

## Clinical Experience with Cryopreserved Allografts for Aortic Infection

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**Abstract:** Treatment of aortic infection continues to pose major challenge for surgeons. This study assessed the clinical profiles and outcomes of patients with aortic infection treated with cryopreserved allograft in our institute. Clinical records were reviewed in 22 allografts implanted in 21 patients from December 1998. The overall in-hospital mortality rate was 36%. The factors (thoracic surgery, positive bacterial study, periaortic abscess, graft infection, no omentopexy, and deep hypothermic circulatory arrest in thoracic surgery) that may affect the in-hospital mortality were examined, and only positive bacterial study was proven to be a significant risk factor. Although the early postoperative courses of patients with abscess formation around the thoracic artificial graft were disappointing, preoperative open drainage and irrigation would improve the outcome. The aorto-esophageal fistula is no longer a fatal illness in this series. (J Jpn Coll Angiol, 2006, 46: 817–822)

**Key words:** allograft, graft infection, infective aneurysm, aorto-esophageal fistula, omentopexy

### Introduction

Treatment of infections of the aorta or aortic prosthesis remains challenging for vascular surgeons. The conventional management of aortic infection includes complete excision of affected aorta, wide debridement of surrounding tissues, and revascularization with extra-anatomic bypass or *in situ* reconstruction. In *in situ* reconstruction, artificial grafts are used due to a shortage of optimal autologous tissues for aortic reconstruction. Therefore, a high re-infection rate discouraged us from performing this approach. Recently cryopreserved allografts became available at the University of Tokyo Hospital. The early to midterm surgical outcome in patients with aortic infection treated with allografts is reviewed.

### Patients and Methods

From December 1998 to October 2005, a total of 22

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cryopreserved aortic allografts were implanted in 21 patients with one recurrence, 8 (36%) for infective aneurysm of the thoracic ( $n = 6$ ) or abdominal ( $n = 2$ ) aorta, and 14 (64%) for prosthetic graft infection of the thoracic ( $n = 12$ ) or abdominal ( $n = 2$ ) aorta. All prostheses but 1 allograft were Dacron grafts. The affected sites were the ascending aorta in 7 patients, the transverse-to-distal arch in 6, the descending in 4 (all cases were with aorto-esophageal fistula), the thoracoabdominal in 1, the pararenal abdominal in 2, and the infrarenal abdominal in 2. There were 14 male and 8 female cases; the mean age was  $58 \pm 11$  years, ranging 31–75. The case details are summarized in **Table 1**.

During this period, 7 patients with suspicious aortic infection underwent *in situ* replacement with crystal violet impregnated Dacron graft or omentopexy only, because of allograft size mismatch or of inactive infection, and were excluded.

#### (1) Perioperative Management

Most patients were transferred from other institutes and

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**Table 1** Characteristics of patients with aortic infection

#	Affected site	Age	Gender	Aorta	Abscess	Omentopexy	Bacteria	Status	Remarks
1	Ascending	75	F	G	Yes	No	MRSA	HD	Died of sepsis-MOF
2	Ascending	56	M	G	Yes	No	MRSE	HD	LVAD, died of heart failure
3	Ascending	33	M	G	Yes	Yes	MRSA	Alive	
4	Ascending	56	F	G	Yes	Yes	MRSA	Alive	Open drainage
5	Ascending	52	M	G	No	No	N/D	Alive	
6	Ascending	61	F	G	No	No	Staphylococcus capitis	Alive	
7	Ascending	57	M	G	No	Yes	N/D	Alive	Redo
8	Arch	53	M	G	Yes	No	$\alpha$ -streptococcus	HD	AEF, died of disruption
9	Arch	69	F	G	Yes	No	MRSA	HD	Died of disruption
10	Arch	62	F	G	Yes	No	N/D	LD	Open drainage, same as #22
11	Arch	63	F	G	Yes	No	N/D	HD	Redo, died of allograft rupture
12	Arch	53	M	N	No	No	N/D	Alive	
13	Arch	31	M	N	No	No	N/D	Alive	
14	Descending	59	M	N	No	Yes	N/D	LD	AEF, died of pneumonia
15	Descending	70	M	N	No	Yes	N/D	Alive	AEF
16	Descending	67	F	N	No	Yes	N/D	Alive	AEF
17	Descending	55	F	N	No	Yes	MRSA	HD	AEF, died of disruption
18	Thoracoabdominal	64	M	G	Yes	No	Proteus vulgaris, Klebsiella pneumonia	HD	Died of sepsis-MOF
19	Pararenal abdominal	54	M	G	Yes	No	N/D	Alive	
20	Pararenal abdominal	52	M	N	No	Yes	Bacteroides fragillis	HD	Died of disruption
21	Infrarenal abdominal	73	M	G	Yes	Yes	Klebsiella oxytoca, Candida albicans	Alive	
22	Infrarenal abdominal	63	M	N	No	Yes	MRSA	LD	Died of arrhythmia

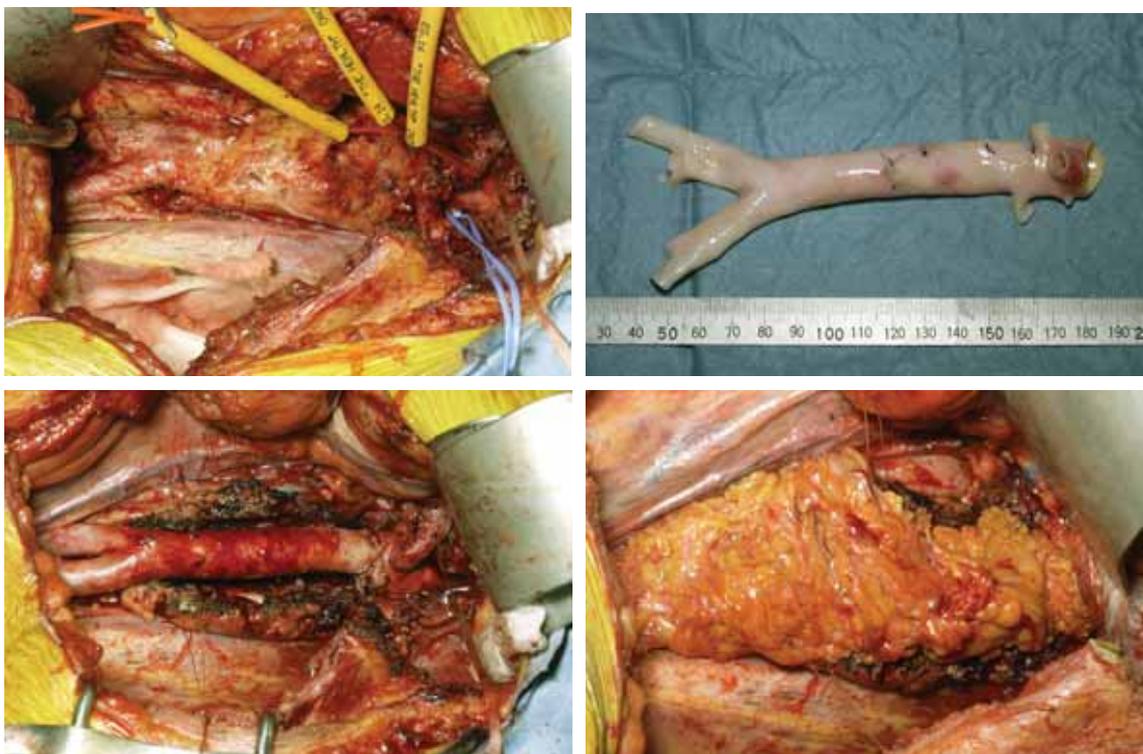
M: male, F: female, G: graft, N: native, MRSA: methicillin resistant staphylococcus aureus, MRSE: methicillin resistant staphylococcus epidermidis, N/D: not detected, HD: hospital death, LD: late death, MOF: multi-organ failure, AEF: aorto-esophageal fistula, LVAD: implantation of left ventricular assist device

had been with intensive antibiotics therapy. Previously, all surgeries were performed on an emergent basis. Since 2 years ago, if abscess formation is detected in an affected site, open drainage and irrigation for a couple of days are performed prior to replacement unless there are no signs of rupture.

Patients with aortic infection in principle underwent *in situ* replacement with cryopreserved allograft with omental wrapping (Fig. 1) whenever possible. If the omentum was not available, suture reinforcement using an allograft strip and/or wrapping with pedicled intercostal muscle flap

were performed to secure anastomosis line. Amikamycin-impregnated fibrin glue was used in all cases to control suture-hole leakage.

Intravenous antibiotics were administered postoperatively based on the results of susceptibility tests until clinical signs of infection diminished. For patients with an infected prosthetic graft remaining partially, lifelong oral antibiotics were given. All survivors underwent CT scanning before discharge from the hospital.



**Figure 1** A case with infective aortic dissection in the pararenal abdominal aorta is shown.

A: Operative view via the retroperitoneal cavity. The silastic slings encircle abdominal branches and a large lumbar artery. The retroperitoneal fatty tissue tightly adhered around the aneurysm.

B: The abdominal aortic allograft harvested from a 30-year-old male donor.

C: The juxtarenal aorta to the common iliac arteries is replaced with the allograft.

D: The allograft is completely wrapped with the omental flap.

A	B
C	D

### (2) Cryopreserved Allograft

Allografts were harvested and cryopreserved at the University of Tokyo Tissue Bank (UTTB). The process of harvesting, storage, and thawing are detailed in Appendix.

### (3) Statistical Analysis

The factors (thoracic surgery, positive bacterial study, periaortic abscess, graft infection, no omentopexy, and deep hypothermic circulatory arrest in thoracic surgery) that may affect the in-hospital mortality were examined using  $2 \times 2$  chi-square test and Fischer's test.

## Results

The in-hospital mortality rate was 36% (8/22), all with uncontrollable infection (sepsis-MOF: 2, anastomosis

disruption: 4, allograft rupture: 1, heart failure: 1). There was no major morbidity in survivors. Late deaths occurred in 3 patients (pneumonia: 1, arrhythmia: 1, recurrent infection: 1) identical with in-hospital death due to allograft rupture. The recurrent case developed inflammatory signs 8 months after initial allograft replacement. The in-hospital mortality rate of the thoracic graft infection accompanied by abscess was significantly high (6/11, 55%).

Among the 6 factors that may affect the in-hospital mortality, only the positive bacterial study showed statistical significance ( $p = 0.031$ ) on the in-hospital mortality (**Table 2**). The species were methicillin-resistant staphylococcus aureus in 6 of 12 cases positive for bacterial study. While both periaortic abscess and no omentopexy had a tendency to contribute to high mortality, they failed to be

**Table 2** Factors for in-hospital mortality (2 × 2 chi-square test and Fischer's test)

		Dead	Alive	p-value
Thoracic or abdominal surgery	Thoracic	7	11	1
	Abdominal	1	3	
Positive or negative bacterial study	Positive	7	5	0.031
	Negative	1	9	
Periaortic abscess, yes or no	yes	6	5	0.183
	no	2	9	
Graft or native aortic infection	Graft	6	8	0.649
	Native	2	6	
Omentopexy, no or yes	no	6	6	0.2
	yes	2	8	
DHCA in thoracic surgery, yes or no	yes	3	3	0.627
	no	4	8	

DHCA: deep hypothermic circulatory arrest

considered statistical significance.

Three of 5 patients with aorto-esophageal fistula, who were operated on immediately after the diagnosis was made based on sentinel hemorrhage, were all alive.

### Discussion

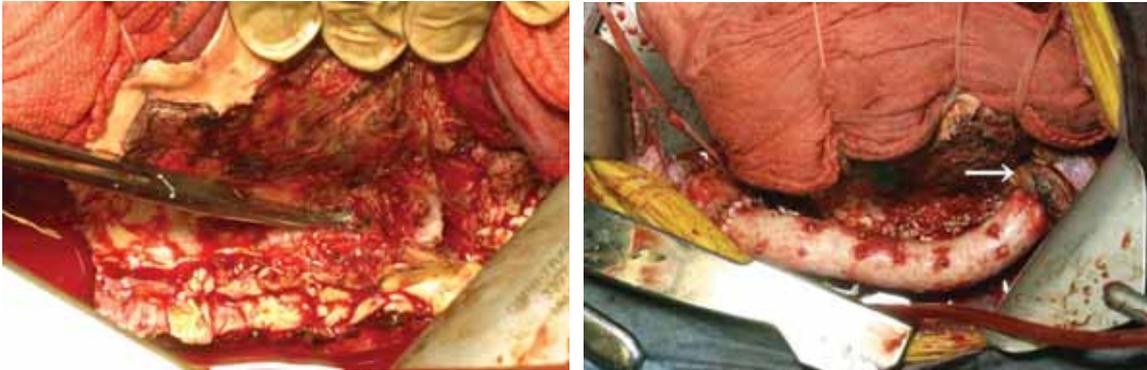
Since Walker et al. described the favorable results with *in situ* reconstruction of the infected abdominal aorta,<sup>1</sup> *in situ* reconstruction had been gaining acceptance as a better technique with less anastomotic disruption than extra-anatomic bypass that often leads to aortic stump rupture.<sup>2</sup> However, the late recurrence rate remained high, 17%, with artificial vascular grafts. The use of cryopreserved allografts has evolved into a distinct method for the surgical treatment of infected aorta. Kieffer et al. verified the effectiveness of *in situ* allograft in 1993,<sup>3</sup> and Vogt et al. demonstrated its superiority over conventional techniques.<sup>4</sup> The 30-day mortality in this paper was 6% for the whole series. Whereas our result, 36% of in-hospital mortality, was considerably higher than that. This might be caused by several reasons. Their series contained lower rate of thoracic cases (33% vs 82%) and prosthetic grafts (57% vs 64%). And, as Vogt et

al. described, technical problems due to the small number of cases treated would also affect the outcome. Although our technique follows the modification in that paper to skip the learning curve, we need more experience.

In this study, only positive bacterial study showed a significant difference on the mortality. More than one half of the patients (7/12) with positive bacterial study died in hospital, while only 1 died in 10 patients without. This fact seems very reasonable. The other factors did not show statistical significance; it is likely that further study with an increased number of patients might reveal a significant difference. Since the number of patients with aortic infection is not large and the spectrum is broad, more experience is required.

#### (1) Timing of Surgery

Timing to operate is also considered to be highly important in improving early results. In our cases, most of them had long been under intensive antibiotics therapy at other hospitals, and the bacterial study often showed multi-drug resistance, otherwise negative. That is why the positive rate of bacterial study is so low (12/22, 55%) in this series.



**Figure 2** Operative view of a case of aorto-esophageal fistula is shown.

A: The top of the forceps is inserted into the esophagus.

B: The descending aorta is replaced with an allograft. The proximal suture line is encircled doubly with the pedicled intercostal muscle flap (arrow). Note that the allograft is upside-down to match the distal anastomotic diameter, and that the allograft is front side-back to control bleeding from the intercostal branches.

A | B

Abscess formation was not rare, manifesting a septic state. Initially we operated on all the patients as soon as possible after the diagnosis was made or on arrival of the patient. But the early postoperative courses of patients with abscess formation around the thoracic artificial graft yielded disappointing results, as we reported previously,<sup>5</sup> and nobody survived. Recently we changed the strategy for such cases to conducting open drainage and irrigation prior to thoracic graft replacement. As a result, no hemorrhage occurs to date. Two of the 3 patients treated with this method survived. Reduction of the number of bacteria, as well as stabilization of inflammation in surrounding tissues, would improve the outcome.

## (2) Aorto-esophageal Fistula

There were 5 patients with aorto-esophageal fistula (AEF) in this series. The AEF has been considered to be a fatal disease with few patients survival.<sup>6</sup> Recently cases of successful surgical treatment by *in situ* replacement with Dacron graft or allograft have been reported.<sup>7</sup> Our strategy for AEF consists of the use of allograft, esophagectomy regardless of the fistula being so small, and omental wrapping<sup>8</sup> (Fig. 2). The fact of 3 in 5 patients being saved demonstrates the use of allograft contributes to an excellent result. One of the death cases was a patient with an anastomotic pseudoaneurysm after graft replacement of the distal aortic arch, and the other

had long been suffering from chronic AEF for over 3 weeks at another hospital, developing abscess by several kinds of multi-drug resistant bacteria in the false lumen of the dissecting aneurysm. If the AEF had been a common kind with communication between the native aorta and the esophagus present, and treated promptly, the surgical results should have been promising with the use of allograft.

## Conclusion

In conclusion, the use of cryopreserved allograft contributed to the improved surgical outcome in patients with aortic infection. The result of those who had negative bacterial study is promising. Treatment for thoracic aortic infection with abscess formation has progressed, and our strategy that consists of preoperative open drainage and irrigation appears to facilitate better outcomes.

## Appendix: Cryopreserved Allograft of UTTB

Written informed consent was obtained from each donor's family, and allografts were harvested with care from multiple organ cadaver donors. Bacteriology and virology tests (hepatitis B and C virus, human immunodeficiency virus 1 and 2, human T-lymphotrophic virus 1, cytomegalovirus) were carried out for all donors. After immersing the allografts in Roswell Park Memorial Institute (RPMI) medium 1640 (Invitrogen, Grand Island, NY, USA) containing four antibiotics (cefmetazole sodium 240  $\mu$ g/mL, lincomycin hydro-

chloride 120  $\mu\text{g}/\text{mL}$ , vancomycin hydrochloride 50  $\mu\text{g}/\text{mL}$ , and polymixin B sulfate 1,000 U/mL) for 24 to 48 hours at 4°C, they were trimmed, with the aortic branches being purse-string-sutured. Then they were soaked in RPMI medium 1640 containing 10% dimethylsulfoxide (Sigma, St. Louis, MO, USA), packed doubly, and frozen in a programmable freezer (Profreezer, Nihon Freezer, Tokyo, Japan). The specimens were cooled from room temperature to -50°C at a rate of 1°C/min and from -50°C to -80°C at 5°C/min. After the temperature of the specimens reached -80°C, they were preserved at -180°C in the vapor phase of liquid nitrogen. The allografts were thawed on request and were transferred to the operating room using a dry-type shipping container. They were placed at room temperature for 7 min. The outer bags were then opened, and the inner bags were placed gently in warm (37°C), sterile saline for 10 min. After the medium thawed completely, the bags were moved into a povidoneiodine solution for 5 min. Then the inner bags were opened, and the allografts were taken, placed in the Alloflow (LifeNet, Virginia Beach, VA, USA), rinsed with 1 L of lactate ringer solution, and carried to the surgical field. The surgeon trimmed them on the operating table.

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