

In situ reconstruction with cryopreserved arterial allograft in mycotic aneurysms or aortoiliac prosthetic grafts infection: a multi-institutional experience

Reconstrução in situ com aloenxerto arterial criopreservado em aneurismas micóticos ou em infecção de enxertos protéticos aorto-iliacos: um estudo multicêntrico

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Abstract

Objective: Aortic prosthetic graft infection remains a highly fatal surgical complication. Recent studies with cryopreserved allografts in the treatment of vascular graft infection suggest improved clinical outcomes. The purpose of this study was to evaluate the efficacy of cryopreserved aortic allografts in the treatment of infected prosthetic grafts or mycotic aneurysms.

Methods: Clinical data of all patients who underwent *in situ* aortic reconstruction with cryopreserved allografts for either infected aortic prosthetic graft or mycotic aneurysms from 1999 to 2003 were reviewed. Relevant clinical variables and treatment outcomes were analyzed.

Results: A total of 18 patients (14 men; overall mean age 62 ± 12 years, range 41-72 years) were identified during this study period. Treatment indications include 12 primary aortic graft infections (67%), four mycotic aneurysms (22%), and two aortoenteric erosions (11%). Transabdominal and thoracoabdominal approaches were used in 14 (78%) and four patients (22%), respectively. *Staphylococcus aureus* was the most commonly identified organism ($n = 11$, 61%). Although there was no intraoperative death, the 30-day operative mortality was 17% (3/18). There were nine (50%) non-fatal complications including local wound infection ($n = 3$), lower extremity deep venous thrombosis ($n = 2$), amputation ($n = 2$), and renal failure requiring hemodialysis ($n = 2$). The average length of their hospital stay was 16.4 ± 7 days. During a mean follow-up period of 8.3 months, reoperation for allograft revision was necessary in one patient due to graft thrombosis. The overall treatment mortality rate was 22% (4/18).

Conclusion: *In situ* aortic reconstruction with cryopreserved allografts is an acceptable treatment modality in patients with infected aortic prosthetic graft or mycotic aneurysms. Our study showed that mid-term graft-related complications such as reinfection or aneurysmal degeneration remained uncommon.

Key words: aortic graft infection, mycotic aneurysm, surgical treatment, cryopreserved graft.

Resumo

Objetivo: A infecção do enxerto protético aórtico continua sendo uma complicação cirúrgica altamente fatal. Estudos recentes com aloenxertos criopreservados no tratamento de infecções de enxerto vascular sugerem melhores resultados clínicos. O objetivo deste estudo foi avaliar a eficiência dos aloenxertos aórticos criopreservados no tratamento de enxertos protéticos infectados ou de aneurismas micóticos.

Métodos: Foram analisados os prontuários médicos de todos os pacientes submetidos à reconstrução aórtica *in situ* com aloenxertos criopreservados, tanto para o enxerto protético aórtico infectado quanto para aneurismas micóticos, no período de 1999 a 2003. Foram analisadas as variáveis clínicas relevantes e o resultado dos tratamentos.

Resultados: Um total de 18 pacientes (14 homens; média de idade 62 ± 12 anos, variação de 41 a 72 anos) foram identificados neste estudo. As indicações para o tratamento incluíram 12 infecções primárias de enxerto aórtico (67%), quatro aneurismas micóticos (22%) e duas erosões aorto-entéricas (11%). Foram utilizadas abordagens transabdominal e tóraco-abdominal em 14 (78%) e quatro pacientes (22%), respectivamente. O *Staphylococcus aureus* foi o organismo mais frequentemente observado ($n = 11$, 61%). Embora não tenha havido morte intra-operatória, a mortalidade pós-operatória, em um período de 30 dias, foi de 17% (3/18). Houve nove (50%) complicações não-fatais, incluindo infecção local do ferimento ($n = 3$), trombose venosa profunda dos membros inferiores ($n = 2$), amputação ($n = 2$) e falha renal com necessidade de hemodiálise ($n = 2$). A média de hospitalização foi de $16,4 \pm 7$ dias. Durante um período de acompanhamento médio de 8,3 meses, a reoperação para revisão do aloenxerto foi necessária em um paciente, devido à trombose do enxerto. A taxa de mortalidade geral foi de 22% (4/18).

Conclusão: A reconstrução aórtica *in situ* com aloenxertos criopreservados é uma modalidade de tratamento aceitável para pacientes com enxerto protético aórtico infectado ou com aneurismas micóticos. Nosso estudo demonstrou que complicações a médio prazo relativas ao enxerto, tais como reinfeção ou degeneração do aneurisma, permaneceram infrequentes.

Palavras-chave: infecção do enxerto aórtico, aneurisma micótico, tratamento cirúrgico, enxerto criopreservado.

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Article submitted on March 28, 2005, accepted on April 25, 2005.

J Vasc Br 2005;4(2):123-8.

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Infected aortic prosthetic graft remains one of the most serious complications of aortic surgery and presents significant treatment challenges.¹ The standard surgical management of total graft excision and extra-anatomic bypass is associated with substantial morbidity, mortality, and rate of limb loss.^{1,2} Aortic allograft has been used as a conduit for arterial reconstruction since the 1950s, when DeBakey and Cooley reported resection and homograft replacement for occlusive and aneurysmal diseases of the aorta in 1954.^{3,4} During the 1960s and 1970s, arterial allografts lost popularity due to concerns of potential risk of later deterioration, availability, and preservation. However, recent studies have demonstrated cryopreserved allograft replacement as an effective and durable alternative for aortic prosthetic graft infection with improved outcomes.⁵⁻⁹ Most reports on in situ aortic allograft reconstruction are from Europe, while studies conducted in the U.S. are scattered and controversial. We herein reviewed our experiences and evaluated the outcomes of cryopreserved allograft replacement for infected aortic prosthetic graft and mycotic aneurysms.

Material and methods

From January 1999 to December 2003, hospital records of all patients who were admitted to the affiliated hospitals of Baylor College of Medicine and Emory University School of Medicine for mycotic aortic aneurysms or suspected aortic prosthetic graft infections were retrospectively reviewed. The four affiliated hospitals included the Methodist Hospital, Houston

Veteran Affairs Medical Center, Emory University Hospital, and Atlanta Medical Center. Patients who underwent surgical intervention for infected aortic grafts or mycotic aneurysms were further evaluated. Those who had intraoperatively confirmed infections and treated with in situ cryopreserved allograft replacement were included in the study. Data were collected with respect to risk factors, preoperative clinical presentations, operative findings, hospital courses, and follow-up evaluations. Types of organisms identified, allograft-related complications, and long-term outcomes were recorded. Patients who had concomitant thoracic graft infections or isolated groin infections without intra-abdominal extensions were excluded from the study.

All cryopreserved allografts were obtained from Cyolife[®] (CryoLife, Inc, Kennesaw, GA, USA) stored at -180 °C to -196 °C and thawed at 37 °C to 42 °C. Matching of blood and tissue compatibility between the cryografts and recipients was not attempted.

Results

Over a 4-year period, a total of 18 patients met the selection criterion. There were 14 men (78%) and four women, with a mean age of 62 years (range, 41-72 years). All patients had multiple medical comorbidities, including coronary artery disease (n = 10), hypertension (n = 16), diabetes mellitus (n = 8), and peripheral vascular disease (n = 14). Twelve patients had long standing histories of tobacco usage (Table 1).

Table 1 - Patient demographics and presentation

Total patients (n)		18
Patient characteristics	Age (range)	62 (41-72)
	Male gender (n, %)	14 (78%)
Co-morbidities	Coronary artery disease (n, %)	10 (56%)
	Hypertension (n, %)	16 (89%)
	Diabetes mellitus (n, %)	8 (44%)
	Smoking (n, %)	12 (67%)
	Peripheral vascular disease (n, %)	14 (78%)
Treatment indications	Primary aortic graft infection (n, %)	12 (67%)
	Aortoenteric erosion (n, %)	2 (11%)
	Mycotic aneurysms (n, %)	4 (22%)
Concomitant groin infection (n, %)		14 (78%)
Interval from original surgery (months)		90 (4-180)

Treatment indications included primary graft infection (n = 12, 67%), mycotic aneurysms (n = 4, 22%), and aortoenteric erosion (n = 2, 11%). Concomitant groin infections were presented in all patients with infected aortic grafts (n = 14). The primary diagnostic modality was an abdominal computer tomography (CT) scan showing evidence of intraabdominal infections in all patients and the diagnosis was further confirmed by intraoperative tissue cultures. The average interval from the original aortic surgeries to the presence of prosthetic graft infection was 90 months, ranging from 4 months to 15 years in those patients who presented infected aortic prosthetic grafts.

All patients were treated with intravenous antibiotics and operative management of graft excision followed by in situ cryopreserved allograft replacement (Table 2). Positive bacterial cultures were confirmed in all the explanted aortic prosthesis or the aneurysmal sac tissue. *Staphylococcus aureus* was the most commonly identified organism, found in 11 patients (61%). The average operating time was 267 minutes (range, 3-5.5 hours) with a 100% technical success rate. The average stay in intensive care was 6 days and the average length of the hospital stay was 16.7 days (range, 9-24 days). All patients received intravenous antibiotics postoperatively followed by long-term oral antibiotics.

Although there was no intraoperative death, the 30-day operative mortality rate was 17%, secondary to multi-organ failure as the result of sepsis (n = 3). In addition, there were 50% non-lethal procedure-related complications, including local wound infection (n = 3), lower extremity deep venous thrombosis (n = 2), renal failure requiring hemodialysis (n = 2), and amputation (n = 2). All patients were available for follow-up with a mean period of 8.3 months (range, 3-18 months). One patient required allograft revision for graft thrombosis (6%) and one died as a result of colocutaneous fistula complications that led to the overall treatment mortality rate of 22% (4/18). There was no evidence of aneurysmal dilatation or disruption on follow-up CT scan evaluations.

Discussion

Aortic prosthetic graft is a rare complication of aortic surgery, occurring in 1 to 2% of patients and the complication rate has been consistent, despite the advances in antibiotics, graft material, and surgical techniques.¹ The standard management of total graft excision and extra-anatomic bypass is associated with substantial morbidities and significant mortality rates ranging from 25 to 75% in reported series.^{1,2}

Table 2 - Treatment strategies and outcomes

Operative approach	Transabdominal (n, %)	14 (78%)
	Thoracoabdominal (n, %)	4 (22%)
Presence of <i>Staphylococcus aureus</i> (n, %)		11 (61%)
Operating time (minutes)		267 ± 53
ICU stay (days)		6 ± 4
Hospital stay (days)		16.7 (9-24)
Follow-up (months)		8.3 (3-18)
Perioperative complications	Local wound infection (n, %)	3 (17%)
	Deep vein thrombosis (n, %)	2 (11%)
	Amputation (n, %)	2 (11%)
	Acute renal failure (n, %)	2 (11%)
Late complication	Graft thrombosis (n, %)	1 (5.6%)
	30-day mortality (n, %)	3 (17%)
Overall mortality (n, %)		4 (22%)

ICU = intensive care unit.

Cryopreserved allograft replacement is an attractive alternative that has been adopted successfully in Europe, while data from the U.S. are scattered and controversial. Our study confirms cryopreserved allograft replacement as an effective strategy for infected aortic prosthetic grafts and mycotic aneurysms.

There are multiple factors contributing to aortic prosthetic graft infection including contamination at the time of implantation, extending infection from the adjacent tissues, seeding from distal sources via hematogenous routine, or erosion into adjacent organs. Manifestation of graft infection may vary widely from days to years depending upon the etiologies of the infection and the physical condition of the patient. The average interval between the original aortic surgeries and the presence of graft infection in our patients was 90 months ranging from 4 months to 15 years. The patient may present with a variety of symptoms, mostly nonspecific, including recurrent fever and chills, groin infection, pulsatile mass or generalized abdominal pain. Rarely, the patients may have gastrointestinal bleeding in the presence of aortoenteric fistula. In the presence of nonspecific symptoms, additional imaging studies are particularly useful in assisting in the diagnosis and operative planning. The most common imaging methods used to evaluate aortic graft infections or aneurysms are ultrasonography, CT scan, and magnetic resonance imaging (MRI).^{10,11} Late aortic graft infections are best evaluated initially by a CT scan or a MRI. CT findings include ectopic gas, perigraft fluid, perigraft inflammatory changes, anastomotic pseudoaneurysm, and thickening of the adjacent bowel. The MRI offers the additional advantage of T2-weighted images to identify perigraft inflammation and minute quantities of perigraft fluid. Sonographic findings of a graft infection include perigraft fluid and pseudoaneurysms. The imaging for infection within a 3-month postoperative period is less diagnostic because of persistent perigraft fluid and inflammatory changes up to 3 months after surgery. Suspected early graft infections often require urgent operative exploration for diagnosis.^{10,11} Due to late presentations of graft infection in our patients, CT scans were particularly informative in confirming the presence of aortic prosthetic graft infection and aiding the operative planning. The presence of saccular aneurysms on CT scans combined with symptoms of infection and positive blood cultures helped identify the mycotic aneurysms in four of our patients.

Treating infected aortic prosthetic graft is extremely challenging. The standard therapeutic option of total graft excision and extra-anatomic bypass is associated with significant mortality and complication rates. O'Hara et al. reviewed their 25 year-experience and demonstrated 0.77% of incidence of aortic graft infection.¹ Despite aggressive surgical treatment including graft excision with and without extra-anatomic bypass in 89% of their patients, they yielded 30-day and 1-year survival of 72 and 42%, respectively. In addition, 27% of the treated patients required major amputation in their series. Similarly, Quinones-Baldrich et al. treated 45 patients with aortic graft infection, including 36 patients who underwent extra-anatomic bypasses.¹² They reported a 30-day mortality rate of 24%, 3-year primary axillo-femoral bypass graft patency rate of 43% and an amputation rate of 34% at 5 years. Their study also suggested that infection in the extra-anatomic bypass graft was the most common cause of recurrent sepsis and the leading cause of late amputations. Nonetheless, the study conducted by Yeager et al. has demonstrated improved overall results. They treated 60 aortic prosthetic graft infections with total excision and extra-anatomic bypass and achieved 30-day mortality and 5-year primary axillo-femoral bypass patency rates of 13 and 73%, respectively.² Despite improved results in some reports, standard surgical treatment of total graft excision and extra-anatomic bypass continues to be associated with substantial complication and mortality rates with potential risk of aortic stump blow out.

The disappointing results of standard surgical treatment have kindled interests in evaluating alternative approaches, such as partial or complete graft preservation, autogenous veins reconstruction, or antibiotic-bonded prostheses. Calligaro et al. investigated partial or complete graft preservation in nine patients and achieved an acceptable perioperative survival rate of 89%.¹³ However, five of the nine patients had limited infection involving the groin only and one of whom had a recurrence that required total excision 6 months later. Additionally, Clagett et al. described using autogenous superficial femoral-popliteal vein (SFPV) as a reconstruction conduit in 41 patients with infected aortic prosthetic grafts and achieved an excellent result of 100% perioperative survival.¹⁴ Nevertheless, they encountered significant perioperative complications associated with vein harvesting including amputation (5%), compartment syndrome (12.3%),

and pulmonary embolism (2.4%). Antibiotic-bonded prosthesis as replacement conduits has been studied as well, with variable success. Koshiko et al. evaluated the efficacy and duration of the antibacterial activity of rifampicin-gelatin grafts in a canine model¹⁵ and concluded that rifampicin-gelatin grafts were valid for *Staphylococcus epidermidis* (*S. epidermidis*) infection, whereas there was no efficacy against more virulent strains of bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* (*E. coli*). Hayes and associates treated 11 patients with major aortic graft infections by total graft excisions and in situ replacements with a rifampicin-bonded prosthesis. They demonstrated a 30-day mortality of 18.2%, but only one of the two patients infected with MRSA survived after 30 days.¹⁶

In situ allograft reconstruction was first described as an effective alternative in treating infected aortic prosthesis in 1991.⁵ Since then, multiple studies have confirmed the efficacy of using allograft replacement for the treatment of prosthetic aortic graft infection.^{7-9,17} Teebken et al. treated 42 patients with in situ cryopreserved allograft reconstruction and achieved a 30-day mortality rate of 14%.⁷ A multi-centered study conducted in Belgium involving 90 patients further confirmed cryopreserved aortic allograft replacement as a promising technique in managing aortic prosthetic graft infections.¹⁷ Kieffer et al. reviewed their extensive experience of treating 179 patients using in situ allograft replacement and compared the results in patients who received fresh allograft versus patients who received cryopreserved allografts.⁶ They achieved an overall early postoperative mortality rate of 20.1% and a 1-year average survival rate of 73%. The allograft-related mortality rate was only 2.2% in their study and all allograft-related deaths and complications were in patients who received fresh allografts. Their observation was confirmed by Litzler et al., who compared cryopreserved to fresh allografts on dogs that were infected with *Staphylococcus aureus* and concluded greater bacterial resistance from cryopreserved allografts than fresh grafts.¹⁸ However, Chiesa et al. did not find a significant difference between fresh and cryopreserved allograft aortic reconstruction.¹⁹ In addition, Knosalla et al. examined the efficacy of allograft replacement in dogs that were implanted with *S. epidermidis* infected aortic prosthetic graft and concluded that cryopreserved aortic allografts were more resistant to reinfection than synthetic grafts after in situ replacement of an infected

prosthetic graft. However, the antibiotic loading of the cryopreserved aortic allograft appears to be essential in obtaining optimal therapeutic effects²⁰ while the study by Rowe et al. failed to demonstrate superior results of cryopreserved allografts over collagen-impregnated Dacron grafts.²¹ Furthermore, allograft-related complications of degeneration and rupture have been reported by some authors²² but not others.²³

Studies on allograft reconstruction for infected aortic prosthesis in the U.S. are scattered. Noel et al. reported the experience of in situ aortic reconstruction using cryopreserved aortic allografts on 56 patients in 31 institutions and demonstrated a 30-day mortality rate of 13% with 4% graft-related mortality. They concluded that in situ aortic reconstruction with an cryopreserved aortic allograft in an infected field carried a high mortality rate and proper caution should be taken even though most deaths were not the result of allograft failure.²⁴ Our experience in treating 18 patients showed no perioperative mortality and an overall mortality rate of 22%. We did not encounter any incidence of allograft infection, degeneration, or disruption over a follow-up mean of 8.3 months. However, we observed one graft thrombosis that required an allograft revision and a 50% non-lethal complication rate including deep venous thrombosis, local wound infection, renal failure, and amputation. Even though allograft-related complications were uncommon in our mid-term evaluation, long-term follow-up is warranted to identify the potential complications of graft infection, thrombosis, or aneurysmal changes.

In conclusion, aortic prosthetic graft is a devastating and potentially lethal complication of aortic surgery that presents significant treatment challenges. Total graft excision followed by in situ cryopreserved allograft reconstruction is an effective alternative with satisfactory mid-term outcomes.

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