Cite this article as: Yousif A, Ali K, Anssar M, Harringer W, El-Essawi A, Brouwer R. A 20-year experience with cryopreserved allografts as the valve replacement of choice in aortic root reconstruction for destructive endocarditis with abscess formation. Interact CardioVasc Thorac Surg 2022; doi:10.1093/icvts/ivac188.

A 20-year experience with cryopreserved allografts as the valve replacement of choice in aortic root reconstruction for destructive endocarditis with abscess formation

Afram Yousif (1) a.*, Khaldoun Alia, Marcel Anssara, Wolfgang Harringera, Aschraf El-Essawi (1) b.† and René Brouwera,†

- ^a Department of Cardiothoracic and Vascular Surgery, Braunschweig Clinic, Braunschweig, Germany
- ^b Department of Cardiothoracic and Vascular Surgery, University of Göttingen, Göttingen, Germany
- * Corresponding author. Department of Cardiothoracic and Vascular surgery, Braunschweig Clinic, Salzdahlumerstraße 90, 38126 Braunschweig, Germany. Tel: +495315952213; e-mail: aframyo@hotmail.com (A. Yousif).

Received 8 March 2022; received in revised form 23 June 2022; accepted 29 June 2022

Key question

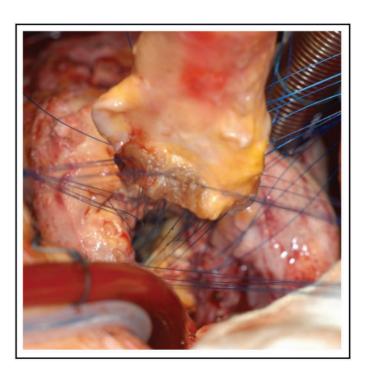
What are the outcomes in patients undergoing aortic allograft replacement in destructive endocarditis with abscess formation?

Key finding(s)

The long-term freedom from re-intervention reached 83.3 % at 10 yrs. with a freedom from re-endocarditis of 95% after 10 yrs.

Take-home message

In abscessed aortic root endocarditis allografts exhibit excellent performance with a low rate of reinfection and reintervention making their use a very desirable option.



Abstract

OBJECTIVES: The aim of this retrospective study was to assess the early- and long-term outcomes following the use of cryopreserved allografts in aortic valve endocarditis with peri-annular abscess formation.

METHODS: From 2001 to 2021, 110 consecutive patients with active infective endocarditis and peri-annular abscess, underwent a cryopreserved allograft root replacement. In 100 patients (91%), the operation was performed <48 h after admission due to refractory heart failure and or septic shock. In 95 patients (86.4%), a redo operation was performed due to a prosthetic valve endocarditis. Preoperatively, 12 patients were dialysis-dependent and 30 patients suffered from a recent stroke.

[†]These authors contributed equally to this work.

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Association for Cardio-Thoracic Surgery.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

RESULTS: The 30-day mortality was 18% (20 patients). Freedom from reintervention was 98.3% (standard deviation: 1.7) at 1 year and 83.3% (standard deviation: 8.5) at 10 years. Four patients required a redo operation. Three patients did develop re-endocarditis. Freedom from re-endocarditis was 95% after 17 years of follow-up. Preoperative dialysis dependency (odds ratio: 22.75, 95% confidence interval: 4.79–108.14, P < 0.001), ejection fraction under 30% (odds ratio: 17.91, 95% confidence interval: 3.27–98.01, P < 0.001) and stroke within 14 days prior to operation (odds ratio: 5.21, 95% confidence interval: 1.28–21.2, P = 0.021) were incremental factors associated with the 30-day mortality.

CONCLUSIONS: In aortic root endocarditis with abscesses formation, cryopreserved allografts exhibit excellent clinical performance with a low rate of reinfection and reintervention, which make its use as valve replacement a very desirable option. Dialysis dependency, ejection fraction under 30% and recent stroke have the highest impact on the 30-day mortality.

Keywords: Cryopreserved allografts • Aortic valve endocarditis • Root abscess • Aortic root reconstruction • Long-term results

ABBREVIATIONS

CI confidence interval

ECLS Extracorporeal life support system

OR Odds ratio

PVE Prosthetic valve endocarditis

SD Standard deviation

INTRODUCTION

Active infective aortic root endocarditis of native or prosthetic valves is a life-threatening condition with mortality ranging between 26% and 75% [1]. In 20% of the cases, burrowing abscesses develop around the annulus with resulting destruction of the aortic root, the aortic-mitral continuity or fistula formation into a cardiac chamber [2, 3]. These life-threatening complications need aggressive debridement of the abscesses and reconstruction of the deformed aortic root with a suitable valve replacement. After surgical treatment, the in-hospital mortality ranges between 10% and 40% [3]. Several factors have been identified as predictors for in-hospital mortality including haemodynamic deterioration due to cardiogenic or septic shock, staphylococcal infection, prosthetic valve endocarditis (PVE) and urgent operation [1, 4, 5].

Currently, the surgeon's armamentarium for aortic root reconstruction consists of cryopreserved allografts, pericardial tissue xenografts, biological aortic root prostheses and mechanical prosthetic valve conduits. Their optimal performance is dependent upon the grafts' resistance to infection and *in vivo* durability. A final discussion as to which valve replacement is superior has not been resolved yet mostly due to the scarceness of randomized studies. Some favour the conventional mechanical or biologic valve prosthesis due to the unavailability of the cryopreserved allograft and the complexity of the implantation technique, whereas others favour the use of the cryopreserved allograft for its tissue characteristics [6–9].

In the past 20 years at our institution, cryopreserved allograft was the valve replacement of choice for reconstruction of the deformed aortic root due to destructive endocarditis with extensive abscess formation. The goal of this single-centre study was first to determine the durability of the cryopreserved allograft by assessing the incidence of surgical reintervention and/or the recurrence of endocarditis and second to identify incremental factors associated with the 30-day mortality after cryopreserved allograft implantation.

PATIENTS AND METHODS

Ethics statement

The local ethical committee (Hannover Medical School—Nr 8718_BO_K_2019) approved the study and waived the need for individual patient consent.

Study design

The study cohort comprised patients who underwent a cryopreserved allograft replacement for reconstruction of the deformed aortic root caused by destructive endocarditis with concomitant periannular abscess formation. The data were retrospectively retrieved from our departments' database and included patients operated between 2001 and 2021. The diagnosis of endocarditis was determined according to the modified Duke criteria [10] and confirmed by histopathological examination and tissue cultures postoperatively.

Once a peri-annular abscess was confirmed or highly suspected in the transoesophageal echocardiography, an allograft was ordered via the German society for tissue transplantation bank. In the case of PVE, the same valve size as in the previous operation was ordered, or one size bigger, if the same size was not available (mostly 23-25 mm). In the case of native valve endocarditis, we anticipated the size to avoid patient-graft mismatch (again mostly 23-25 for women and 23-27 mm for men). If the diagnosis was confirmed intraoperatively the allograft was used, otherwise, it was kept frozen and returned to the tissue bank. Patients treated otherwise were not included in our analysis. Primary outcomes included 30-day mortality as well as long-term survival and long-term freedom from reendocarditis and reintervention. Reoperation was defined as any operation that repairs or replaces the previously implanted allograft. Re-endocarditis was defined as any infection involving the operated valve according to the modified Duke criteria and histological confirmation of endocarditis at reoperation. Secondary outcomes included factors associated with the 30-day mortality. The EuroSCORE was calculated based on a set of predefined preoperative risk factors [11]. Anti-bacterial therapy was antibiogram dependent and in compliance with the guidelines. It was always continued intravenously for 6-8 weeks following the procedure. Patients with an isolated allograft implantation received Heparin in a prophylactic dose up till discharge. Afterwards, no further anticoagulants were prescribed. Further therapies were dependent on concomitant procedures or comorbidities of the patients. Patients with an additional coronary artery bypass grafting received Aspirin 100 mg once a day, patients with an additional tricuspid valve or mitral valve reconstruction and/

Table 1: Patient demographic and baseline characteristics

Characteristics	N (%)
Number of patients	110
Age (years) median (25th to 75th percentile)	70 (60, 75)
Gender, male	87 (79%)
BMI (kg/m^2)	
<25	37
25-29.9	41
≥30	32
COPD	14 (13%)
Pulmonary hypertension	13 (13%)
PAVD	33 (30%)
CVD	57 (52%)
DMII	24 (22%)
IDDMII	9 (8%)
Rhythm disturbances	60 (55%)
ĀF	39 (35%)
Complete AV block	12 (11%)
PM-dependent	9 (8%)
Ejection fraction	
>50%	56 (51%)
30-50%	46 (42%)
<30%	8 (7%)
NYHA class	
I-II	12 (11%)
III-IV	98 (89%)
Active endocarditis and root abscess	110 (100%)
Preoperative dialysis dependent	12 (11%)
Preoperative stroke	30 (27%)
<2 weeks before surgery	16
>2 weeks before surgery	14
Previous heart surgery	95 (86%)
Isolated aortic valve replacement	42
Aortic valve replacement:	
+CABG	21
+Ascending aortic replacement	12
+Ascending, arch and frozen ET	1
+CABG and ascending aortic replacement	4
+Mitral or tricuspid valve surgery	5
David procedure and ascending aortic replacement	3
+Arch replacement	1
Homograft aortic valve replacement	2
Freestyle aortic root replacement	2
CABG and ascending aortic replacement	2

AF: atrial fibrillation; BMI: body mass index; CABG: coronary artery bypass grafting; COPD: chronic obstructive pulmonary disease; DMII: diabetes mellitus type II; IDDMII: insulin-dependent diabetes mellitus type II; MVR: mitral valve replacement; NYHA: New York Heart Association classification; PAVD: peripheral arterial vessel disease; PM: pacemaker; SD: standard deviation; TV: tricuspid valve.

or replacement or atrial fibrillation received oral anticoagulation with phenprocoumon.

Allograft function was assessed with echocardiography in all patients before discharge. The mean and peak transvalvular gradients as well as the degree of valve incompetence were reported. Follow-up data were obtained prospectively during follow-up visits or by contacting cardiologists, general practitioners or the patients themselves.

Surgical details

Surgery was performed after standard median sternotomy with the use of cardiopulmonary bypass and crystalloid cardioplegia under mild systemic hypothermia (32°C). The aortic valves, native or

Table 2: Isolated microorganisms Causative microorganism N (%) 21 (19) Staphylococcus aureus Staphylococcus coagulase negative 5 (5) Staphylococcus epidermidis 14 (13) 7 (6) Streptococcus species Enterococci 28 (25) Miscellaneous 10 (9) No microorganism identified 25 (23)

prosthesis were resected and the deep abscesses fully debrided. After anti-septic irrigation, the coronary ostia were excised using the button technique. The proximal anastomosis between the cryopreserved allograft and left ventricle outflow tract was performed using single interrupted 4-0 polypropylene sutures, placing them circumferentially around the annulus, ensuring full-thickness bites of tissue. In case of an aortoventricular dehiscence, closure of the septal defect was achieved with the attached aortic-mitral 'curtain' of the cryopreserved allograft. The coronary ostia were re-implanted as buttons into the cryopreserved allograft conduit. Other intra-cardiac defects were closed with either autologous or bovine pericardium. In case of proximal and/or total aortic arch replacement, deep hypothermic circulatory arrest was applied. The operative procedure is described more extensively in Supplementary Material, Fig. S1.

Statistical analysis

The distribution of the continuous variables was analysed with normality plots. If they were normally distributed, the mean and standard deviation (SD) were used, if not the median with the 25th and 75th percentiles were used. Categorical variables are presented as total count and percentage of the group. Missing values were excluded listwise and excluded from all analyses. Multicollinearity among 2 or more independent variables was ruled out by the Variance Inflation Factor and Condition index. Overall survival was examined by the Kaplan-Meier estimate with 95% confidence interval (CI). Freedom from events (re-endocarditis and reintervention) was adjusted for competing risk with mortality using the Fine-Gray method. Pre- and intraoperative variables were tested in a univariable fashion as a pre-screening method and variables with a P < 0.25 were included in the model. The lowest Akaike Information Criterion Value in combination with the highest Pseudo R² (Nagelkerke) determined which model fitted best for the data and the predictive strength. A forward multivariable logistic regression analysis was run to find the adjusted odds ratio (OR) for each variable with 95% CI. Statistical analysis was performed using SPSS version 28 (IBM142 Corp., Armonk, NY, USA) and R-software (version 2.2-10. Copyright ©2020 the R Foundation for Statistical Computing) was used for data analysis. P-values < 0.05 are considered statistically significant.

RESULTS

Preoperative demographic characteristics

One hundred and ten consecutive patients (87 males, 79.1%) with a median age of 70 years underwent a cryopreserved

Table 3: Intraoperative data

Type of operation	N (%)
Ascending aortic replacement	110 (100)
CPB time, min, median (25th to 75th percentile)	254 (241, 254)
Cross-clamp time, min, median (25th to 75th percentile)	174 (165, 174)
Aortic arch replacement	11 (10)
Proximal	8 (7)
Total	3 (3)
Coronary artery bypass graft	27 (25)
Mitral valve surgery	16 (15)
Repair	5 (5)
Replacement	11 (10)
Tricuspid valve surgery	7 (6)
Repair	4 (4)
Replacement	3 (2)
Carotid endarterectomy	2 (2)
Atrial repair	6 (6)
ASD closure	1 (1)
VSD closure	1 (1)
PM removal	9 (8)
Need for IABP	3 (3)
Need for ECLS	5 (5)

ASD: atrial septal defect; CPB: cardiopulmonary bypass; ECLS: extra corporeal life support system; IABP: intra-aortic balloon pump; PM: pacemaker; VSD: ventricular septal defect.

allograft replacement. The majority of the patients (N = 98, 89%) were classified as New York Heart Association Class III or IV, while 25 (23%) of them were in septic shock. Twelve patients (11%) were dialysis dependent at the time of admission. Thirty patients (27%) had a recent, likely septic, stroke, 14 of them within 2 weeks prior to surgery. In 27 patients, the diagnosis was confirmed by a cerebral computed tomography scan and in 3 patients by a magnetic resonance imaging scan. All of these patients had a stable neurological condition prior to surgery so that their neurological impairment was not seen as a contraindication for surgery.

Twelve patients (11%) had a complete atrioventricular block. An urgent (within 48 h after admission) or emergent operation was performed in 100 patients (91%) due to congestive heart failure, septic shock, presence of large vegetations, severe aortic regurgitation, fistulas or recurrent systemic embolization. Eighty-six (78%) underwent reoperative sternotomy and 9 patients (8%) underwent second or third reoperative sternotomy. Of these, 50 patients had a previous bio-prosthetic aortic valve replacement and 35 patients a mechanical aortic valve replacement. Three patients had a previous endocarditis of which 2 were operated in another clinic. In 15 patients (14%), a native valve endocarditis was found, of those 3 had a bicuspid valve.

The median logistic EuroSCORE of the whole group was 17.8% (25th to 75th percentile: 9.6–35.4). The miscellaneous primary operations are listed in Table 1. A causative microorganism was identified in 85 (77.3%) patients (Table 2). In 25 patients (23.7%), the blood and histopathological cultures remained sterile as blood culture-negative endocarditis group.

Intraoperative characteristics

Twenty-seven patients underwent a concomitant coronary artery bypass grafting, in 12 of those, coronary artery bypass grafting was needed due to severe ostial calcification and or

 Table 4:
 Postoperative data

Characteristics	N (%)
30-day mortality	20 (18%)
New-onset renal failure	17 (15%)
LCOS	20 (18%)
Need for IABP	3 (2%)
Postoperative bleeding requiring rethoracotomy	24 (22%)
Requiring CPB	4 (3%)
Respiratory failure requiring reintubation	13 (12%)
Neurologic events	
Stroke	3 (2%)
Intracranial haemorrhage	1 (1%)
Delirium	29 (26%)
Sternal infection	1 (1%)
Sepsis	11 (10%)
Postoperative rhythm disturbances	
Atrial fibrillation	8 (11%)
Complete AV-block requiring PM implantation	28 (26%)
Ventricular fibrillation	2 (2%)
Blood product transfusion (units)	Mean (SD)
PRBCs	11.7 (9)
FFP	12.7 (10)
PLT	2.1 (2)
ICU-stay, days	10 (15)
Hospital stay, days	16 (12)

CPB: cardiopulmonary bypass; FFP: fresh frozen plasma; LCOS: low cardiac output syndrome; PLT: platelet concentrates; PRBC: packed red blood cells.

destruction by the abscess formation and in one case a vein graft interposition between the coronary ostium and the allograft was needed. Eight patients required a proximal aortic arch replacement and 3 patients a total arch replacement. Other surgical characteristics and intraoperative details are summarized in Table 3.

Early mortality and morbidity. The operative 30-day mortality was 18% (20 patients). Causes of death were multi-organ failure (n=11), low cardiac output syndrome (n=4), intraoperative death due to haemorrhagic shock (n=1), cerebrovascular accident (n=2), pulmonary haemorrhage (n=1) and one with sudden cardiac death. In 7 patients, a preoperative complete atrioventricular block persisted postoperatively, while 21 patients developed a new atrioventricular clock postoperatively, all requiring a pacemaker implantation. The other postoperative data are listed in Table 4.

Allograft function before hospital discharge. Mean transvalvular gradient was 4.5 (SD: 2.2) mmHg, with a peak transvalvular gradient of 8.3 (SD: 4.1) mmHg. All patients had no or trivial aortic valve incompetence.

Factors associated with 30-day mortality. Predictors of 30-day mortality are presented in Table 5. Multivariable analysis identified the following variables as statistically significant: preoperative dialysis dependency (OR: 22.75, 95% CI: 4.79–108.14, P < 0.001), ejection fraction under 30% (OR: 17.91, 95% CI: 3.27–98.01, P < 0.001) and stroke within 14 days prior to operation (OR: 5.21, 95% CI: 1.28–21.2, P = 0.021; Table 6).

Follow-up. The mean follow-up time was 4.0 years (range 0-17.1 years) with a follow-up index of 0.48 (SD: 0.39). During the

Table 5: Univariable logistic regression analysis for 30-day mortality

Characteristics	Odds ratio (95% CI)	P-value
Gender	1.6 (0.43-6.0)	0.48
Prior cardiac surgery	3.5 (0.43-28.3)	0.24
CPB time	0.1 (0.99-1.0)	0.87
Aortic cross-clamp time	1.0 (0.99-1.0)	0.65
COPD	3.0 (0.88-10.2)	0.08
Pulmonary hypertension	2.3 (0.62-8.2)	0.22
Extracardiac arteriopathy	2.9 (1.01-7.89)	0.04
Coronary artery disease	0.95 (0.35-2.4)	0.86
Rhythm disorders	1.39 (0.89-2.16)	0.15
DMII	3.08 (1.08-8.77)	0.04
Ejection fraction under 30%	5.38 (1.22-23.73)	0.03
NYHA III/IV	2.70 (1.11-6.55)	0.03
Preoperative dialysis	23.73 (5.57-101.1)	< 0.001
Prior stroke	0.23 (0.05-1.08)	0.06
Stroke within 14 days prior to operation	4.85 (1.54-15.28)	0.007
Concomitant aortic arch surgery	3.50 (0.89-13.82)	0.07
BCNIE	0.32 (0.07-1.50)	0.15
Staphylococcal infection	2.0 (0.75-5.33)	0.17
Streptococcal infection	1.89 (3.34-10.52)	0.47
Enterococcal infection	0.97 (0.32-2.97)	0.96

BCNIE: blood culture-negative infective endocarditis; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; DMII: diabetes mellitus type II with or without insulin dependency; NYHA: New York Heart Association classification.

Table 6: Multivariable logistic regression analysis for 30-day mortality

Characteristics	Odds ratio (95% CI)	P-value
Preoperative dialysis dependency Ejection fraction under 30%	22.75 (4.79–108.14) 17.91 (3.27–98.01)	<0.001 <0.001
Stroke within 14 days prior to operation	5.21 (1.28-21.2)	0.021

CI: confidence interval.

follow-up period, another 36 patients died from various causes: 6 patients due to heart failure; 5 patients due to sepsis and multi-organ failure, of which none due to re-endocarditis, 3 patients due to renal failure; 2 patients due to respiratory failure; 2 patients due to a cerebrovascular accident; 2 patients due to bleeding complications and 7 patients due to natural non-cardiac-related death (see Supplementary Material). In 9 patients, cause of death was unknown. One patient was lost to follow-up. The long-term survival was 67.6% (SD: 0.4) at 1 year, 51.2% (SD: 0.5) at 5 years, 31.4% (SD: 0.6) at 10 years and 19.4% (SD: 0.6) at 15 years (Fig. 1).

Four patients required a redo operation, 2 due to recurrent endocarditis after 1.4 and 6 years of follow-up and 2 due to structural graft degeneration after 2.6 and 8.1 years of follow-up, respectively. Freedom from reintervention was 98.3% (SD \pm 1.7) at 1 year, 90.8% (SD \pm 5.7) at 5 years and 83.3% (SD \pm 8.5) at 10 years (Fig. 2A).

Three patients did develop re-endocarditis (2.7%). Two of these patients needed a reoperation, one patient was treated medically. Overall absence of recurrent endocarditis was 95% up to 17 years of follow-up (Fig. 2B).

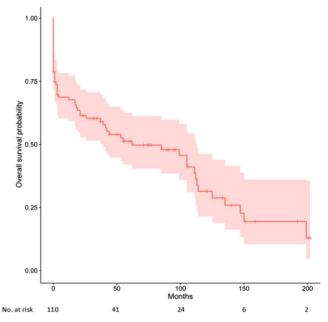


Figure 1: The Kaplan-Meier survival curve after allograft implantation for native and prosthetic valve endocarditis.

DISCUSSION

In infective endocarditis, the choice of valve and/or conduit is guided by factors such as the presence of PVE, the integrity of the aortic root, need for anticoagulation, the availability of cryopreserved allografts and surgical experience [1, 7]. In the case of an intact aortic root, the preference for mechanical or bio-prosthetic valves is understandable, but in cases of invasive infective endocarditits (IE) with concomitant peri-annular abscesses, the role of aggressive debridement and root replacement rather than simple aortic valve replacement is crucial. In our series, all patients had extensive aortic root abscess and 86% had PVE, some of those underwent multiple reoperative sternotomies. At presence, there are no prospective randomized studies to support decision-making in this subpopulation. However, in a systematic review and meta-analysis, Yanagawa et al. [12] examined 2232 patients in 18 observational studies to compare the outcomes between allograft and conventional prosthesis for native valve endocarditis (NVE) and PVE. The median number of patients with PVE in these studies was 30%. No differences were found in early mortality or stroke nor in long-term outcomes of all-cause mortality, recurrent endocarditis and reoperation between allograft versus all conventional prosthesis. However, there were significantly more reoperations with allograft as compared to the mechanical prosthetic valves. Furthermore, there was a higher incidence of peri-annular abscess, root replacement and reoperation for PVE in the allograft cohort, with significantly longer cardiopulmonary bypass and cross-clamp times. This could implicate a greater disease burden in this cohort. Given that there was no statistical difference in operative mortality between these groups, one could presume that allografts may have better outcomes in these high-risk patients. Like others, we contend that the use of allografts in this subset of patients may offer distinct surgical technical advantages for several reasons [6-9, 13]. First, the complex reconstruction after aggressive debridement of the root can be better accommodated by the allografts due to its tissue components such as the aortomitral

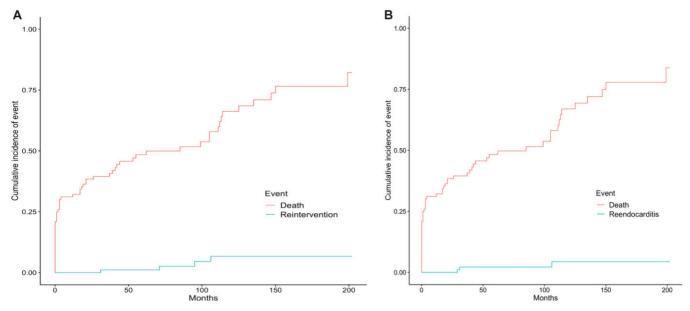


Figure 2: (A) Freedom from reintervention adjusted for competing risk with mortality. (B) Freedom from re-endocarditis adjusted for competing risk with mortality.

continuity, the anterior leaflet of the mitral valve and the muscular tissue of the left ventricular outflow tract. This tissue support allows for filling the large tissue spaces left after wide debridement, which prosthetic stented or stentless conduits cannot. Second, their superior haemodynamics, presumed bacterial resistance, low incidence of reinfection, the avoidance of warfarinrelated complications and very low thrombotic event rates. Thus, all these advantages make the allograft an ideal substitute with good clinical outcomes [14–16].

However, relatively young patients may face reoperations in the long run due to structural valve deterioration or calcification of the cryopreserved allograft, which is a concern [12, 17, 18]. Despite this drawback of structural valve degeneration, we believe that the abovementioned advantages, including infection control and mitigation of IE-related mortality, outweigh this long-term risk. Moreover, in the case of allograft degeneration, valve-in-valve transcatheter aortic valve replacement may then offer a realistic solution especially in older patients [19, 20].

The second goal of this study was to find factors associated with the 30-day mortality. We found that preoperative dialysisdependent patients with aortic root endocarditis were almost 23 times more likely to die within 30 days of postoperative hospital stay than those who were not dialysis dependent. The reason for this highly significant association is multifactorial. First, dialysisdependent patients are classified under chronic reno-cardiac disease type 4, which is characterized by accelerated ischaemic and calcified valvular heart disease. In addition, chronic pressure and volume overload will eventually deteriorate the left ventricular function [21]. Second, dialysis-dependent patients are prone to staphylococcal infections, sepsis, thrombosis and infective endocarditis due to the frequent use of vascular access devices [22, 23]. These factors are known to portend a higher 30-day mortality as well [1, 16-19]. Finally, acute renal failure is strongly related to the severity of postoperative haemodynamic deterioration caused by cardiogenic- or septic shock. Therefore, the surgical treatment for bacterial endocarditis in these patients is more demanding due to extensive comorbid conditions. In spite of these complex circumstances and higher operative risk, however, the guidelines still recommend adhering to the accepted indications for surgical treatment of infective endocarditis [24, 25].

Another strong incremental factor associated with the 30-day mortality is recent stroke within 14 days prior to operation. These patients with recent stroke without intracranial bleeding were 5 times more likely to die within 30 days of hospital stay than those without preoperative neurological event. This risk factor not only influences the proper timing of surgical intervention but also the choice of prosthesis. Okita et al. [26] retrospectively investigated the effect of the timing of surgery for active IE in patients with cerebral complications. In 568 patients, non-haemorrhagic cerebral infarction was present in 118 patients, 54 patients had intracranial haemorrhage and 396 had no cerebral event (control group). Delayed surgery of more than 2 weeks after cerebral infarction, resulted in a higher incidence of hospital death compared to those who underwent surgery within 7 days. In contrast, patients with intracranial haemorrhage who underwent surgery within 7 days had a higher incidence of hospital death compared to those, in whom surgery was delayed for more than 8 days. They concluded that early surgery in active IE patients with cerebral infarction is safe. Delahaye et al. [27] concluded that there is no benefit and even potential harm in delaying surgery. So, there is substantial evidence that early operation in IE is beneficial, unless the patient suffers major intracranial bleeding or severe neurological deficits. Finally, this comorbidity also justifies the use of allografts even in younger patients regarding the risks associated with anticoagulation in the early postoperative period.

Finally, in the perioperative period, 6 patients needed an extracorporeal life support system (ECLS) as a temporary circulatory and respiratory support. They suffered from refractory septic shock with profound left ventricular impairment. They had no lactate clearance, mixed venous saturation (Svo2) <55%, cardiac index <2 l/min/m², mean arterial pressure <65 mmHg in spite of maximum vasoactive inotropic support and adequate antibiotic treatment. These highly critical clinical circumstances urged us to implant the ECLS as ultima ratio therapy in an attempt to restore the oxygenation to the tissue,

to enhance the circulation and restraining the adverse effects of cardiac depression and vasoplegia. However, our experience shows that, even though ECLS is highly effective in bridging the patient from the operation room to the ICU, 5 of the 6 patients could not be weaned from the ECLS and died. Only 1 patient, who received his ECLS preoperatively, survived. This poor survival coincides with those reported by others and confirms that the role of ECLS in refractory septic shock is still very limited or even futile [28–30].

Strengths and limitations

The strength of this study is that it describes the dedicated approach with cryopreserved allograft as the conduit of choice for aortic valve endocarditis with annular abscess formation. On the other hand, due to the retrospective nature and the lack of routine structured follow-up in our clinic, a reasonable risk factor analysis for the long-term mortality was not feasible, nor were details of long-term valve function available.

CONCLUSIONS

In aortic root endocarditis with abscesses formation, cryopreserved allografts exhibit excellent clinical performance with a low rate of reinfection and reintervention, which makes its use as valve replacement a very desirable option, particularly in the setting of reoperation and or multiple reoperations. Preoperative dialysis dependency, ejection fraction under 30% and stroke within 14 days prior to operation were incremental factors associated with the 30-day mortality.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

Conflict of interest: none declared.

Data availability

All relevant data are within the manuscript and its Supporting Information files.

Author contributions

Afram Yousif: Conceptualization; Data curation; Formal analysis; Methodology; Writing—original draft; Writing—review & editing. Khaldoun Ali: Writing—review & editing. Marcel Anssar: Writing—review & editing. Wolfgang Harringer: Formal analysis; Writing—review & editing. Aschraf El-Essawi: Conceptualization; Formal analysis; Methodology; Supervision; Writing—original draft; Writing—review & editing. René Brouwer: Conceptualization; Formal analysis; Methodology; Supervision; Writing—review & editing.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Satsuki Fukushima, Mikalai Shchatsinka and the other anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

- [1] Luehr M, Bauernschmitt N, Peterss S, Li Y, Heyn O, Dashkevich A *et al.* Incidence and surgical outcomes of patients with native and prosthetic aortic valve endocarditis. Ann Thorac Surg 2020;110:93–101.
- [2] Leontyev S, Davierwala PM, Krögh G, Feder S, Öberbach A, Bakhtiary F et al. Early and late outcomes of complex aortic root surgery in patients with aortic root abscesses. Eur J Cardiothorac Surg 2016;49: 447–54.
- [3] d'Udekem Y, David TE, Feindel CM, Armstrong S, Sun Z. Long-term results of surgery for acute infective endocarditis. Eur J Cardiothorac Surg 1997;11:46–52.
- [4] Haydock D, Barratt-Boyes B, Macedo T, Kirklin JW, Blackstone E. Aortic valve replacement for active infectious endocarditis in 108 patients. A comparison of freehand allograft valves with mechanical prostheses and bioprostheses. J Thorac Cardiovasc Surg 1992;103:130-9.
- [5] Said SM, Abdelsattar ZM, Schaff HV, Greason KL, Daly RC, Pochettino A et al. Outcomes of surgery for infective endocarditis: a single-centre experience of 801 patients. Eur J Cardiothorac Surg 2018;53:435–9.
- [6] Perrotta S, Aljassim O, Jeppsson A, Bech-Hanssen O, Svensson G. Survival and quality of life after aortic root replacement with homografts in acute endocarditis. Ann Thorac Surg 2010;90:1862–7.
- [7] Musci M, Weng Y, Hubler M, Amiri A, Pasic M, Kosky S et al. Homograft aortic root replacement in native or prosthetic active infective endocarditis: twenty-year single-center experience. J Thorac Cardiovasc Surg 2010:139:665–73
- [8] Lopes S, Calvinho P, de Oliveira F, Antunes M. Allograft aortic root replacement in complex prosthetic endocarditis. Eur J Cardiothorac Surg 2007;32:126–30.
- [9] David TE, Gavra G, Feindel CM, Regesta T, Armstrong S, Maganti MD. Surgical treatment of active infective endocarditis: a continued challenge. J Thorac Cardiovasc Surg 2007;133:144-9.
- [10] Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633–8.
- [11] Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9-13.
- [12] Yanagawa B, Mazine A, Tam DY, Jüni P, Bhatt DL, Spindel S et al. Homograft versus conventional prosthesis for surgical management of aortic valve infective endocarditis: a systematic review and meta-analysis. Innovations (Phila) 2018;13:163-70.
- [13] Antunes MJ. Is allograft aortic valve replacement still an option? When, which, where? J Thorac Cardiovasc Surg 2018;156:1366-7.
- [14] Nappi F, Avtaar Singh SS, Timofeeva I. Learning from controversy: contemporary surgical management of aortic valve endocarditis. Clin Med Insights Cardiol 2020;14:1179546820960729.
- [15] Nappi F, Nenna A, Petitti T, Spadaccio C, Gambardella I, Lusini M et al. Long-term outcome of cryopreserved allograftfor aortic valve replacement. J Thorac Cardiovasc Surg 2018;156:1357–1365.e6.
- [16] Steffen V, Marsch G, Burgwitz K, Kuehn C, Teebken OE. Resistance to infection of long-term cryopreserved human aortic valve allografts. J Thorac Cardiovasc Surg 2016;151:1251-9.
- [17] Joudinaud TM, Baron F, Raffoul R, Pagis B, Vergnat M, Parisot C et al. Redo aortic root surgery for failure of an aortic homograft is a major technical challenge. Eur J Cardiothorac Surg 2008;33:989–94.
- [18] Crestanello JA. Aortic homografts: unrealized expectations and hard reoperations at the end. I Thorac Cardiovasc Surg 2018;156:1351-2.
- [19] Kowert A, Vogt F, Beiras-Fernandez A, Reichart B, Kilian E. Outcome after homograft redo operation in aortic position. Eur J Cardiothorac Surg 2012;41:404–8.
- [20] Greco R, Muretti M, Djordjevic J, Jin XY, Hill E, Renna M et al. Surgical complexity and outcome of patients undergoing re-do aortic valve surgery. Open Heart 2020;7:e001209.
- [21] Di Lullo L, Bellasi A, Barbera V, Russo D, Russo L, Di Iorio B et al. Pathophysiology of the cardio-renal syndromes types 1–5: an uptodate. Indian Heart J 2017;69:255–65.
- [22] Raza S, Hussain ST, Rajeswaran J, Ansari A, Trezzi M, Arafat A et al. Value of surgery for infective endocarditis in dialysis patients. J Thorac Cardiovasc Surg 2017;154:61–70.e6.
- [23] Rankin JS, Milford-Beland S, O'Brien SM, Edwards FH, Peterson ED, Glower DD et al. The risk of valve surgery for endocarditis in patients with dialysis-dependent renal failure. J Heart Valve Dis 2007;16: 617-22.

- [24] Pettersson GB, Hussain ST. Current AATS guidelines on surgical treatment of infective endocarditis. Ann Cardiothorac Surg 2019;8:630-44.
- [25] Leither MD, Shroff GR, Ding S, Gilbertson DT, Herzog CA. Long-term survival of dialysis patients with bacterial endocarditis undergoing valvular replacement surgery in the United States. Circulation 2013;128:344–51.
- [26] Okita Y, Minakata K, Yasuno S, Uozumi R, Sato T, Ueshima K et al. Optimal timing of surgery for active infective endocarditis with cerebral complications: a Japanese multicenter study. Eur J Cardiothorac Surg 2016;50:374-9.
- [27] Delahaye F, Antchouey AM, de Gevigney G. Optimal timing for cardiac surgery in infective endocarditis: is earlier better? Curr Infect Dis Rep 2014;16:411-3.
- [28] Riera J, Argudo E, Ruiz-Rodríguez JC, Ferrer R. Extracorporeal membrane oxygenation for adults with refractory septic shock. ASAIO J 2019;65:760-8.
- [29] Pagani FD. Extracorporeal membrane oxygenation for septic shock: heroic futility? J Thorac Cardiovasc Surg 2018;156:1110-1.
- [30] Falk L, Hultman J, Broman LM. Extracorporeal membrane oxygenation for septic shock. Crit Care Med 2019;47:1097–105.