A REVIEW ON THE USE OF CRYOPRESERVED AORTOILIAC ALLOGRAFTS

Aortic grafts can be used to bypass a blocked artery or repair damage from trauma, infection, or aneurysm in order to restore blood flow from the heart to the lower body. These grafts may be autograft, allograft, or synthetic. While uncommon, aortic graft infections occur in 0.2 - 5.0% of open aortic reconstruction surgeries and are linked to significant morbidity and mortality [1]. These rare infections are difficult to treat. The treatments, such as extra-anatomic bypass and neo-aortoiliac system procedure (NAIS) with the femoral vein, also have substantial risk of complications [1-3]. One study using graft excision with extra-anatomic bypass reported an aortic stump blowout rate of 25%, lower limb amputation rate of 16%, and an infection rate of 27% at one-year [4]. O'Hara et al. found a rate of 27% for major amputation following reconstruction with graft excision and extra-anatomic bypass; however, the authors commented that this number was artificially low because other patients who likely would have needed amputation died soon after surgery [3]. Similarly, a study by Quinones-Baldrich reported an amputation rate of 34% at 5 years after extra-anatomic bypass, while Seeger reported a 5-year amputation rate of 18% [5, 6]. Studies by both Reilly and Campbell demonstrated recurrent infection rates of 20% and 13%, respectively, using extra-anatomic bypass or a neo-aortoiliac system [2, 4]. As an alternative to autograft or synthetic grafts, cryopreserved aortoiliac allografts may be used in aortic reconstruction surgeries.

One advantage of using cryopreserved aortoiliac allografts compared to singular veins or arteries is that they have branch vessels which allow connections to neighboring vessels at the implantation site, potentially reducing the risk of ischemia and contributing to limb preservation [1]. Additionally, while cryopreserved donor vein or femoral artery allografts must be altered on the back table in operating rooms in order to fit a patient's aortic diameter and anatomic specifications, a cryopreserved aortoiliac allograft can be patient-specific size-selected to minimize preparation time. Two recent studies by The Vascular Low-Frequency Disease Consortium found substantially reduced complications when using cryopreserved aortoiliac allografts [1, 7]. The study took place at 14 sites, including The Mayo Clinic, and found that the use of cryopreserved aortoiliac allografts reduced the mortality rate, the risk of recurrent infection, and limb loss compared to other treatment options. Results from the study include a 75% survival rate at 1 year, only a 4% infection rate, and a 97% limb salvage rate in a patient population with a mean age of 65 years old. These data indicate that using these allografts could substantially decrease complications after aortic reconstruction.

Literature Review of Cryopreserved Aortoiliac and Arterial Allografts

- **Philpott, JM, and Zemlin, CW. Aortic reconstruction for an infected stent graft with a composite homograft. The Journal of Thoracic and Cardiovascular Surgery, Volume 153, Issue 5, e73 - e75.**

This case study examined the outcome of using a composite allograft to repair a previously-implanted, infected thoracic endovascular repair graft. The patient was a 56 year-old man with

an infected and severely inflamed arch pseudoaneurysm measuring 9.6 cm and rapidly enlarging. The descending thoracic aorta (DTA) was infected with methicillin-sensitive *Staphylococcus aureus*. On the morning of the surgery, the patient was in shock with renal failure and an acute stroke, but could follow commands, and therefore the surgeon moved to proceed as a life-saving measure. The surgical team constructed an arch-DTA composite graft using 4 cryopreserved allograft elements sewn together: a reversed root-arch segment, an ascending aorta segment, and two adolescent DTAs that were joined longitudinally. The lengthy surgery included bypass of 450 minutes and total cross-clamp time of 262 minutes. The patient survived the procedure and had an intact, reconstructed aorta 2 years later. The surgeon concluded that ***"Although technically challenging, composite homograft repairs offer a viable solution to these frequently mortal complications."***

- **Smeds, MR, et al. Treatment and outcomes of aortic endograft infection. J Vasc Surg 2016;63:332-40.**

This retrospective study reviewed a multi-center database for the outcomes of patients diagnosed with endograft infections after undergoing thoracic endovascular repair or abdominal endovascular repair between January 2004 and January 2014. Two-hundred and six patients suffered from infection at an average of 22 months post-implant. Ninety-five percent of these patients had surgery to address the infection, with 90% undergoing *in situ* aortic replacement. Of these individuals, 54 received a cryopreserved allograft, 21 a neoaortoiliac system, 111 a prosthetic system (of which 83% were soaked in antibiotics), and 11 had axillary-(bi)femoral bypass. The perioperative mortality rate was 11%. Nineteen of the replacement grafts were removed primarily due to the prosthetic graft not being soaked in antibiotic as well as some of the cases with extra-anatomic bypass. The authors concluded: "***The better option for repair in our series was use of cryopreserved allograft or the femoral-popliteal vein (NAIS) for aortic reconstruction."***

- **Harlander-Locke, M.P. et al. The use of cryopreserved aortoiliac allograft for aortic reconstruction in the United States. J Vasc Surg. 2014 Mar;59(3):669-74.**

In 2014, Harlander-Locke et al. reported the results of a multicenter study using cryopreserved aortoiliac allograft for aortic reconstruction [1]. The study examined results of 220 patients from 14 medical institutions. The outcome measures were culture positive or culture negative infections, enteric fistula/erosion, infected pseudoaneurysm near the aortic graft, and other. During the follow-up period (30 ± 3 months), the results indicated that aortic reconstruction using cryopreserved aortoiliac allografts (CAA) resulted in low explant rate (10%) as well as low complication and reinfection rates. Harlander-Locke noted that CAA were a viable alternative to other grafting options for *in situ* reconstruction in part due to a 0% early limb loss rate, and 97% limb salvage at 5 years. The author concluded: ***"We believe that CAA should be considered a first line treatment of aortic infections."***

- **Brown K.E. et al. Arterial reconstruction with cryopreserved human allografts in the setting of infection: A single-center experience with midterm follow-up. J Vasc Surg. 2009 Mar;49(3):660-6.**

Brown et al. conducted an investigation of cryopreserved human allografts (CHA) used in vascular reconstruction between February 1999 and June 2008. The CHAs were aortoiliac or thoracic allografts. Fifty-two patients (mean age 66 years) had vascular reconstruction for iliofemoral/femoral-popliteal arterial, abdominal aortic, or prosthetic infections. The authors also examined results for 53 non-CHA patients with similar age and procedures. The CHA patients had a 30-day mortality rate of 5.2% compared to non-CHA of 7.5% with one year mortality rates of 7.0% and 13.2% respectively. The authors concluded that: ***"In the setting of infection, cryopreserved human allograft arterial reconstruction is a viable alternative to traditional methods of vascular reconstruction in patients without available autogenous conduit and when expedient reconstruction is required."***

- **Zhou W. et al. *In situ* reconstruction with cryopreserved arterial allografts for management of mycotic aneurysms or aortic prosthetic graft infections: a multi-institutional experience. Tex Heart Inst J. 2006;33(1):14-8.**

In this study, Zhou followed 42 patients (mean age 63 ± 13 years) who underwent *in situ* aortic reconstruction with cryopreserved arterial allografts to treat primary aortic graft infections (81%), mycotic aneurysms (22%), or aortoenteric erosions (5%). Arterial allografts included 24% tube grafts and 76% bifurcated tube grafts. Thirty-day graft-related mortality rate was 17% due to complications from sepsis (N=7), and the nonfatal complication rate was 50% (N=21). Nonfatal complications included "local wound infection (n=8), lower-extremity deep venous thrombosis (n=5), renal failure requiring hemodialysis (n=2), and amputation (n=6)." Overall mortality rate was 21% (N=9), and there was no sign of aneurysmal dilatation on follow-up CT scans. ***"In situ aortic reconstruction with cryopreserved allografts is an acceptable treatment method in patients with infected aortic prosthetic graft or mycotic aneurysms."***

- **Kieffer E. et al. Allograft replacement for infrarenal aortic graft infection: early and late results in 179 patients. J Vasc Surg. 2004 May; 39(5):1009-17.**

Kieffer et al. retrospectively compared the use of fresh allografts to cryopreserved human allografts for infrarenal aortic graft infections in 179 patients (111 fresh and 68 cryopreserved). Grafts included a segment of infrarenal aorta or descending thoracic aorta as well as various lengths of the iliac and femoral arteries. Indications included primary graft infections (69.8%) and secondary aortoenteric fistulas (AEF; 30.2%). Four early postoperative allograft-related deaths occurred due to allograft rupture in patients who had received fresh allografts. Significant risk factors for early mortality included septic shock, emergency allograft replacement, surgical complication, and need for repeat operation. The difference for

cryopreserved allograft recipients compared to fresh allograft recipients for these risk factors neared statistical significance (P= 0.07). Dilation of the aortic portion of the allografts occurred in four fresh allografts from the descending thoracic aorta. Two fresh allograft recipients died at 10 and 27 months due to late aortic rupture. The authors concluded that: ***"Complications [following aortic reconstruction] are significantly reduced by using cryopreserved allografts rather than fresh allografts and by not using allografts obtained from the descending thoracic aorta."***

- **Vogt P.R. et al. Cryopreserved arterial allografts in the treatment of major vascular infection: A comparison with conventional surgical techniques. J Thorac Cardiovasc Surg. 1998 Dec;116(6):965-72.**

Vogt et al. studied 72 patients (median age 62 years) who presented with mycotic aneurysms (N=29) or infected vascular prostheses (N=43) of the thoracic or abdominal aorta between 1990 and 1996. Patients either received cryopreserved arterial allograft (N=34) or were treated with conventional surgery (N=38) that involved *in situ* reconstruction with a new prosthesis (N=20) or excision of the infected prosthesis and extra-anatomic bypass grafting (N=18). Cryopreserved arterial allograft demonstrated significantly superior performance to conventional surgery in disease-related survival free of reoperation (P=0.0001), hospitalization (P=0.002), incidence of complications (P=0.005), elimination of infection (P=0.001), and costs associated with treatment (P=0.005) among others. The authors concluded that ***"the use of cryopreserved arterial allografts is a more effective treatment for mycotic aneurysms and infected vascular prostheses than conventional surgical techniques".***

- **Leusèche G. et al. Long-term results of cryopreserved arterial allograft reconstruction in infected prosthetic grafts and mycotic aneurysms of the abdominal aorta. J Vasc Surg. 2001 Oct;34(4):616-22.**

Leusèche et al. collected outcome data from 28 patients (mean age 64 years) after cryopreserved arterial allograft reconstruction using descending thoracic aorta, aortoiliac, or iliac and femoral arteries obtained from brain dead donors. All patients presented with abdominal aortic infection. Twenty-three were aortic prosthetic graft infections, and five were mycotic aortic aneurysms, 3 of which had ruptured. Thirteen patients underwent allograft aortic reconstruction as an emergency procedure and fifteen as a planned procedure. Treatment-related mortality was 17.8% over the follow-up period (mean 35 months, range 6-101 months). All five patients who died from graft-related causes had undergone complete aortic or graft excision. Of note, no patients experienced recurrent infection or amputation following reconstruction up to the mean follow-up of 35 months. Additionally, no patients "received long-term (>3 months) antibiotic therapy." The 3 year primary patency rate was 81% and the 3 year secondary patency rate was 96%. ***"Reconstruction with cryopreserved arterial allografts should be regarded as a safe temporizing maneuver to help eradicate infection and permit subsequent reconstructions with prosthetic material when necessary."***

Discussion

While autogenous deep lower limb veins can be used for aorta reconstruction, autografts have an associated risk of donor site morbidity that may include pain or infection at the harvest site. The use of allografts does not carry this risk and may be the preferred grafting solution so long as efficacy and safety are comparable to autograft or other synthetic options. A study by Clagett et al. reported a complication rate of 49% with lower limb autograft, including a 5% amputation rate and 12.3% compartment syndrome rate [8]. However, another investigation by Nevelsteen et al. and associates (1995) used autogenous lower extremity deep veins as arterial conduits to treat prosthetic infections after reconstructive aortoiliac surgery. The authors reported no occurrences of recurrent infection and only one patient later received an above-knee amputation due to "concomitant femoropopliteal occlusion in the presence of a patent deep venous aortofemoral graft" [9]. Some physicians recommend the use of autogenous or allogeneic grafting over extra-anatomic bypass in younger patients due to the lower risk of long-term graft failure. Conversely, the higher risk for long-term graft failure using extra-anatomic bypass is considered more acceptable in older patients [6, 10]. Autograft harvesting and subsequent reconstruction creates more physiological stress compared to the recovery associated with extra-anatomic bypass using allograft. Given these concerns, the use of cryopreserved aortoiliac arteries has become more common.

In their study of cryopreserved allograft aortoiliac arteries for aortic reconstruction in patients with cases of infected grafts, Harlander-Locke reported a 24% complication rate, half of that seen in the Clagett et al. study, which used autografts [1]. These results may be due to properties of cryopreserved allografts. Cryopreservation has been shown to reduce the risk of graft dilation following implant compared to fresh allografts [11]. Harlander-Locke et al. reported dilation in the aortic portion of five fresh allografts, four of which were harvested from the descending thoracic aorta. Additionally, two "late lethal aortic ruptures" occurred in patients who received fresh allografts. Harlander-Locke et al. suggested that cryopreservation methods "preserve the integrity of the collagen matrix, which is believed to be responsible for fewer graft-related complications and higher graft patency rates" [1].

The clinical evidence for using cryopreserved allografts in aortic reconstruction has been accumulating for the last several decades. It shows that these allografts are an efficacious and safe alternative to autograft, with the added benefit of avoiding the potential of donor site pain or infection.

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