ABSTRACT
An observational analysis of cryopreserved homografts utilization at the vascular surgery service of Hospital Pasteur (UDELA-ASSE Montevideo, Uruguay) was done. The experience includes 68 patients with 82 grafts in 15 years. Patients who had prosthetic infection or venous bypass in lower limbs, lower limb critical ischemia in the absence of venous grafts, and in chronic hemodialysis patients with arteriovenous fistulas repeated infections, or infectious foci were included. Other patients with rare diseases are also described. The feasibility of alternative homograft use in difficult cases to resolve, where there is no consensus in the literature, was also evaluated. It is concluded that the cryopreserved homograft constitute a valid therapeutic resource for selected cases.

KEY WORDS: Homograft, cryopreserved artery, bypass infection, critic ischemia.

INTRODUCTION
Arterial grafts are not a recent invention; in 1912 Alexis Carrel published his experimental results with two different biological grafts. The first one was a human popliteal artery heterograft replacing the abdominal aorta of a dog, and the second one was a dog external jugular vein homograft replacing the thoracic aorta. The autopsies of these dogs showed after 4 and 2 years, respectively, permeable dilatations, which were rather larger in the case of the heterograft. Despite these experimental results, it was only in the 1950s that a new advance in this field was made as a consequence of the development of venous autografts in medium-sized arteries.
by Kunlin in 1948⁷. Then, Gross in 1949³, and Dubost⁴ and Outdot⁵ in 1951 resumed the use of biological grafts. Despite the initial enthusiasm, their use fell at the end of the decade as a result of a study by Szilagyi et al⁶. The study suggested that the long-term degradation of such homografts was almost inevitable as a consequence of an immune reaction of the recipient, thus determining a high incidence of dilatation, calcification and thrombosis. Although this technique was at an initial stage in terms of tissue extraction conditions and conservation methods, Szilagyi’s permeability after 5 years was 38%⁷. The work of Szilagyi coincided with the appearance of synthetic prostheses as known today. These prostheses soon began to be widely used despite the risk of infection ranging between 1% and 6%⁸. On November 6, 1957, Carlos Ormaechea in Uruguay⁹-¹⁰ made the first aortic replacement in Latin America using a freeze-dried homograft. Based on the good results achieved by Donalson¹¹ in the treatment of bacterial endocarditis, and disappointed by the results of the classic treatment of prosthetic infections as well as by the experimental work of Wesley Moore¹², the team of the vascular surgery service of Hospital Pitié Salpetrière decided to study the result of managing arterial infections through arterial homografts in situ¹³,¹⁴.

The work of Wesley Moore¹² compares biological grafts and prostheses in terms of infection resistance and showed that biological grafts – whether homografts or autografts – have better results, suggesting as responsible mechanisms the high concentration of ATBs in mediums for conservation, the high adhesiveness of ATBs to arteries, the absence of fibrin deposits and the anti-adherence role of graft cells. These pieces of work¹²-¹⁴ are our basis for the treatment of patients with infections of stents or autologous bypasses.
As regards the revascularization of lower limbs, the most representative work, in our opinion, is that of Albertini et al. It is a multisite study that analyzes 165 bridges in 148 patients—123 of them with previous revascularizations. In short, results show primary permeability of 48%, 35% and 16% after one, three and five years, respectively, as well as secondary permeability of 60%, 42% and 26%, plus limb salvage of 83%, 76% and 74%. The third group of patients is that of hemodialysis patients with infection of vascular accesses for hemodialysis or infectious foci not in remission. As for vascular accesses, there is experience in the use of cryopreserved saphenous heterografts and homografts with variables, but generally with poor results, and finally in the use of cryopreserved arterial homografts.

This paper was intended to present the 15-year experience with the use of cryopreserved homografts in peripheral vascular surgery.

**MATERIALS AND METHODS**

A retrospective, descriptive, observational study was conducted by reviewing the medical records in the database of our service, including all patients treated with cryopreserved homografts. Infections of aortic prostheses were treated by choice with cryopreserved anatomic homografts, using abdominal aorta, thoracic aorta or iliac segments. In the case of iliac-femoral infections, femoral-popliteal segments of choice were used. Femoral-popliteal segments were used also at infrainguinal level, after having ruled out the possibility of using the saphenous vein (determined by prior use, by Doppler ultrasound test or by intraoperative scanning). The purpose of the procedure in these groups was to maintain the viability of limbs and to control the infectious process locally.

In patients with critical ischemia without infection, the criterion for inclusion was: absence of ductus venous (previously used, ruled out by Doppler ultrasound test or by intraoperative scanning), and with exit at least through a leg axis, properly perfusing the foot. Those patients that were not candidates for bypass with autologous vein (non-revascularizable) were ruled out. The purpose of the procedure was to maintain the viability of limbs in patients who otherwise would undergo amputation.

Patients with vascular accesses for hemodialysis were admitted to the protocol because of: absence of venous capital suitable for fistula creation, repeated infection of accesses, chronic infection of accesses and/or infectious foci not treatable remotely. In this case, the purpose of the procedure was to control repeated infections and then, in the absence of active septic foci, to use synthetic materials again, as described by other authors.

For all procedures, cryopreserved homografts were used. They were approved and provided by the National Institute of Organ, Tissue and Cell Donation and Transplantation of Uruguay. Tissues were obtained in the context of multiorgan retrievals in patients with brain
death and then were processed, cryopreserved and bacteriologically approved under the Institute’s protocols.

RESULTS

The series consists of 68 patients who underwent 82 procedures between the years 2000 and 2014. Fifteen patients were treated for infections (aortoiliac infections, femorofemoral crossover bypasses or femoropopliteal bypasses). Twenty-eight patients presented critical ischemia without infection. Four of them underwent two surgeries (two due to the degradation of the graft, one due to occlusion and the other one due to bilateral surgery). Three patients had infection and associated critical ischemia. On the other hand, out of 19 patients with vascular accesses for hemodialysis, two had undergone three procedures and six had undergone two procedures. The series is completed with: an aortic aneurysm in an infant aged 6 months, who underwent an aortobiliac bypass procedure with a femoral artery bifurcation (only one prior report in the literature); a femoral pseudoaneurysm in an intravenous drug user; and a replacement of an artery and the iliac vein in an infected retroperitoneal tumor.

In the group of infections (n = 15), nine aortoiliac infections were treated and the segments used were three thoracic aortas and six aortobifemoral segments. Out of these patients (n = 9), four overcame their disease for more than a year (three of them alive have been under follow-up examination for 98, 58 and 40 months, whereas the other one died after 13 months from laryngeal neoplasm), three died from sepsis with permeable graft, and two died from graft complications. As for the six patients with infections of femorofemoral crossover bypass, two died without infection, two were permeable after 55 and 76 months, and two were occluded but asymptomatic. Out of those with femoral-popliteal bypass associated with infection (n = 3), one was permeable after 22 months, one was amputated and died from sepsis, and the other one was occluded with closed stage IIIb claudication.

In the group with critical ischemia without infection (n = 28), the materials used were single long axes extending consistently from the iliac to a variable distal area. The results of distal revascularizations are shown in the chart with 24-month maximum permeability and seven early failures (Figure 1). On follow-up, eight patients were lost and five saved their limbs despite the occlusion of the bridge.

In the group of arteriovenous fistulas (n = 19), the segment used was the femoral artery (common and superficial or just superficial, according to the convergence of sizes). Maximum permeability was after 66 months (Figure 2). Seven patients were lost on follow-up and eight patients in evolution received new fistulas with PTFE.

Regarding the other cases, the infant with aortic aneurysm died a year later from unknown cause (associated with multiple congenital pathologies). The patient with femoral pseudoaneurysm survived and needed urgent mitral valve replacement in the immediate
Figure 1. Distant permeability in the group of patients with ischemia (n = 28) (Kaplan Meier).

Figure 2. Distant permeability in the group of patients with arteriovenous fistulas for hemodialysis (n = 19) (Kaplan Meier).
postoperative period. The patient with artery and iliac vein replacement due to a retroperitoneal tumor had an asymptomatic thrombosis of the venous replacement, with the artery remaining permeable on follow-up.

**DISCUSSION**

While the viability of cryopreserved grafts, mainly in the long term, is still not clear, there are several series reporting good results. In the dramatic scenario of a vascular surgeon faced with an infected bypass, this tool reduces the burden. Castier et al published in 2005 and then in 2010 the experience with 36 patients, in which patients with bypass infection were treated with cryopreserved arterial grafts. After three years, results showed 87% limb salvage with 57% primary permeability and 78% secondary permeability. Brown et al also had good medium-term results, presenting in this series of 57 cases patients with primary arterial infection. In addition, this author compared this group with 53 patients treated, during the same period, with extra anatomic bypass, also associated with infection. Mortality after one year was 7% and 13.2%, with better results for cryopreserved grafts.

These grafts were used also for popliteal artery aneurysms, assuming that no autologous grafts were available. A series of 54 patients with very good results has been published recently. After five years, primary and secondary permeability was 88% and 98.1%, respectively.

Another series, published in 2014, shows good results in patients with critical ischemia, without autologous graft and with active infection (either ulcers, trophic lesions or gangrene). Distal bridging was performed in more than half the cases. The 13 lower limbs treated in the series were saved, while 18-month permeability was 58.6%.

In those cases where there is no cryopreservation banking, like in Wayne et al in Australia, fresh artery was used, which is more controversial and not widespread.

No rejections of cryopreserved arterial grafts have been described, apart from a recently published case where there was aneurysmal degeneration one month after the bridging. The solution, which was satisfactory, consisted of the replacement with another new cryopreserved graft. This raises the possibility, apparently uncommon, of the rejection of these grafts due to their immunogenicity.

Also, cryopreserved internal saphenous vein homografts have been used as grafts for greater consistency in infrapopliteal bypasses. A series published in 2010 refers to the 15-year experience of Randon et al. One hundred and two internal saphenous vein grafts were used in 92 patients, with permeability similar to that of the autologous vein. It should be noted that, in all cases, low immunosuppression doses were associated for the first year.
To further explore this issue, mention should be made of the 2013 paper by Jashari, which is a 20-year record of the European Union. After being harvested, 1,250 arterial segments, accounting for 32%, were ruled out because of morphological alterations (acquired), bacteria or others; 2,506 segments were implanted in 1,600 patients. While the main indication (65%) was infection, at the other end, the smallest group corresponded to the use of aorta for trachea replacement in patients with oncologic resection of trachea (0.4%).

In a nutshell, we conclude that cryopreserved homografts are reliable alternatives, once approved by tissue banks according to their processing protocols. Their use is best indicated in vascular infections, as definitive treatment or as bridging treatment to control the infection. In comparison with the analyzed series, our series assumes more significance since it provides a larger number of cases. In patients with other unusual pathological situations like those referred to above (arteriovenous fistulas, pseudoaneurysms), arterial homografts are a valid alternative. Long-term multisite prospective studies to confirm their actual usefulness are still pending.

REFERENCES


