

EDUCATIONAL ARTICLE

Grafts and Graft Materials as Vascular Substitutes for Haemodialysis Access Construction

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Apart from long-term central venous catheterisation, the insertion of an arteriovenous graft (AVG) remains the only option to allow continued haemodialysis when the patient's superficial veins have been exhausted. Although, expanded PTFE has become the graft of choice for haemodialysis access throughout the world, many other organic or semi-organic materials are currently available for AVG construction. These are less prone to steal syndrome, easier to handle, more resistant to infection and may have similar, if not better, long term patencies.

Keywords: Vascular access; Haemodialysis; Prosthetic grafts.

Introduction

The best prosthetic material for arteriovenous graft fistula (AVG) construction in patients on chronic haemodialysis (HD) with unsuitable superficial vessels remains a matter for debate, as there have been no large prospective, randomized trials; moreover, the materials have been used under different circumstances and the methods for reporting patency have not been uniform. This review covers currently available autogenous, allogenic, xenogenic or synthetic grafts for AVG construction, including some that have been abandoned in favour of new materials with better compliance and fewer complications.¹

Graft Materials

The ideal vascular graft for patients on HD should be easy to handle, closely mimicking the native vessels, nonthrombogenic, immunologically inert, resistant to

infection and puncture trauma, able to retain tensile strength, and manufactured at a reasonable cost.

Biological grafts

Autogenous greater saphenous vein would appear to be the obvious conduit for AV bridge graft construction but has generally given disappointing results with patency rates of 20% at 2 years,² although cumulative patencies of 89, 89 and 72% have been reported at 1–3 years, respectively, in a recent small retrospective review of forearm AVGs.³ Saphenous vein can also be used to construct a spiral vein graft in the lower limb, which gives encouraging patency at 5 years.⁴ However, the increased operating time for saphenous vein harvesting, delayed healing of the thigh wound, and the need to preserve it for peripheral vascular or coronary arterial revascularization have turned attention to other vascular substitutes.

Homologous saphenous veins, obtained by stripping varicose veins, has been used with excellent results, whether prepared 'in house'^{5–7} or commercially (Vascogref, Bioprotec, Varivas). We have found that them easy to handle and it is not rejected immunologically, although other investigators have found them to cause allosensitization.⁸

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Denatured homologous vein grafts have given variable results with one-year primary patencies of 30–57%.^{9,10}

Initial enthusiasm for cryopreserved venous homografts (saphenous or femoral vein), with reports of a two-year cumulative patency of 100% without allograft rejection^{10,11} has been tempered by subsequent reports of graft infections and allograft rupture.¹²

Denatured arterial homografts have also been given poor results due to an inflammatory response and interactions between host and graft cells, and graft degeneration.¹³

Human umbilical vein, first used by Dardik,¹⁴ showed poor overall patency rates in two early studies, with frequent thrombosis and infection rates of over 20% in a mean 8.5 month follow-up.^{15,16} Moreover, it is expensive and difficult to handle because of the disparity in thickness between the umbilical vein and the host vessels.

Bovine Carotid Artery, a pre-treated heterograft, was first described for AVG construction in 1972. The long term patency rates were inferior to other graft materials and it suffered graft disintegration,¹⁷ although overall patencies of 79, 69, 63 and 51% at 1–4 years, respectively, were observed by some investigators.¹⁸ On the other hand, Metha reported a primary patency for bovine carotid grafts of 16% and the secondary patency of 39%, at 3 years in a large retrospective study in 1991,¹⁹ which is significantly inferior to those reported for PTFE (22 and 54%). Other prospective studies have shown these two graft materials to give similar results²⁰ but bovine carotid artery is now rarely used,²¹ due to the high incidence of aneurysms²² and infections in up to 25%.²³

Biohybrid and bioresorbable prostheses, graft pretreatment with endothelial cell culture, methods of affixing antibiotics, anticoagulants and growth factor to graft surfaces are under investigation to enhance the results of prosthetic vascular materials, as biologic materials facilitate cell repopulation and tissue remodeling.

The Omniflow prosthesis is formed from gluteraldehyde-tanned ovine collagen, which is grown around a polyester mesh. This biosynthetic device obtained by inserting polyester mesh-covered mandrils beneath the cutaneous trunci muscle of Australian adult sheep for a period of 12–14 weeks, is stabilized using gluteraldehyde and may be prepared in straight or J- or U- curved configurations; this collagen-encapsulated graft is easy to handle, with reduced thrombogenicity, low rates of infection, a low incidence of aneurysm formation and satisfactory long-term results with overall patencies of 77–71% and 48–45% at one and 4 years.²⁴ The current Omniflow II vascular

graft has a more resistant mesh but requires delicate manipulation, avoiding cross clamping the graft with metal instruments and traction during the passage through the tunnel.

Another modern bioprosthesis, bovine mesenteric vein, obtained by a patented process of gluteraldehyde cross linking and gamma radiation has physiological properties similar to those of the human saphenous vein, due to its high elastin to collagen ratio. In a recent multicenter study comparing it with synthetic grafts, bovine mesenteric vein had lower rates of re-operation per year (0.97 with bovine mesenteric vein vs 1.37 for synthetic), a lower incidence of thrombosis (0.78 vs 1.36), a 3.7 fold less frequent infection (0.05 vs 0.2) and higher patencies, both primary (36 vs 28% at 12 months) and secondary (66 and 60% vs 56 and 43% at 12 and 24 months, respectively).²⁵

The original bovine ureteric graft, prepared by gluteraldehyde fixation and detergent processing was prone to aneurysmal changes.²⁶ A modified preparation procedure to chemically-fix and decellularize the graft (synergraft),²⁷ eliminates this problem and has been recently adopted, because of optimal handling characteristics, the uniform diameter, the correct thickness of the graft wall to withstand even high arterial pressures and the absence of valves or tributaries. In the early preparation, this modified xenograft, showed reversible edema of the limb and a redness of the overlying skin in about 40% of limbs in which the graft had been implanted but this problem seems to have been overcome by further modifications. Additional advantages of this graft are the virtually unlimited supply, the simple storage, no need of time-consuming preparation or rinsing procedures and high resistance to infection.

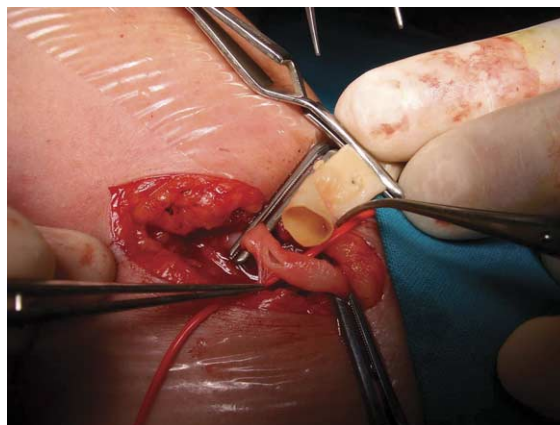


Fig. 1. An organic prosthesis of 6 mm in diameter is anastomosed to the left brachial artery of 2.9 mm. The arteriotomy should not be over 2.3 mm, to reduce the risk of steal syndrome.



Fig. 2. A straight AVG in the upper arm in a child, showing the 'pleating' of the organic prosthesis during the arterial anastomosis to taper the graft and match it to the arteriotomy.

Modern biological materials, such as bovine ureter, cryopreserved vein¹² and bovine mesenteric vein²⁸ show less anastomotic site compliance mismatch, a reduced tendency to thrombose, reduced intimal hyperplasia at the venous end of the AVG,²⁹ a reduced risk of steal syndrome due to the ability to 'pleat' the graft (Figs. 1 and 2) thereby reducing its diameter to match a smaller arteriotomy,³⁰⁻³² a reduced risk of infection, a considerable reduction in re-operations to maintain the patency and better results than PTFE.^{25,33}

Synthetic grafts

The modern era of synthetic vascular grafts began with the search for an inert graft material, but it was soon realized that healing of vascular prostheses occurs by interaction with the blood elements and the surrounding tissue,³⁴ leading to incorporation and endothelialization of the graft.

Polytetrafluoroethylene (PTFE) (Fig. 3) gained popularity as graft material in the expanded form (ePTFE), due to increased porosity, better tissue adhesion, the lack of requirement to preclot prior to implantation and improved pliability, in comparison with polyethylene terephthalate (Dacron).

Expanded PTFE was first used as a conduit for vascular access in the late 1970's³³ and has since become the most popular graft material, despite its high incidence of occlusion, (usually due to myointimal hyperplasia at the venous end), seroma formation, high infection rates and suboptimal patency rates. Primary patency rates of 28% at 12 months have been reported for ePTFE AVGs²⁵ with secondary patency rates of 76% at 6 months,³⁵ 55-59% at 12 months^{25,36,37} and 43% at 24 months,²⁵ respectively.

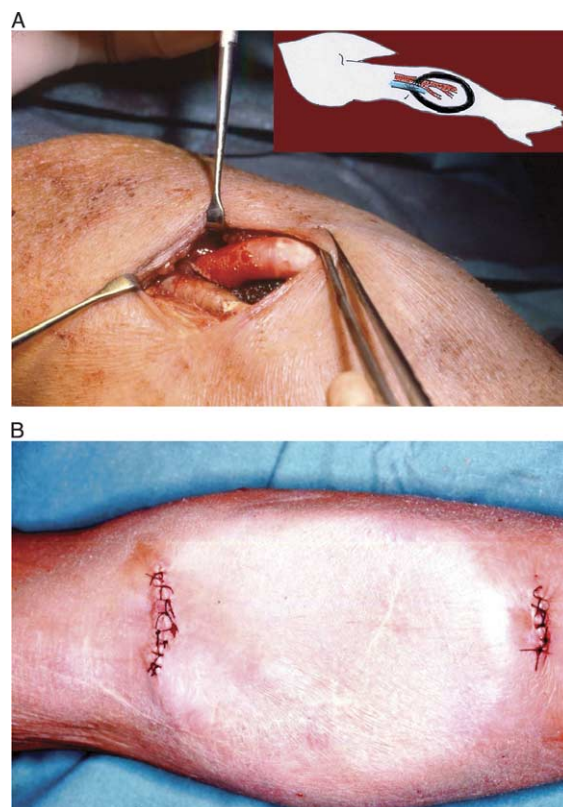


Fig. 3. A forearm PTFE loop graft: (A) the arterial anastomosis (a) between a tapered e-PTFE and the right brachial artery has been completed. Some oozing of blood through the PTFE can be seen. The venous anastomosis (b) is to a vena comitans of the brachial artery (rather than the cephalic or basilic veins since if these were present an autologous brachial fistula would have been constructed). (B) The completed PTFE loop after skin closure showing the graft in a subcutaneous tunnel in the forearm, with a distal counter-incision. The scars of previous failed access sites are also seen.

Further modifications of standard PTFE have been introduced (impra or goretex, thin walled, tapered, stretch, higher porosity PTFE, carbon-coated, heparin-bounded, fibroblast growth factors impregnation, the addition of external rings to enhance kinking and crush resistance) but have failed to improve patency.^{38,39} Similarly, other PTFE modifications, such as the diastat graft, which is a self-sealing PTFE-silicone graft, and plasma-TFE, developed to allow an early cannulation and avoid the need for temporary dialysis catheter, had patency rates similar to standard PTFE. The addition of an expanded cuff to a PTFE graft (Venaflo) to obviate the problem of outflow venous stenosis has been found to improve patency.⁴⁰

The Hemasite®, a transcutaneous button, as external part of a titanium nonthrombogenic tube, connected to the side of a PTFE internal arteriovenous bypass graft with the advantage of avoiding the need for skin puncture⁴¹ is no longer available.

The first generation of polyester-polyurethane vascular grafts (vascugraft) was hydrolytically unstable. A polyether-based polyurethane (Pulse-Tec), relatively insensitive to hydrolysis, used for AVGs, underwent biodegradation *in vivo* due to an oxidative process.⁴² One of the latest attempts to create a self-sealing vascular access for immediate use is a three-layered polyetherurethaneurea with non-porous layer under the luminal surface (Vectra®, made by Thoralon®) gave similar patency rates compared to PTFE grafts.⁴³ Such polyurethane grafts elongate with time and the incidence of pseudointima formation near the venous anastomosis is higher than for ePTFE grafts. Moreover, early cannulation seems to damage the graft material as shown by color Doppler ultrasound.⁴⁴

A more porous polyurethane vascular graft coated with a gelatin-heparin matrix and reinforced on the outside with knitted dacron fibers to prevent aneurysm formation (corvita), seems to have no clinical advantage over PTFE, with a reported cumulative patency of 53% at 1 year⁴⁵ and a similar long term patency.⁴⁶ Another major concern about polyurethane grafts is the potential carcinogenic effect of 2,4-toluene diamine, one of its degradation products.⁴⁷

Despite major advances in vascular grafting, the search of small diameter vascular substitutes is far from complete.

Graft Configurations

The forearm loop between the brachial artery and one of the available veins in the antecubital fossa (Fig. 3 (A) and (B)) and the straight AVG in the upper arm between the brachial artery and the axillary vein (Fig. 2) (or the proximal brachial or basilic vein) are the most popular graft configurations, but a number of anatomical variations may be used, depending on the patient's remaining vessels. Greater secondary patencies have been reported with the looped forearm AVG by most⁴⁸⁻⁵⁰ but not all observers.⁵¹ However, every effort should be made to preserve the available vessels of uremic patients by creating the most distal AV graft or fistula possible, and adopting a strategy for a sequential graft placement.⁵²

The straight forearm configuration between the radial artery at the wrist and an antecubital vein⁵³ should be avoided, because of an increased risk of early thrombosis. Ischaemia due to steal syndrome is also a problem because of the relatively poor inflow through the radial artery. Ideally, one of the venae comitantes of the brachial artery should be used rather than the superficial veins as outflow for a straight or looped forearm AVG graft, because if the basilic or



Fig. 4. The 'O' shaped AVG in the distal third of the upper arm preserves more proximal sites for potential future straight AVGs. The compliance of the biological graft is crucial for this technique, as the prosthesis is placed between the brachial artery and its vena comitans in a very narrow loop. This AVG is functioning well at 9 years.

cephalic veins are still available they should be used instead to construct an autogenous AVF with the brachial artery.

The elasticity and compliance of the graft are crucial for some techniques, such as the 'O' shaped AVG with a narrow loop in the distal third of the upper arm (Fig. 4) between the brachial artery and its vena comitans or the basilic vein,⁵² in order to preserve more proximal locations for potential future straight AVGs. Modern biological grafts are more suited to this configuration.

AVGs in the lower limb have generally given less encouraging results than for the upper limb, because of increased rates of infection (41%), ischaemia (11%), and 2-year primary and secondary patency rates of only 19 and 54%, respectively.⁵⁴ However, groin access is a useful option when upper extremities are unavailable and peritoneal dialysis has failed.

The lower extremity may be also used for a saphenous vein loop fistula between great saphenous vein anastomosed in an end-to-side fashion to superficial femoral artery^{55,56} or to the popliteal artery.⁵⁷ However, prosthetic grafts shorten the operation time, reduce wound-healing problems and preserve the saphenous vein for future myocardial or peripheral revascularization.

A careful policy of native vessel preservation should also be adopted in the lower limb to maximize the use of potential access sites in each extremity: the distal superficial femoral artery and saphenous vein should be used first for positioning an AVG in a straight configuration, as his subsequently converted to a loop configuration after failure, leaving a segment of the old AVG temporary to allow early needling and minimize the use of a central venous catheter.⁵² The

common femoral artery and superficial femoral vein may be also employed, if necessary, for a looped AVG.

The axillary (or subclavian) artery can be used for a loop AVG, with the ipsilateral axillary or jugular vein as outflow, as well as for placing a straight AVG anastomosed to the contralateral axillary or jugular veins.^{58,59}

Long axillo-femoral grafts⁶⁰ are prone to repeated thromboses, especially in hypotensive patients. Moreover, when large vessels, such as the axillary artery and femoral veins, are employed severe venous or arterial problems may follow AVG thrombosis.⁶¹

Central vein occlusion, ischaemic steal syndrome and cardiac failure may be indications for creating arterio-arterial vascular access grafts run superficially in the lower limb,⁶² or on the chest wall.⁶³

More heroic access configurations, such as anastomosis to the right atrial appendage through a median sternotomy⁶⁴ and to the renal vein⁶⁵ to bypass central venous obstruction should be avoided if possible in favour of a permanent central venous catheter.

Graft complications

There are differences between graft materials with regard to the type and the incidence of complications. The high surface thrombogenicity of the AVG may be the cause of early thrombosis, in the absence of other factors, such as technical error, compressing haematoma/seroma or proximal venous occlusion.

Perigraft seroma is a typical early complication of PTFE AVGs.²⁶ The most frequent late complication in AVGs, particularly synthetic grafts, is stenosis at the venous anastomosis due to development of myointimal hyperplasia. Concomitant thrombosis requires revisional surgery to preserve other access sites for future use: surgical correction using an interposition graft^{66,67} is generally preferred to endovascular repair, because of its better long-term results.⁶⁸ Multiple stenoses within an AVG at needling sites do not generally need of surgical correction.

As the graft is only a porous scaffold, a minimum of three weeks is required before using an AVG to allow capillary ingrowth, surface re-endothelialization and host incorporation. The premature needling of an AVG is associated with puncture site bleeding and false aneurysm formation.

Tunneling too superficially, the use of anticoagulants and infection are also potential causes of false aneurysm development, skin erosion, infection and hemorrhage. High systemic blood pressure, venous hypertension due to a compromised venous outflow, atherosclerosis⁶⁹ and graft wall degeneration may lead

to true aneurysms later on. Biological grafts, especially those treated by glutaraldehyde, are reported to be more prone to biodegradation and aneurysm formation or dilatation. Cannulation technique is also important for prevent graft degeneration.⁷⁰ the 'rope ladder' technique is, in our experience, much better for AVGs than the 'area puncture' and 'buttonhole' techniques.

Vascular access-induced peripheral ischaemia, or steal syndrome, is more frequent in forearm PTFE-AVGs than radio-cephalic AVFs (4.3–6 vs 1–1.8%)⁷¹ and may be due to peripheral arteriosclerosis, diabetes, too large anastomosis, anatomical anomalies of the palmar arch, age, previous ipsilateral AVFs and high flow. If left untreated, it may lead to digital gangrene or even hand amputation.⁷² In addition, to preoperative investigations (bilateral measurement of arm and digital blood pressures, digital/brachial pressure indices and, in selected cases, upper limb angiography or magnetic resonance angiography), the best way to prevent steal syndrome is by restricting the arteriotomy to less than 80% of the arterial diameter. Biologic grafts are preferable, although more expensive than PTFE grafts, as they can more easily be pleated to match the graft to a smaller arteriotomy.

Currently, the most frequent cause of AVG failure is stenosis or thrombosis of the great veins, due to central vein catheterization, which leads to increased recirculation, decreased urea clearance, swelling and even ulceration of the ipsilateral limb. Percutaneous transluminal angioplasty, with or without stenting is helpful, but restenosis usually occurs within few months so that graft ligation may become necessary.

Graft Infection

The risk of infection of AVGs is significantly greater than AVFs.⁷³ This is important because dialysis access-related infection is associated with substantial morbidity and mortality.⁷⁴

Oral linezolid is a new treatment option in the management of methicillin-resistant *Staphylococcus aureus* (MRSA) infections, and seems to have significantly better outcomes than intravenous vancomycin.⁷⁵

Surgical treatment strategies vary according to the time of onset of the infection, the patient's clinical condition, the access site, the nature of the graft material and its anatomical position. Immediate removal of the access graft should be performed in cases of early (within 1 month) infections arising close to arterial anastomosis or in deep infection in lower limb AVGs. By contrast, a conservative approach may be adopted in late AVG infections away from the arterial anastomosis, such as superficial infections in



Fig. 5. (A) An infected forearm AVG has been just treated by partial excision; a new organic interposition graft is anastomosed in an end-to-end fashion to the arterial limb of the old AVG. (B) The new interposition graft bypasses the infected area involved through a new, concentric, subcutaneous tunnel. (C) The skin incisions are closed and covered with occlusive dressing. (D) The infected area is treated by removing the AVG and leaving the wound to heal by second intention.

true graft aneurysms or in midgraft AVG infections, as shown in Fig. 5. Primary removal of the entire graft should be reserved for extensive infections of synthetic AVGs.

In a prospective study of Minga,⁷⁶ of more than 500 dialysis patients over a 4.5 year-period, 90 (18%) functioning PTFE-AVGs were removed because of infection. During the same period, there were 1.1 graft-years of follow-up, yielding a rate of 8.2 infections/100 graft-years and 1% of related-deaths. In a recent retrospective study,⁷⁷ significantly better results were obtained with 863 AVGs performed in the upper (701) or in the lower (116) limb between January

1990 and June 2005, using biologic/semibiologic materials, in comparison with previous studies on PTFE AVGs (2.6 infections/100 graft-years were observed over 2.3 graft-years of follow-up), with a significantly lower incidence of functioning graft loss for infection (2.9%) and of related deaths (0.1%).

Conclusion

Organic and semi-organic materials for AVG construction offer advantages over synthetic materials, with easier to handling, a lower incidence of 'steal

syndrome', wider possibilities for the preservation of the patient's native vessels and a lower incidence of infection. Thrombogenicity of the luminal surface is the most common cause of AVG occlusion. Biological prostheses give more satisfactory results for revision vascular access surgery, prolong access patency and improve the quality of life, even in difficult patients.

Key Summary

- Biologic/semibiologic grafts give better long term patencies, a lower incidences of infection and steal syndrome, a very low incidence of stenosis at the venous end and easier redo-surgery in comparison with synthetic grafts.
- The creation of loop or straight AVGs should not simply depend on the preference of the vascular surgeon: every effort must be made to preserve the native vessels of uremic patients, using the most compliant graft and a critical strategy for sequential AVG placement
- The improved compliance of biological/semibiological grafts is advantageous when crossing joints and allows some techniques which would otherwise not be possible, helping to preserve the vascular system for future access sites
- Avoid synthetic prostheses in the elderly, diabetics and very young patients, as they are more prone to infection and steal syndrome
- The arteriotomy should not exceed 80% of the arterial diameter to avoid a steal syndrome: the advantage of biologic or semibiologic materials is that they may be easily 'pleated' to match the length of the arteriotomy.
- Avoid puncturing biological AVGs for a minimum of 3 weeks after implantation to prevent bleeding or false-aneurysm formation
- An aggressive surgical approach limits the consequences of AVG infection
- It is important to minimize central venous catheter use.

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