In Situ Reconstruction with Cryopreserved Arterial Allografts
for Management of Mycotic Aneurysms or Aortic Prosthetic Graft Infections: a Multi-Institutional Experience

We designed this study to evaluate a multi-institutional experience regarding the efficacy of cryopreserved aortic allografts in the treatment of infected aortic prosthetic grafts or mycotic aneurysms. We reviewed clinical data of all patients from 4 institutions who underwent in situ aortic reconstruction with cryopreserved allografts for either infected aortic prosthetic graft or mycotic aneurysms from during a 6-year period. Relevant clinical variables and treatment outcomes were analyzed.

A total of 42 patients (37 men; overall mean age 63 ± 13 years, range 41–74 years) were identified during this study period. Treatment indications included 34 primary aortic graft infections (81%), 6 mycotic aneurysms (22%), and 2 aortoenteric erosions (5%). Transabdominal and thoracoabdominal approaches were used in 38 (90%) and 4 patients (10%), respectively. Staphylococcus aureus was the most commonly identified organism (n=27, 64%). Although there was no intraoperative death, the 30-day operative mortality was 17% (n=7). There were 21 (50%) nonfatal complications, including local wound infection (n=8), lower-extremity deep venous thrombosis (n=5), amputation (n=6), and renal failure requiring hemodialysis (n=2). The average length of hospital stay was 16.4 ± 7 days. During a mean follow-up period of 12.5 months, reoperation for allograft revision was necessary in 1 patient due to graft thrombosis (6%). The overall treatment mortality rate was 21% (n=9).

In situ aortic reconstruction with cryopreserved allografts is an acceptable treatment method 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 were uncommon. (Tex Heart Inst J 2006;33:14-8)
suspected aortic prosthetic graft infections. These institutions include 1) Baylor College of Medicine, Houston, Texas; 2) Emory University School of Medicine, Atlanta, Georgia; 3) Medical College of Georgia, Atlanta, Georgia; and 4) Yale University School of Medicine, New Haven, Connecticut. Patients who underwent surgical intervention for infected aortic grafts or mycotic aneurysms were further evaluated. Those who had intraoperatively confirmed infections and had been 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 Cryolift® (CryoLife, Inc; Kennesaw, Ga), stored at –180 to –196 °C and thawed at 37 to 42 °C. Matching of blood and tissue compatibility between the cryografts and recipients was not attempted.

Results

Over a 6-year period, a total of 42 patients met the selection criteria. There were 37 men (88%) and 5 women, with a mean age of 63 ± 13 years (range, 41–74 years). All patients had multiple comorbidities, including coronary artery disease (n=28, 67%), hypertension (n=26, 62%), diabetes mellitus (n=14, 33%), and peripheral vascular disease (n=31, 74%). Twenty-four patients (57%) had long-standing histories of tobacco usage.

Treatment indications included primary graft infection (n=34, 81%), mycotic aneurysm (n=6, 14%), and aortoenteric erosion (n=2, 5%). The primary diagnostic method was an abdominal computed tomographic (CT) scan, which showed evidence of intra-abdominal infections in all patients; the diagnosis was confirmed by intraoperative tissue culture. The average interval from the original aortic surgery to the manifestation of prosthetic graft infection was 92 months, and ranged from 4 months to 15 years in those patients who presented with infected aortic prosthetic grafts.

All patients received intravenous antibiotics and operative management of graft excision, followed by in situ cryopreserved allograft replacement (Fig. 1). Tube grafts were used in 10 patients (24%), and bifurcated grafts were used in 32 patients (76%). Proximal anastomoses were performed at the level of the descending thoracic aorta, suprarenal aorta, and infra-renal aorta in 2 patients (5%), 5 patients (12%), and 35 patients (83%), respectively. Distal anastomoses were performed at the level of the infra-renal aorta, iliac artery, and femoral artery in 10 patients (24%), 3 patients (7%), and 29 patients (69%), respectively. Regarding the operative approach, thoracoabdominal incision was used in 4 patients (10%); transabdominal midline and retroperitoneal incisions were used in 36 patients (86%) and 2 patients (5%), respectively. The mean aortic clamp time was 55 minutes (range, 39–105 minutes). At the completion of the anastomotic reconstruction, suture line bleeding was noted in 10 patients (24%), who were all treated with BioGlue surgical adhesives (CryoLife). Because of the underlying infectious surgical environment, Teflon pledges were not used to reinforce the suture line.

Positive bacterial cultures were confirmed in all the explanted aortic prostheses and in the aneurysmal sac tissue. *Staphylococcus aureus* was the most commonly identified organism, found in 27 patients (64%). The average operating time was 267 minutes (range, 3–5.5 hours), and the technical success rate was 100%. 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% due to multiorgan failure secondary to sepsis (n=7). In addition, 50% of the patients had nonlethal procedure-related complications, including local wound infection (n=8), lower-extremity deep venous thrombosis (n=5), renal failure requiring hemodialysis (n=2), and amputation (n=6). All patients were available for follow-up for a mean period of 12.5 months (range, 3–39 months). One patient required allograft revision for graft thrombosis (6%), and one died as a result of complications from a colocutaneous fistula, which led to the overall treatment mortality rate of 21% (n=9). There was no evidence of aneurysmal dilatation or disruption on the evaluation of follow-up CT scans.

Discussion

Infection of aortic prosthetic graft material is a rare complication of aortic surgery that occurs in 1% to 2% of patients, and the complication rate has been consistent despite advances in antibiotics, graft material, and surgical techniques.1 The standard management of total graft excision and extra-anatomic bypass is associated with substantial morbidity and with significant mortality rates, ranging from 25% to 75% in reported series.1,2 Replacement of the infected prosthesis with cryopreserved allograft is an attractive alternative that has been adopted successfully in Europe, while data from the United States has been scattered and controversial. Our study confirms cryopreserved allograft replacement as an effective strategy for treating infected aortic prosthetic grafts and mycotic aneurysms.

Multiple factors contribute to aortic prosthetic graft infection, including contamination at the time of implantation, the extension of infection from adjacent tissues, seeding from distal sources via hematogenous routes, or erosion into adjacent organs. Manifestation of graft infection may vary widely, from days to years, depending upon the origin of the infection and the physical condition of the patient. The average interval between the original aortic surgeries and the manifestations of graft infection in our patients was 90 months (range, 4 months to 15 years). The patient may present with a variety of symptoms, mostly nonspecific and including recurrent fever and chills, groin infection, pulsatile mass, and generalized abdominal pain. Rarely, patients have gastrointestinal bleeding in the presence of aortoenteric fistula. When symptoms are nonspecific, additional imaging studies such as CT scanning are particularly useful in assisting in the diagnosis and in operative planning. The most common imaging methods used to evaluate aortic graft infections or aneurysms are ultrasonography, CT scanning, and magnetic resonance imaging (MRI).10,11 Late aortic graft infections are best evaluated initially by a CT scan or an MRI. Computed tomographic findings include ectopic gas, perigraft fluid, perigraft inflammatory changes, anastomotic pseudoaneurysm, and thickening of the adjacent bowel. The MRI offers the additional advantage of T1-weighted images to identify perigraft inflammation and minute quantities of perigraft fluid. Sonographic findings indicative of graft infection include perigraft fluid and pseudoaneurysms. Imaging for infection within 3 postoperative months is seldom 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 in aiding operative planning. The presence of saccular aneurysms on CT scans, combined with symptoms of infection and positive blood cultures, helped to identify mycotic aneurysms in 4 of our patients.

Treating infected aortic prosthetic graft material is extremely challenging. The standard therapeutic option of total graft excision and extra-anatomic bypass is associated with significant mortality and complication rates. In reviewing their 25-year-experience, O’Hara and associates1 found a 0.77% of incidence of aortic graft infection. Despite aggressive surgical treatment, including graft excision with and without extra-anatomic bypass in 89% of their patients, they obtained 30-day and 1-year survival rates of 72% and 42%, respectively. In addition, 27% of the treated patients in their series required major amputation. Similarly, Quinones-Baldrich and coworkers12 treated 45 patients with aortic graft infection, including 36 patients who underwent extra-anatomic bypasses. They reported a 30-day mortality rate of 24%, a 3-year primary axillofemoral bypass graft patency rate of 43%, and a 5-year amputation rate of 34%. 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 amputation. Nonetheless, a study conducted by Yeager and colleagues13 demonstrated improved overall results in treating 60 aortic prosthetic graft infections with total excision and extra-anatomic bypass: Yeager achieved 30-day mortality and 5-year primary axillofemoral bypass patency rates of 13% and 73%, respectively. Despite improved results in some reports, the standard surgical treatment—total graft excision and extra-anatomic bypass—continues to be associated with substantial rates of mortality and complication, such as the risk of aortic stump blowout.

The disappointing results of standard surgical treatment have kindled interest in evaluating alternative
approaches, such as partial or complete graft preservation, autogenous vein reconstruction, and antibiotic-bonded prostheses. Calligaro and associates\textsuperscript{13} investigated partial or complete graft preservation in 9 patients and achieved an acceptable perioperative survival rate of 89%. However, 5 of the 9 patients had limited infection involving only the groin, and 1 had a recurrence that required total excision 6 months later. Additionally, Clagett and colleagues\textsuperscript{14} achieved an excellent result of 100% perioperative survival using autogenous superficial femoral–popliteal vein as a reconstruction conduit in 41 patients who had infected aortic prosthetic grafts. Nevertheless, they encountered significant perioperative complications associated with vein harvesting; these included amputation (5%), compartment syndrome (12.3%), and pulmonary embolism (2.4%). Antibiotic-bonded prosthesis has been studied as replacement conduit, and it has shown variable success. Koshiko and colleagues\textsuperscript{15} evaluated the efficacy and duration of the antibacterial activity of rifampin-gelatin grafts in a canine model and concluded that they were effective against \textit{S. epidermidis} infection, but not against more virulent strains of bacteria, such as methicillin-resistant \textit{S. aureus} (MRSA) and \textit{Escherichia coli}. Hayes and associates\textsuperscript{16} treated 11 patients, all with major aortic graft infection, by total graft excision and in situ replacement with a rifampin-bonded prosthesis. They had a 30-day mortality rate of 18.2%, but only 1 of the 2 patients infected with MRSA survived after 30 days.

In situ allograft reconstruction was first described as an effective alternative in treating infected aortic prosthesis in 1991.\textsuperscript{17} Since then, multiple studies have confirmed the efficacy of using allograft replacement for the treatment of prosthetic aortic graft infection.\textsuperscript{7-9,17} Teebken and associates\textsuperscript{7} achieved a 30-day mortality rate of 14% in 42 patients treated with in situ reconstruction by means of cryopreserved allograft. A multi-center study involving 90 patients in Belgium further demonstrated that cryopreserved aortic allograft replacement is a promising technique for the management of aortic prosthetic graft infections.\textsuperscript{17} Kieffer and associates\textsuperscript{8} reviewed their extensive experience in treating 179 patients using in situ allograft replacement: they compared the results in patients who had received fresh allograft with the results in patients who had received cryopreserved allografts. 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 and coworkers,\textsuperscript{19} who compared cryopreserved to fresh allografts, in dogs that were infected with \textit{S. aureus}, and encountered greater bacterial resistance from cryopreserved allografts than from fresh grafts. However, Chiesa and colleagues\textsuperscript{20} did not find a significant difference between fresh and cryopreserved allograft aortic reconstruction. In addition, Knosalla and associates\textsuperscript{21} examined the efficacy of allograft replacement in dogs that had been implanted with \textit{S. epidermidis}-infected aortic prosthetic grafts and concluded that cryopreserved aortic allografts were more resistant to reinfection than are synthetic grafts after in situ replacement. However, the antibiotic loading of the cryopreserved aortic allograft appears to be essential in obtaining optimal therapeutic effect,\textsuperscript{20} and the study by Rowe and associates\textsuperscript{22} failed to demonstrate superior results of cryopreserved allografts over collagen-impregnated Dacron grafts. Furthermore, allograft-related complications of degeneration and rupture have been reported by some authors,\textsuperscript{23} but not by others.\textsuperscript{24}

Studies in the United States on allograft reconstruction for infected aortic prosthesis are scattered. Noel and associates\textsuperscript{24} reported the 31-institution experience of in situ aortic reconstruction using cryopreserved aortic allografts on 56 patients and demonstrated a 30-day mortality rate of 13%, with 4% graft-related mortality. They concluded that in situ aortic reconstruction with cryopreserved aortic allograft in an infected field carried a high mortality rate and that proper precautions should be taken, even though most deaths were not the result of allograft failure.\textsuperscript{25}

Our experience in treating 42 patients showed no intraoperative deaths and an overall mortality rate of 21%. We did not encounter any instances of allograft infection, degeneration, or disruption over a mean follow-up of 12.5 months. However, we observed 1 graft thrombosis that required an allograft revision and a 50% nonlethal complication rate that included deep vein 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 change.

The current study contains several limitations. Bias may have been introduced by the retrospective nature of the study. In addition, a variety of surgical approaches, with varying anastomotic reconstructive techniques, were used in our patients. While the data represent a multi-institutional experience, the variations in surgical experience among surgeons from these hospitals may contribute to a wide range of clinical outcomes. Last, the relatively small sample size of our patients is insufficient to enable a conclusive treatment recommendation in patients with infected prosthetic aortic grafts.

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

References
