuspid valve endocarditis	2.579 (1.187–5.6)	0.01	2.105 (0.935–4.741)	0.07
PVE	2.145 (1.257–4.183)	0.04	1.956 (0.957–3.294)	0.124
Postoperative ECMO	10.176 (3.476–29.794)	<0.001	2.039 (0.576–12.927)	<0.001

CI: confidence iterval; ECMO: extracorporeal membrane oxygenation; PVE: prosthetic valve endocarditis.

Table 4: Events recorded during the follow-up as a whole and according to surgical indication

Follow-up events	Total (*n* = 95)	NVE (*n* = 28)	PVE (*n* = 57)	AVD (*n* = 10)	*P*-Value
IE, *n* (%)	7 (7)	2 (7)	4 (7)	1 (10)	0.9
SVD, *n* (%)	17 (18)	8 (29)	2 (4)	7 (70)	<0.001
Homograft dehiscence, *n* (%)	1 (1)	0	1 (2)	0	–
Reoperation, *n* (%)	25 (26)	10 (36)	7 (12)	8 (80)	0.005
Prosthetic AVR	14	6	1	5	
Prosthetic AVR + MVR	2	1	1	0	
TAVR	3	0	1	1	
Prosthetic ARR	1	2	0	2	
Homograft ARR	3	1	2	0	
Homograft re-suturing	1	0	1	0	
Prosthetic MVR	1	0	1	0	
Periprocedural mortality, *n* (%)	4 (16)	1 (10)	3 (43)	0	0.2

ARR: aortic root replacement; AVD: aortic valve disease; AVR: aortic valve replacement; IE: infective endocarditis; MVR: mitral valve replacement; NVE: native valve endocarditis; PVE: prosthetic valve endocarditis; SVD: structural valve deterioration; TAVR: transcatheter aortic valve replacement.

Table 5: Echocardiographic data of patients reoperated or not for structural valve deterioration during the follow-up period

Echocardiographic variable	No reoperation (*n* = 36)	Reoperation for SVD (*n* = 17)
Ascending aorta diameter (mm), median (IQR)	32 (30–36)	35 (32–41)
LA diameter (mm), median (IQR)	45 (41–51)	53 (49–60)
LVEDD (mm), median (IQR)	56 (50–59)	63 (53–65)
LVESD (mm), median (IQR)	37 (35–40)	44 (34–52)
Interventricular septum (mm), median (IQR)	11 (10–13)	12 (9–14)
LVEF (%), median (IQR)	55 (50–63)	60 (48–63)
PAPs (mmHg), median (IQR)	31 (28–40)	48 (39–60)
Peak aortic gradient (mmHg), median (IQR)	12 (7–19)	39 (20–50)
Aortic valve regurgitation, *n* (%)		
Mild	12 (33)	0
Moderate	6 (17)	4 (24)
Severe	0	13 (76)
Mitral valve regurgitation, *n* (%)		
Mild	14 (39)	3 (18)
Moderate	1 (3)	7 (41)
Severe	1 (3)	0
Tricuspid valve regurgitation, *n* (%)		
Mild	8 (22)	6 (35)
Moderate	3 (8)	3 (18)
Severe	1 (3)	1 (6)

IQR: interquartile range; LA: left atrial; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; PAPs: systolic pulmonary artery pressure; SVD: structural valve deterioration.

(29 [24–38] vs 32 [36–42] years; *P* = 0.76). The mean survival time free from SVD did not differ between patients operated with the full root replacement and patients operated with the free-hand subcoronary technique (19.2 ± 2 vs 17.1 ± 1.8 years; *P* = 0.5).

Overall mean homograft survival (defined as CAH survival until replacement or patient death) was 10.1 ± 0.9 years (median 10.2 [1.5–15.7] years) (Fig. 6). The difference in mean homograft survival time stratified for preoperative diagnosis was not significant: 12.2 ± 1.9 years in patients with AVD, 10.8 ± 1.7 in patients with NVE and 9.9 ± 1.5 in patients with PVE (*P* = 0.7) (Fig. 7) (Video 1).

DISCUSSION

We reported our very long-term experience with aortic homograft utilization in patients with complex aortic valve or root endocarditis and found that AVR or ARR with a CAH is associated with satisfactory hospital survival, in spite of the often critical patient presentation at surgery, and good long-term results despite the need for reoperation. The latter is comparable to the expected need for reintervention after AVR or ARR using biological prostheses in patients with similar age at operation [7, 8].

In our series, CAH was predominantly used in patients with IE, especially in patients with PVE. Aortic homograft has been considered the gold standard in the treatment of NVE, PVE and multiple valve endocarditis complicated by annular abscess and ventricular-aortic discontinuity, because of its intrinsic resistance to infection and great versatility, which allows an extensive debridement of infected tissue and left ventricular outflow reconstruction, closure of annular abscess, ventricular septal defects, fistulae and MV perforation [3, 9]. Such interventions are technically demanding and imply a substantial operative morbidity and mortality; in our series, the periprocedural mortality was 12% which is perhaps lower than most previously reported mortality

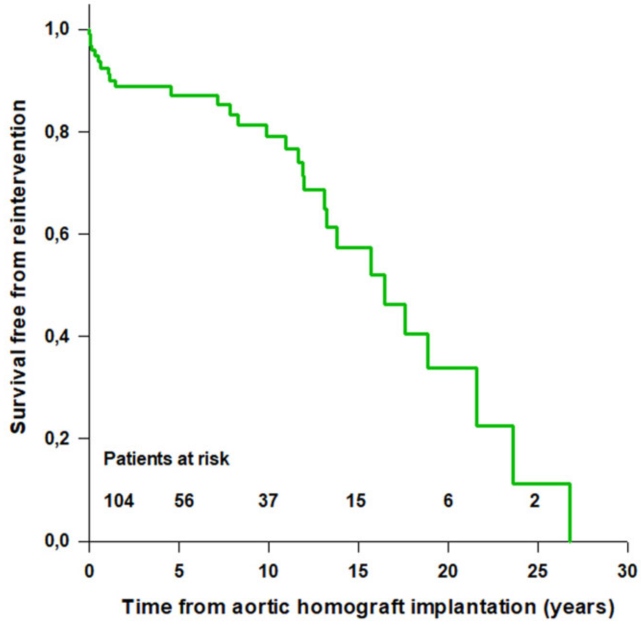


Figure 4: Survival free from reintervention after aortic homograft implantation.

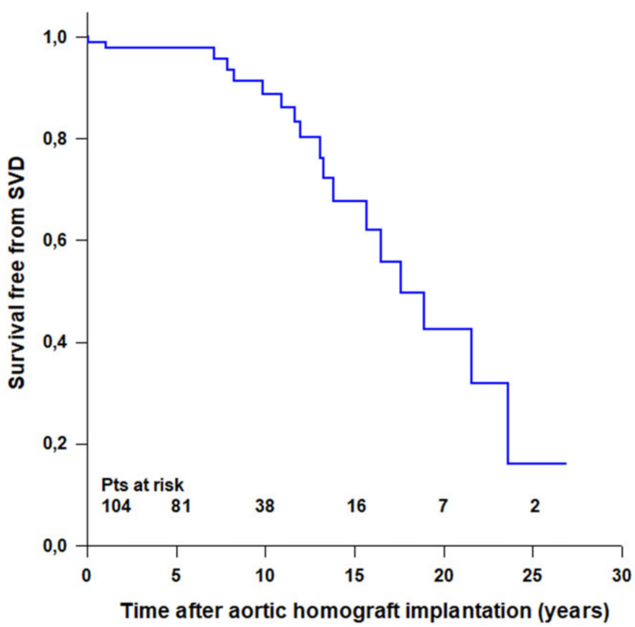


Figure 5: Survival free from structural valve deterioration.

rates as high as 25.4% [9–14]. The high operative mortality is a consequence of the severity of the disease and also of the clinical status of the patient at the time of surgery. Multivariate analysis showed that age >65 years, annular abscess and heart failure requiring postoperative ECMO were independent risk factors for mortality; of note PVE was not a risk factor for mortality *per se* but it became such when an aortic root abscess and/or involvement of the tricuspid vale were present. In our series, patients with PVE were older and had more annular abscess, multiple valve involvement and Gerbode defect, requiring a more extensive surgery to allow a complete debridement of all infected tissue, with significantly longer CPB and aortic cross-clamping times and greater need for pacemaker implantation for third-degree atrioventricular block. However, in contrast with previous reports showing a better survival in patients with NVE compared to patients with PVE [12], we did not find any difference in early- and long-term survival between patients with NVE and patients with PVE. These findings are in line with Solari *et al.* [10] who showed similar 30-day mortality in NVE and PVE. Previous reports showed a similar mortality between single and multiple valve endocarditis [15, 16]. In the present series, patients with single valve involvement had a better survival compared to patients with multiple valve involvement, even if the difference did not reach the statistical significance. These results suggest that radical and aggressive intervention is fundamental to completely eradicate the infection and achieve good early and long-term results. Aortic homograft represents the ideal substitute in this context because it allows to reconstruct the aortic valve and root, as well as other cardiac structures damaged by the infection [17]. In addition, several reports indicate a low valve reinfection in aortic homograft ranging from 3.8% to 6.8% [9, 10, 12, 18, 19]. Accordingly, in the current series, reinfection was 7%, thus similar to previously reported results. Some authors reported a higher incidence of recurrent endocarditis in patients treated with mechanical or biological valve prostheses than in patients treated with a homograft [20], while others failed to demonstrate a significant benefit when using aortic homograft with regard to resistance to reinfection when compared with xenografts or mechanical prostheses in the setting of IE [21]. One of the main concerns with the use of aortic homograft is durability, especially in younger patients, and technical challenges posed by reintervention for homograft failure due to heavy calcification, often leading to difficulties in mobilization of the coronary buttons and postoperative bleeding. More recent adoption at our unit of rapid deployment sutureless bioprostheses or TAVI for homograft valve reintervention in heavily calcified conduits has significantly reduced the risk of intraoperative complications. In our series, 26% of the patients underwent reoperation, mainly for SVD, at a median time of 11.6 [3.8–15.9] years after CAH implantation. This

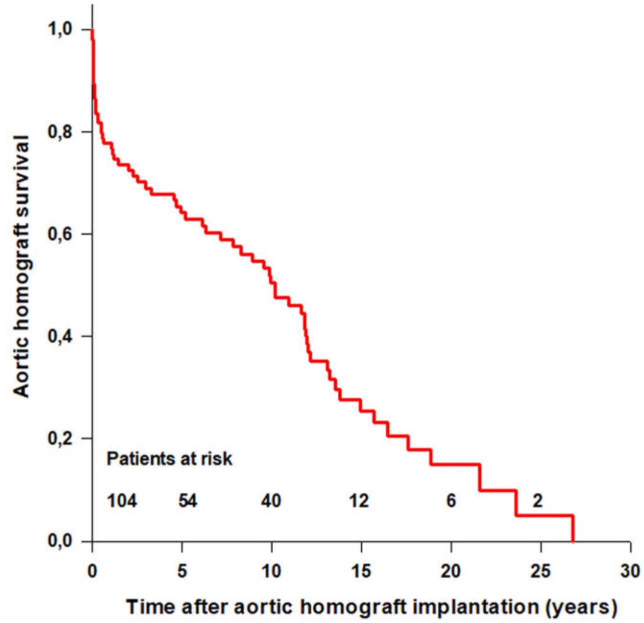


Figure 6: Aortic homograft survival after implantation.

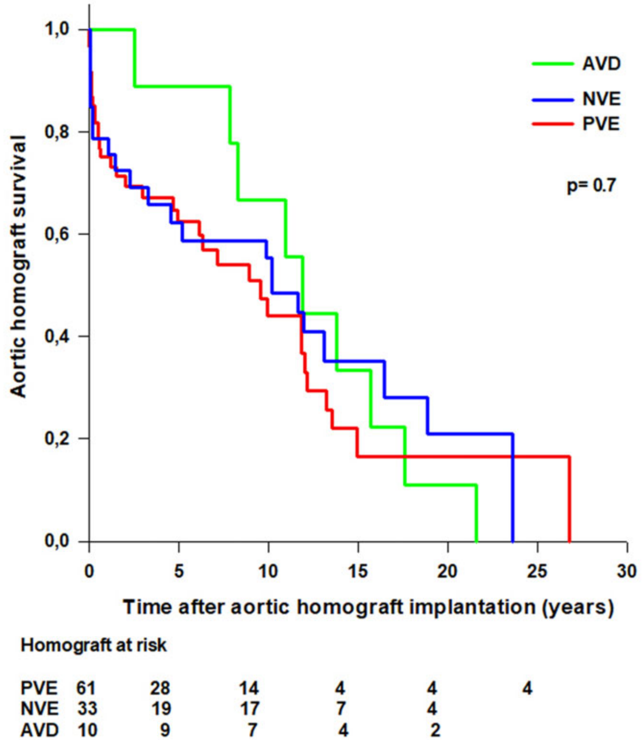
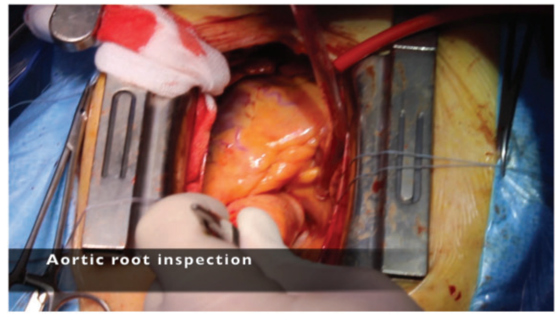


Figure 7: Aortic homograft survival according to surgical indication. AVD: aortic valve disease; NVE: native valve endocarditis; PVE: prosthetic valve endocarditis.

finding is in line with expected reoperation rate after bioprosthetic AVR in patients presenting for surgery at age <60 years [22].

Hospital mortality at CAH reoperation was 16%, which may be higher than previously reported mortality rates ranging between 3.8% and 8.9% [14, 23–25], and is possibly related to the number of prior operations (often 2 or more) and reinfection. Despite the need for reoperation with the attendant morbidity, long-term outcomes are good with the mean patient survival time of 13.9 ± 1.2 years; overall survival rates were 91.3%, 82.6%, 71.1%, 60.1%, 39.8% and 37.2% at 30, 1, 5, 10, 15 and 20 days, respectively, which are similar to those reported in the literature for patients with IE treated using aortic homografts [9, 10, 12, 18, 19].

Superior haemodynamic and avoidance of anticoagulation, particularly advantageous for women of childbearing age or for elderly patients with multiple co-morbidities, are the absolute benefits of aortic homograft utilization [26]. The scarce availability of human allograft tissue, as well as the lack of surgical expertise in complex aortic root surgery in many Cardiac Units, remains the major limitations to wider adoption of CAH employment. Therefore, general consensus regarding the use of aortic homografts over the use of standard prostheses for AVR or ARR, including the setting of NVE or PVE, has not been reached and it is unlikely that it will be in the future. Studies comparing mechanical composite graft, biological valve conduit and homograft root replacement in the context of IE found no significant differences in major complications and early or late mortality [11, 21] and concluded that complete eradication of infected tissue is more important than conduit choice in determining outcomes. In selected young patients with acute endocarditis with a low rate of recurrent infection, the Ross procedure could be an alternative to prosthetic valve replacement or homograft implantation



Video 1: Technique for aortic valve replacement with free-hand aortic homograft using the subcoronary intact non-coronary sinus technique.

[27, 28]. Ratschiller *et al.* [27] reported their experience on 19 patients with aortic valve IE aged 35.9 ± 11.5 years and showed a 5.3% mortality at 30 days; during a mean follow-up of 12.0 ± 5.7 years, they found no case of recurrent endocarditis affecting the autograft, while 3 patients (15.8%) underwent reoperation for autograft aneurysm and 1 patient was reoperated 1.8 years after the Ross procedure for homograft endocarditis. Another report on 42 patients (mean age 34 ± 8 years) showed a perioperative mortality of 4.7% and survival at 10 and 15 years of 87 ± 5% and 81 ± 8%, respectively; during a median follow-up of 10 years (4–21 years), 8 patients (19%) underwent repeat surgery for autograft and/or homograft dysfunction at a median time of 8.4 years (3 months to 18 years), while the rate of recurrent endocarditis was 7% [28]. In patients with complex IE, however, the Ross procedure may be challenging due to the concomitant need to reconstruct the fibrous skeleton of the heart, including the left and right trigones. To this end, the aortic homograft with the anterior mitral leaflet seems ideally suited, whereas the pulmonary autograft represents, in our opinion, a second choice. Furthermore, the Ross procedure inevitably adds pulmonary valve morbidity to an often times two-valve or three-valve procedure, in cases of complex IE. This may potentially put all cardiac valves, semilunar and atrioventricular alike, at risk of further complications.

In our experience, aortic homograft is ideally suited for reconstruction of the aortic valve and the aortic root with satisfactory hospital survival, compatible with a critical patient presentation at surgery, and good long-term results despite the need for reoperation. The current trend towards the application of transcatheter valve replacement or, when not feasible, AVR using sutureless bioprosteheses holds great promise in terms of a decrease in morbidity associated with reoperations (often multiple), particularly when dealing with heavily calcified CAH.

Limitations

This study has limitations due to the retrospective observational design where selection bias is unavoidable. In addition, the study covers a very long period and pre- and postoperative management of the patients could have changed over time. Therefore, the study results should be interpreted with caution.

CONCLUSION

Extensive surgical debridement is essential to ensure early- and long-term disease in patients with IE complicated by annular abscess and other cardiac structures destruction. Aortic homograft is a safe and effective option and should be available for patients with complex IE as it allows healing from infection and reconstruction of the aortic valve and aortic root with very satisfactory early and late results.

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Data Availability Statement

All relevant data are within the manuscript.

Author contributions

Antonella Galeone: Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Supervision; Writing—original draft. **Diletta Trojan:** Data curation; Methodology. **Jacopo Gardellini:** Data curation; Methodology. **Renato di Gaetano:** Data curation; Methodology. **Giuseppe Faggian:** Writing—review & editing. **Giovanni Battista Luciani:** Conceptualization; Supervision; Writing—review & editing.

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