In situ Arterial Allografts: a New Treatment for Aortic Prosthetic Infection

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Introduction

During the last decade the most widely favoured management for aortic graft infection required a radical approach with total graft removal, aortic stump closure, and extra-anatomic grafting through uninfected tissues. Staging of the procedures – initial extra-anatomic bypass followed by either immediate or interval graft excision vs. the more traditional single operation of graft excision followed by lower extremity revascularisation – seems to give the best results. Unfortunately, this management strategy results in several significant problems. Extra-anatomic bypass patency rates can be very disappointing, in particular in patients with extensive vascular occlusive disease who require axillounilateral profunda or popliteal bypasses. In addition to the high rate of thrombosis, recurrence of infection in an extra-anatomic bypass graft occurs in about 20% of cases. Aortic stump blowout is still an unresolved issue. Although recent studies have shown that the risk of disruption of the aortic closure is minimised by careful surgical technique, it continues to be a much feared and frequently quoted early and late problem, with an incidence of 20% or more. Stump blowout is almost always fatal and reinfection of extra-anatomic prosthetic grafts often causes limb loss or death.

In situ graft reconstruction has been reported as an attractive treatment alternative because of its relative technical ease, theoretically better long-term patency rates, and potential avoidance of aortic stump blowout. Although it can be a rational treatment option for localised or circumscribed aortic infection, it does not seem reasonable in the case of diffusely infected abdominal aortic prosthetic grafts, where graft removal and extra-anatomic grafting are required. Furthermore, placing a prosthesis in a contaminated field surely risks reinfection of the graft, with early recurrent rupture or false aneurysm of the proximal aortic anastomosis. Towne et al. have emphasised the subtle clinical presentation of patients with Staphylococcus epidermidis graft infections. The low virulence of this organism permits treatment by partial excision of the grossly involved graft segments, debridement of perigraft tissue and adjacent artery, and in situ replacement of another prosthesis. Conversely, according to these authors in situ replacement for Gram-negative infection and for coagulase-positive staphylococcus infections is not recommended, and subsequent infection of previously uninvolved graft segments may be expected.

Experimental studies have shown that collagen rifampicin-bonded grafts reduce the incidence of graft colonisation after in situ replacement of an infected graft. Based on these excellent results, gelatin-sealed grafts soaked with rifampicin were implanted in situ in five patients with aortic prosthetic infection not suitable for graft excision and extra-anatomic bypass. Despite promising early results, further observation of the patients is necessary to exclude recurrent graft infection. Also, grafts infected with bacteria resistant to rifampicin remain an unresolved issue.

A controversial strategy including complete graft preservation to treat selected aortobifemoral prosthetic graft infection has been recently reported. Preservation of the entire graft is only recommended when the graft is patent, the anastomoses are intact, the patient does not have sepsis, and cultures of the wound do not yield pseudomonas. Treatment adjuncts include repeated, radical operative wound debridement and rarely rotational muscle flaps. Once again, in case of anastomotic haemorrhage, graft thrombosis, or persistent drainage of purulent material the

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authors advocate graft excision and extra-anatomic bypass. The limited number of patients with aortic prosthetic infections so treated does not allow any firm conclusions to be drawn.

In order to avoid the risk of persistent or recurrent graft infection and the hazards of aortic stump complications, different types of autogenous reconstructions have been reported.\(^\text{18-22}\) The autogenous approach was originally advocated by Ehrenfeld et al.,\(^\text{18}\) who reported reconstructing the aortoiliac segments by disobliterating occluded aortoiliac segments, coupled with arterial and venous autografts, after extensive debridement of the infected area. However, the presence of degenerative or aneurysmal changes in the native arterial segments contraindicating endarterectomy and the lack of suitable greater saphenous veins (GSV) limit the use of these procedures, which are always technically demanding. The risk of secondary failure of disobliterated arterial segments and GSV is also a major concern.\(^\text{20,21}\) More recently, the use of GSV alone,\(^\text{19}\) lower extremity deep veins (DV) alone,\(^\text{22}\) or both GSV and DV\(^\text{22}\) has been reported. Harvesting of DV was well tolerated, without disabling chronic venous stasis, although it is obviously contraindicated in cases of previous deep venous thrombosis. Furthermore, the use of GSV has been associated with development of focal stenoses and diffuse neointimal hyperplasia.\(^\text{21}\) The possibility of future dilatation of thin wall DV in an aortic position can also be expected.

Arterial allografts

Allograft aortic replacement is not a new technique. Experimental studies were carried out by Carrel\(^\text{23}\) early in this century and the first clinical use goes back to the early years of vascular surgery.\(^\text{24,25}\) Although clinical results were encouraging, several drawbacks were soon recognised.

Despite the organisation of arterial banks, procurement and preservation of human allografts were fraught with difficulties. The available methods of sterilisation and storage were certainly a major contributing factor to the secondary dilatation and calcification observed in a significant number of patients.\(^\text{26,27}\) Finally, the development of suitable arterial prostheses led to abandonment of arterial allografts in the early 1960s. Prosthetic infection soon appeared, however, as a rare but dreadful complication.

During the last two decades our policy for the treatment of this devastating complication shifted from partial graft removal to total graft removal, associated with lower limb revascularisation by either extra-anatomic bypasses or in situ autogenous reconstructions. Despite a progressive decrease in mortality and morbidity, our experience of these conventional methods of treatment was disappointing. Encouraged by the excellent long-term results reported by cardiac surgeons following allograft replacement for management of infections involving the ascending aorta\(^\text{28,29}\) and from a very active local multi-organ transplant tissue retrieval program, we decided to investigate allograft replacement in the management of arterial infections.

Our first patient was operated upon in October 1988\(^\text{30}\) and a series of 43 consecutive patients was reported in 1993.\(^\text{31}\) As of October 1995, 100 consecutive patients with infected infrarenal aortic prosthetic grafts underwent in situ replacement with preserved allografts in our department.\(^\text{35}\) Twenty-seven patients had a graft-enteric fistula. Twenty-six patients needed emergency procedures because of acute bleeding, septic complications and/or lower limb ischaemia, while 74 patients had planned operations.

Technique

Our technique of procurement and preservation of allografts has been previously described.\(^\text{31}\) Arterial allografts were harvested from cadavers as part of a multi-organ transplant tissue retrieval program. Bacteriological and virology tests were routinely performed among donors. The whole length of the descending thoracic aorta, aortic bifurcation, iliac and femoral arteries were obtained. Hypogastric and deep femoral arteries were transected 2-3 cm distal to their origins in order to allow revascularisation of the corresponding arteries of the recipient. A fragment of the retrieved arterial allograft was routinely cultured for bacteriological control. Allografts were stored in 500 ml of preservation medium containing heparin and antibiotics. Allografts were implanted after a minimum interval of 48 h, to decrease cellular antigenicity and a maximum interval of 21 days, to avoid late degenerative changes. Because of the limited number of available allografts, matching blood and tissue compatibility between recipient and donor was not attempted.

Before implantation a fragment of allograft and a few millilitres of the preservation medium were sent to the bacteriology laboratory. The aortic stump and periprosthetic infected tissues were carefully debrided. The periprosthetic fluid and part of the infected prosthetic graft were sent for bacteriological culture. The allograft was implanted in situ, using polypropylene
running sutures for proximal and distal anastomoses. All infected prosthetic material was usually removed at the same operation. Associated reconstructions of lower limb and/or visceral arteries were performed in a significant number of patients (Figs. 1 and 2). Retroperitoneal and inguinal drainage were used routinely.

All patients received broad-spectrum antibiotics perioperatively that were replaced by selective antibiotics according to culture results. Antibiotics were maintained for at least 6 weeks. None of the patients received long-term or indefinite antibiotic therapy.

**Results**

Twenty-four patients died during the early postoperative period. More than half of deaths were due to septic complications. The overall mortality of the present series (24%) is quite disappointing, compared to the 12% mortality among the 43 patients we reported in 1993. However, in the present series mortality rate was 38% in patients with aortoenteric fistulas, and 19% in patients with isolated prosthetic infection. Even more striking was the difference of mortality rates among patients undergoing emergency operations because of haemorrhagic, septic or ischaemic complications, and patients undergoing planned operations (46% vs. 16%, respectively). All surviving patients had postoperative arteriography before discharge. Routine follow-up included duplex scanning at 3-monthly intervals. Late computed tomography (CT) scanning and/or aortography were performed depending upon the results of duplex scanning. There were 13 late deaths, of whom two were due to aortic rupture. During follow-up 20 occlusive lesions were observed and 15 required reoperation which was always successful. Ultrasonography and CT scanning showed aortic dilatation with mural thrombosis in five patients. In all of these cases descending thoracic aortic allografts had been used for replacement of the infrarenal aorta. As of yet, none have had to be reoperated upon. Three patients had major amputations because of pre-existing irreversible ischemia. No patients had secondary amputations.
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Discussion

Although the overall survival rates of our series are less promising than our preliminary experience, in situ allograft replacement has several undeniable advantages in the management of infected infrarenal aortic prosthetic grafts. Experimental studies suggested that fresh allograft arteries are suitable materials for arterial reconstruction in infected fields because they function as a vascular conduit and allow resolution of infection by conventional antibiotic therapy. This avoids complications related to aortic stump pathology as well as occlusion or infection of prosthetic extranatomic bypasses. The risk of persistent or recurrent infection of in situ prosthetic replacement is also significantly reduced, even though not completely eliminated. Furthermore, availability of long bifurcated grafts makes the procedure feasible in all cases and technically much easier than autogenous in situ reconstructions using endarterectomy, venous or arterial autografts or a combination of these. Associated visceral reconstructions, if indicated, are also feasible. More importantly, there were no early or late amputations in our patients secondary to failure of arterial allograft reconstruction, an outcome not matched by any of the conventional methods. Nevertheless, arterial allograft replacement raises several theoretical as well as practical problems:

1) Availability of arterial allografts is rather limited at present, because of donor shortage and legal problems. The organisation of arterial banks has just begun and will probably develop in the next years. However, according to experimental as well as clinical studies, there is no hard evidence to choose between fresh allografts stored at 4°C in a preservation medium, which we used to reduce allograft antigenicity, and cryopreserved grafts, which have the distinct advantage of avoiding all risks of viral contamination.

2) Perioperative mortality of in situ arterial allograft replacement remains high and is by far greater than mortality of prosthetic aortic replacement in a non-infected field. Aortic allograft replacement can be a rather aggressive operation, entailing a repeat laparotomy, the possibility of significant blood loss and long operative times along with the necessity of suprarenal clamping in a significant number of cases. Unfortunately, patient selection is difficult due to the unfavourable outcome of spontaneously evolving prosthetic infections and the need for emergency operation in case of haemorrhagic, ischaemic or septic complications. Some of our patients, in poor general condition, without emergency indications might have benefited from a two-stage operation, including local treatment of the main complications (drainage of closed collections, direct suture of leaking anastomoses, direct suture repair of enteric fistulas), with allograft aortic replacement and removal of all prosthetic materials performed as a secondary procedure after adequate preparation of the patient. Septic shock was the leading cause of mortality in our series. Patients usually had long-standing infections secondary to multiple multi-resistant organisms, including mycobacteria and fungi, and had undergone multiple redo palliative operations. Of the utmost importance, therefore, is early treatment of the patient as soon as signs of prosthetic infection appear, and replacement of broad-spectrum antibiotics by selective antibiotics, according to cultures from blood, perigraft collections, and infected graft fabric.

3) Resistance of allograft to infection cannot be considered complete, especially when dealing with highly virulent organisms and incompletely debrided infected tissues. In our series one patient died 13 days postoperatively from septic rupture of his native aorta proximal to the allograft anastomosis, probably because of highly virulent infection and insufficient debridement of the infected aorta. Besides appropriate antibiotic therapy, coverage of the aortic allograft with viable tissue such as omentum or rotational muscle flaps as well as drainage or even continuous irrigation of contaminated fields with antibiotics or povidone-iodine solution, are all important adjuncts to eradicate infection.

4) Long-term results of arterial allografts are still a cause for concern. Although the methods of allograft procurement and storage are at present totally different from those utilised in the 1950s, the risks of allograft degenerative changes cannot be overlooked. All of our patients had routine duplex scanning during the follow-up. CT scanning and/or aortography were performed depending on the results of ultrasound studies. Dilatation of the allograft was observed in only a few patients in whom thoracic aortic allografts (elastic arteries), had been used for replacement of the infrarenal aorta. None has yet been reoperated upon. However, at 2 years of follow-up, occlusive lesions were observed in about 25% of external iliac and femoral arterial allografts (muscular arteries), requiring redo operations for ischaemic symptoms. Although the cause was probably intimal hyperplasia in the majority of cases, typical histological signs of chronic rejection were observed, i.e. intimal proliferation of myofibroblastic cells, medial smooth muscle necrosis and adventitial inflammatory cells infiltration. Secondary and late deterioration of allografts, therefore, are probably partly immunological.
in origin.\textsuperscript{35,36} Matching of blood and histocompatibility between recipient and donor was not attempted in our series because of the lack of available allografts. The development of arterial banks should make this possible in the near future. Although immunosuppressive treatment can delay intimal thickening\textsuperscript{36} and improve long-term patency of arterial allografts,\textsuperscript{35} it is obviously contraindicated in infected patients.

Conclusions

The use of arterial allografts is certainly not the “ideal” solution for the treatment of aortic prosthesis infection. In situ reconstructions with either autogenous DV or antibiotic-bonded grafts may be valuable alternatives, even though further evaluation of these materials is needed. Nevertheless, arterial allografts deserve ongoing research, regarding their resistance to infection, antigenicity, mechanical properties and preservation techniques, in order to better understand their biological behaviour and better define the indications and modalities for their clinical use. Our results have encouraged us to continue to offer in situ allograft replacement to patients with abdominal aortic infected grafts.

References

32. Kieffer E, Plissonnier D, Bahini A et al. In situ allograft replacement of infrarenal aortic prosthetic grafts: results in 100 consecutives patients. Submitted for publication.
34. Baccourty C, Koskas F, AURC. Axillofemoral bypass and aortic

