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Materials Used for Hemodialysis Vascular Access: Current Strategies and a Call to Action

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Renal replacement programs are an integral therapeutic part of end-stage renal disease. However, the increasing lack of donor organs, associated with an increasing number of patients requiring permanent hemodialysis necessitates the implantation of a hemodialysis access. However, natural vessels are often not or no longer usable after long-standing dialysis. Therefore, arteriovenous grafts, that is, polytetraflouroethylene (PTFE) grafts, are used at increasing frequency. However, PTFE grafts especially are associated with two untoward consequences: high rates of arteriovenous access thrombosis and infection. In this review, current strategies are discussed and requirements for future graft materials are defined. Biological implants show relative resistance to infection and rejection. Therefore, biological implants seem to provide the most useful tool in managing complications associated with hemodialysis vascular access. Thus, it is time to develop new strategies and new graft materials that fulfill the "physiological" requirements of an optimal vascular access to prolong patient survival on dialysis, reducing morbidity and escalating costs.

Keywords: hemodialysis; vascular access; dialysis; shunt; arteriovenous; renal end-stage disease

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Introduction

Although intermittent hemodialysis for the treatment of patients with acute renal failure was introduced by Kolff in 1943, the development of chronic hemodialysis therapy for end-stage renal disease was not feasible until the introduction of the external arteriovenous shunt by Quinton and colleagues in 1960. Six years later, Brescia and coworkers developed an endogenous radiocephalic arteriovenous fistula.[1] Prosthetic subcutaneous fistulae used as an interpositional bridge were developed shortly thereafter.[2] Although in an area characterized by rapid technical development, no major advances on permanent grafts and only minor refinements in the biomaterials and contours of prosthetic bridge grafts have been made. Thus, over the past 3 decades, the development of permanent hemodialysis access slowed down significantly. During this time of "nondevelopment," the rapid growth of end-stage renal failure programs has been accompanied by a tremendous increase in hemodialysis vascular access–associated morbidity worldwide.

Most recent evidence suggests that access-related morbidity accounts for at least 25% of all hospital stays of these patients. In the 1st year of dialysis, costs associated with vascular access may constitute up to 50% of all patient care costs.[3-5] In addition to the enormous financial burden, the frequency and unpredictability with which hemodialysis vascular access thrombosis occurs remain enormous frustrations. The same is true for infectious complications.

Infectious complications continue to be among the foremost causes of morbidity and mortality in hemodialysis patients. The tremendous risk of death caused by infection in end-stage renal disease patients is probably best highlighted by Sarnak and

Jaber, who compared annual mortality rates caused by sepsis in such patients with the general population.[6] In their study, which relied on data from the United States Renal Data System for the years 1994 to 1996, a 100– to 300–fold higher risk of death caused by sepsis was found in patients with end-stage renal disease. Stratification for age, gender, and the presence of diabetes did not show a significantly altered magnitude of such risk posed by the status of end-stage renal disease.

A major risk factor for infection and bacteraemia is the hemodialysis access itself.[7-11] The incidence of infection caused by the hemodialysis vascular access is highest with central venous catheters and lowest when a native arteriovenous fistula is used.[8,9,11] Especially prosthetic arteriovenous grafts composed of polytetraflouroethylene (PTFE), which has become a widely used alternative when a native arteriovenous fistula is not surgically feasible, is plagued by infection very often.[12-15]

None of the materials currently used for hemodialysis access fulfill the requirements of an optimal access graft. Thus, the purpose of this review is to give an overview of materials experimentally or clinically used for vascular access and to discuss advantages and disadvantages of these materials.

Arteriovenous Hemodialysis Access

Arteriovenous hemodialysis accesses include native arteriovenous fistulas and synthetic arteriovenous grafts.

Autogeneous Arteriovenous Fistulae

First choice of arteriovenous hemodialysis access is the Brescia Cimino radiocephalic fistula.[1] It offers reported patency rates of 64% to 72% and 37% to 72% at 3 and 5 years, respectively.[16-19] Although a surgical end-to-side technique is associated with a lower incidence of venous hypertension symptoms in the hand, neither the side-to-side technique, as described originally, nor the end-of-vein-to-side-of-artery technique is superior in terms of overall patency.[20] If there are no suitable vessels at the wrist, brachiocephalic or elbow fistulae present the next best choice.[21,22] This vascular access allows for patency rates of 50% to 70% and 34% to 53% at 3 and 5 years, respectively.[23-26] Besides low infection, low thrombosis, and so forth, both types of fistulae can be fashioned under local anesthesia, and they

have low complication rates in comparison to other forms of access. They are also relatively resistant to infection compared with constructions using PTFE grafts. Despite infection of 0% to 6% for wrist fistulas[18,27] and 8% to 10% for elbow fistulas,[25,26] the rate of fistula loss due to infection is low: 0% to 1% for both types of construction.[16,18,23,25,27] However, brachiocephalic fistulas, although to a lesser extent than arteriovenous accesses of the lower limb, are associated with a high incidence (10% to 20%) of vascular steal phenomena.[23,28] "Steal" means a significant proportion of the arterial flow to be shunted back toward the heart with more distal vascular areas becoming ischemic. Diabetes and preexisting vascular disease represent risk factors for arterial steal. Clinically, a patient presents with classical signs of distal limb ischemia that develops gradually within weeks after fistula construction or, occasionally, as acute nerve ischemia in the postoperative period. In a proportion of patients, symptoms improve without treatment if they persist; however, treatment options include banding or plication of the fistula, with intraoperative flow monitoring to assess the required degree of luminal narrowing.[29] It may also be possible to ligate the artery to the arm distal to the fistula anastomosis. Successful restoration of function has been reported in more than 90% of patients using this latter technique.[30,31] If such interventions are unsuccessful, ligation of the fistula is required.

Another alternative is the transposed autologous brachiocephalic arteriovenous fistula. It is fashioned by mobilizing the basilic vein from its subfascial bed, transposing it to a subcutaneous tunnel on the anterior surface of the arm, and anastomosing it to the brachial artery at the level of the antecubital fossa.[20,22] The procedure is technically feasible in 95% to 98% of cases[29,32] owing to the subfascial location of the vein protecting it from previous venipuncture. It has the advantages of resistance to infection as well as requiring only 1 anastomosis. This latter feature has the double benefit of avoiding the proximal anastomosis associated with outflow stenosis in PTFE grafts and not compromising the insertion of a prosthetic graft at a later date, should this become necessary. Secondary patency rates of these alternatives are roughly equal, with 3-year patency rates ranging from 43% to 64% for transposed brachiocephalic fistu-

lae[24,26,33,34] and 40% to 59% for PTFE arteriovenous grafts.

Other disadvantages of autogeneous arteriovenous fistulae are long periods of maturation (up to 4 months for wrist fistulae) and a resulting high proportion of fistulae that fail before being used for dialysis (11% to 30%).[18,19,23,27] Attempts to improve the rate of maturation have included hand exercise, with or without a light tourniquet; however, there is no evidence to support this approach. Although some studies have reported higher rates of primary failure, delayed maturation, and lower patency rates in wrist fistulae, especially in the elderly[35] and diabetic[36] patient, other studies have reported no differences in outcome in elderly and diabetic patients[37,38]; an appreciable number of patients with diabetes achieve successful dialysis via radiocephalic fistulae (30% to 80%),[36,39] with no differences in dialysis efficiency between diabetic and nondiabetic patients.[36]

Venous occlusive disease is another complication of arteriovenous fistulae. More than 60% of arteriovenous fistulae fail because of thrombosis in the venous circulation.[40] These stenoses are histologically characterized by neointimal hyperplasia,[41,42] a pathological response of vascular tissue injury.[43] Stenosis in an autogeneous arteriovenous fistula occurs predominantly within 2 to 3 cm of the arteriovenous anastomosis, or at needling sites and calcified venous valves.[44] Central venous stenosis, typically subclavian vein stenosis, accounts for roughly 40% of venous stenoses associated with arteriovenous fistulae.[45] Central venous cannulation, a nondenuding stretching injury produced by blood flow at arterial pressure, as well as endothelial trauma from repeated venipuncture with a subsequent release of mitogens from the activated platelet plug required to stop bleeding,[46] are discussed as underlying pathomechanisms.

PTFE Arteriovenous Grafts

In the absence of suitable superficial veins in the arm, the next best type of access is a choice between the insertion of a prosthetic arteriovenous graft and the transposed autologous brachiocephalic arteriovenous fistula.[47] In practice, however, use of artificial grafts appears to be predominant, as shown by a large US national survey (1995) conducted by the Centers for Disease Control and involving 224,954 hemodialysis patients. According to these data, only 22% of patients were dialysed through a native arteriovenous fistula, although an autologous vascular access is superior to PTFE grafts.[48] In the United States, the majority of current arteriovenous grafts are made of PTFE material. These grafts have gained widespread popularity because of ease of placement at sites where it is surgically unfeasible to create a native arteriovenous fistula. However, this surgical success has created 2 untoward consequences: high rates of arteriovenous access thrombosis and infection.[13,14,28,49,50] In the United States, the vast majority of arteriovenous access-related infections are associated with PTFE grafts.

Expanded PTFE was first used as a conduit for vascular access by Volder and coworkers.[51] PTFE has the advantage of easy handling and ready availability, it can be inserted under local anesthesia in a wide variety of configurations (depending on the available vascular anatomy), and, if necessary, it can be needled immediately for hemodialysis (see Table 1).

However, in comparison to transposed brachiocephalic arteriovenous fistulas, PTFE grafts are associated with much higher complication rates.[34] The primary patency rate for PTFE grafts is significantly lower than for brachiocephalic fistulae and requires up to 1 to 4 further procedures per year to maintain patency.[52] In general, large centers with active prospective surveillance programs present secondary patency rates for PTFE grafts of approximately 50% at 3 years. This is achieved at the expense of a 3- to 6-fold increase in the number of procedures compared to native fistulas.[53]

More than 80% of all PTFE grafts fail because of thrombosis in the venous circulation.[40] Of these, 50% to 70% occur within 3 cm of the graft-to-vein anastomoses.[54,55] Central venous stenoses associated with arteriovenous PTFE grafts—typically subclavian vein stenoses—account for roughly 20% of venous stenoses.[44] Differences in the incidence and distribution of venous stenosis related to arteriovenous fistulae and arteriovenous grafts are largely due to an accelerated rate of stenosis at the graft-to-vein anastomosis associated with the PTFE grafts.[53] They reflect different etiological factors in each type of fistula. As described above, in autogeneous arteriovenous fistulae, these include a nondenuding

Table 1 | **FEATURES OF CURRENTLY KNOWN BIOLOGICAL VASCULAR ACCESSES**

Type of Vascular Access Material	Origin	Choice	1 Year	3 Years	5 Years	Infection	Disadvantages
			PATENCY RATE				
Radiocephalic fistula	Biological (autogenous)	1st		64%-72%	37%-72%	0%-6%	Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia Steal phenomenon
Brachiocephalic and elbow fistulae	Biological (autogenous)	2nd		50%-70%	34%-53%	8%-10%	Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia Steal phenomenon
Transposed brachiocephalic arteriovenous fistula	Biological (autogenous)	3rd		43%-69%	No data	8%-10%	Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia
Polytetraflouroethylene (PTFE)	Artificial	4th	79.0%	40%-59%	No data	8%-19%	No resistance against infection Vast majority of infections are associated with PTFE 3- to 6-fold increase in the number of procedures to maintain patency (as compared to native fistulae) More than 80% of PTFE grafts fail due to thrombosis Size mismatches between native vessels and PTFE graft Accelerated intimal hyperplasia High primary (graft) and secondary (access care) costs
Bovine carotid arteries	Biological (xenogeneic)	No use	73%-75%	No data	No data	9%-10%	High primary (graft) and secondary (access care) costs Difficult to obtain High rate of pseudoaneurysm formation Graft rejection? Long periods of maturation Graft thrombosis within 12 months (53%)
Human umbilical vein graft	Biological (allogeneic)	No use	No data	No data	No data	High rates of infection	High primary (graft) and secondary (access care) costs Difficult to obtain High rate of pseudoaneurysm formation Graft rejection? Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia
Cryopreserved vein grafts	Biological (allogeneic)	Last choice	72%-75%	No data	No data	No data	Graft thrombosis within 12 months (22%) Intimal hyperplasia Graft rejection? Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia
Fresh human saphenous veins	Biological (allogeneic)	Last choice	82.0%	No data	No data	No data	Graft thrombosis within 12 months (17%) Intimal hyperplasia Graft rejection? Long periods of maturation Degeneration because of repeated needle puncture Intimal hyperplasia

stretching injury produced by blood flow at arterial pressure and endothelial trauma from repeated venipuncture with a subsequent release of mitogens from the activated platelet plug required to stop bleeding.[46] With PTFE grafts, the accelerated intimal hyperplasia found in proximity to the anasto-

mosis is due to a combination of flow turbulence, surgical trauma, compliance mismatch between vein and graft,[56] and the release of growth factors from fibrin and platelets that accumulate on the luminal surface.[57] Attempts to address some of these problems by increased graft compliance[58] or reduced thrombogenicity[57-61] are largely experimental and have produced mixed results. A wider use of pharmaceutical agents to reduce intimal hyperplasia seems warranted, but there are few reported trials of such agents in the context of hemodialysis vascular access.

If both the nondominant and dominant arm vessels are exhausted, remaining options for long-term access are leg or thigh grafts involving the subclavian or axillary vessels. The patency rate of PTFE thigh grafts has been reported to be approximately 50% at 2 years.[28] Graft infection is a particular risk in the groin, and it is associated with anastomotic dehiscence, hemorrhage, and death. The incidence of groin infection in PTFE grafts ranges from 16% to 35%,[28,62] and other reports of mixed PTFE and biological arteriovenous thigh grafts describe a leg amputation rate of 22% and a mortality rate of 18% attributable to infection.[63] Another complicating factor is the high incidence of peripheral vascular disease in renal patients with resulting high rates of steal phenomena (16%) and subsequent amputation (7%).[52] Due to these risks, the insertion of leg grafts should be seen as a last resort in those for whom all other options for long-term access have been exhausted.

Alternative Biological Implants

Bovine Carotid Arteries and Umbilical Veins

An alternative approach for vascular access using biological graft material was introduced by Rosenberg and coworkers in 1964.[64] After extensive evaluation in animal studies, bovine carotid grafts were applied as conduits in vascular surgery in 1966.[65] For clinical use, the bovine carotid artery is removed from the calf, and enzymatic digestion is performed with ficin, which removes all muscular and elastic material and leaves an essential collagenous tube. Subsequently, tanning is accomplished by submersing the tube in 1.3% dialdehyde starch solution, providing improved cross-linking of colla-

gen fibers. This procedure was believed to provide a nonantigenic graft.[65,66] After adequate checks for possible leaks, the graft is slid onto a glass rod and placed in tubes containing a sterilizing solution prepared with 1% propylene oxide in 40% aqueous ethyl alcohol. The grafts vary from 20 cm to 45 cm in length; diameters range from 8 mm to 12 mm.

Before 1980, many groups described the usefulness of bovine heterografts for chronic venous access in patients in whom direct arteriovenous fistula construction was impossible.[67,68] Reported advantages were an immediate use and a high rate of patency (97.5%). Despite early usage, immediate complications were described to be minimal and the long-term complication rate satisfactory (12-month cumulative patency rate of 73.9%).[69] Others reported on its disadvantage of being expensive and occasionally difficult to obtain and advocated PTFE grafts to be superior. Later on, advantages of early PTFE grafts were described as the ability to withstand infection at the puncture site, the ease of repair after the development of false aneurysms in these puncture sites, and the apparent low rate of development of pseudointimal proliferation at the venous anastomosis compared with the rather high rate with bovine heterografts.[70] Subsequently, in the early 1980s, it was concluded that bovine carotid grafts used for vascular access suffered unacceptable rates of infection and aneurysmal degeneration; they have generally been discarded as a vascular conduit for dialysis.

Another biological material used for hemodialysis access was the modified human umbilical vein, which was developed and introduced in the 1970s, too. After a period of about 10 years, like bovine heterografts, this material suffered a similar fate and likewise is now only rarely used.[71]

Cryopreserved Vein Grafts

A relatively new approach to prevent or at least to minimize access-related infectious complications is the use of cryopreserved superficial human femoral veins as arteriovenous access grafts (CryoLife Inc., Kennesaw, GA, USA). Natural grafts like these have the ability to revascularize their vessel walls in vivo and thus allow the patient to fight and resist infection. Since 1996, more than 500 cryopreserved superficial femoral vein allografts have been

implanted for hemodialysis access, preferentially in the setting of local or systemic infection. Initial results reported by Matsuura and coworkers show a remarkable absence of graft-related infection and rejection. Between 1996 and 1999, they implanted 48 cryopreserved femoral vein grafts in 44 patients. The indication for implantation included patients with infected PTFE arteriovenous grafts (20 patients), sepsis and persistent bacteremia (14 patients), and those who had cryovein arteriovenous grafts implanted for previous multiple graft failures and compromised venous outflow (10 patients). During the same time, 68 patients underwent placement of brachial artery-to-axillary vein arteriovenous grafts using PTFE step grafts (Impra Inc., Phoenix, AZ, USA). However, there were no cases of implantation of PTFE grafts into septic patients or infected fields. Life table analysis indicated a significant difference regarding primary patency between PTFE (69%) versus cryopreserved vein grafts (49%, $P < 0.01$). However, there was no statistically significant difference in the 12-month secondary patency for the cryovein (75%) versus the PTFE grafts (79%, $P = 0.519$). Furthermore, hemodialysis access–related complications such as puncture site bleeding or pseudoaneurysm formation were not seen in the cryovein homograft. As surgeons face older patients with multiple failure of access sites, Matsuura and coworkers concluded that maintaining patency of the few remaining conventional angioaccess locations, especially in the presence of infection, becomes an important priority. They thus stated that because of the relative resistance to infection, cryopreserved homografts provide a useful tool in managing sites of arteriovenous graft infections that might otherwise have been lost for future angioaccess.[72] Observations made by Baraldi and coworkers underscore these findings. They reported on 59 patients who received fresh or cryopreserved femoral human vein arteriovenous grafts. Acturial patency rates after 1 year were 82% and 72%, respectively. Although no early thrombosis was observed, 17% of fresh and 22% of cryopreserved vein grafts developed thrombosis during the 12-month follow-up. In most cases, this was explained as a result of myointimal hyperplasia in the perianastomotic area of the venous outflow.[73]

There is an ongoing debate among angiologists about whether rejection occurs in venous allografts. Baraldi and coworkers further examined the occurrence of T lymphocyte subsets (CD3, CD4, CD8, and CD4/8), as well as lymphcytotoxic antibodies, before and on days 15 and 30 following implantation of fresh and cryopreserved human femoral veins (allogeneic). Because they did not find evidence of an immunologic activation, they concluded that rejection is not a major cause of failure in cryoveins[74] even in the absence of ABO and HLA-A-B compatibilities.

The low rate of infection as well as the absence of graft rejection in these preliminary reports is promising for patients who have suffered from repeated PTFE graft infections and exhaustion of dialysis arteriovenous access sites. Here, cryopreserved vein allografts may be placed at new sites, but placement at old graft sites seems to be possible despite the presence of intercurrent PTFE graft infection. In such clinical scenarios, Matsuura and colleagues advocate one operation in which the cryovein graft is created at the same site while the infected PTFE graft is being removed. This leads to salvage of angioaccess sites that would have otherwise been abandoned. In keeping with the same concept, lower rates of arteriovenous access-related infection were also observed with the use of denatured homologous vein grafts, as opposed to PTFE grafts, in a prospective randomized multicenter trial.[75]

Features of the "Optimal" Hemodialysis Access

There is an increasing majority of end-stage renal disease patients in whom an arterialized autogenous venous conduit cannot be constructed or is not durable. Therefore, a substitute conduit must be used. Characteristics of the ideal biomaterial for this purpose include appropriate sizes to match host vessels, mechanical strength, low thrombogenicity, rapid and complete "healing" in subcutaneous tissues, ease of handling by the surgeon and by the dialysis technician or nurse, resistance to infection, structural durability in the face of repeated needle punctures, a low incidence of hyperplastic intimal reactions at interfaces with artery and vein, and low cost.

The luminal surface of an ideal graft must be thromboresistent, while the external surface should

Table 2 | FEATURES OF THE "OPTIMAL" HEMODIALYSIS ACCESS

Appropriate size to match host vessels
Mechanical strength
Low thrombogenicity/complete endothelialization
Rapid/complete healing
Ease of handling by technicians/nurses
Resistance to infection
Structural durability in face of repeated needle puncture
Low incidence of hyperplastic intimal reactions
Low costs

rapidly be incorporated into the surrounding tissues. The tendency toward thromboresistance versus thrombogenicity of biomaterials used in vascular access grafts is largely determined by surface characteristics, types of proteins that selectively and actively adsorb to the graft,[76-78] and the cells that tend to adhere to the graft material.[79] Inflammation at the host-biomaterial interface as a result of bioincompatibility may contribute to the development of intimal hyperplasia in PTFE grafts.[80-83] A potential mechanism in PTFE may be its strong hydrophobic material, which may increase platelet activation.[84-86] Furthermore, macrophages adhere readily to PTFE and become activated with the production of reactive oxygen species and membrane-associated interleukin-1 and tumor necrosis factor-a (TNF-a).[78,87] Endothelial cells adherent to PTFE bind human leukocytes more readily than control endothelial cells.[88]

A major biological problem with PTFE grafts is their failure to achieve complete in vivo endothelialization.[38] This leads to repetitive episodes of platelet deposition and inflammatory cell activation (platelets, neutrophils, macrophages).[89] It has been suggested that there may be better perigraft tissue in-growth and endothelialization using high-porosity, nonreinforced PTFE grafts (compared to the standard lower porosity reinforced PTFE grafts in clinical use) or with the use of vascular endothelial growth factor.[90-92] Recently, experimental approaches such as the application of shear stress on endothelial cells or retroviral transfection of endothelial cells[93,94] have been shown to increase retention of endothelial cells on graft material in vitro (see Table 2).

Areas of Active Investigation

Research in vascular prostheses for hemodialysis remains in its infancy. Relatively little is understood about basic blood/surface/host tissue interactions in general; furthermore, the response of various biografts to the special setting of the end-stage renal disease patient—high blood pressures and flows, altered platelet and endothelial cell biology, accelerated atherosclerosis, and thrice-weekly dialysis sessions characterized by multiple needle punctures, the administration of heparin, hypotension or hypertension, and extrinsic compression—further complicate any understanding of the natural history of the vascular biograft in the dialysis patient.

What is known about blood/surface physics and chemistry includes the following. The "optimal" or "critical" surface tension (a function of flow pattern and rate) approximates 10 to 45 dyn/cm: The likelihood of thrombosis rises geometrically at surface tensions below or above this range. Surface composition is relevant to graft patency: Crystalline polymers are more reactive with respect to platelets and leukocytes, whereas hydrophilic surfaces without ionic charge or strong hydrogen bonding appear to minimize thrombosis. Deposition of serum proteins from flowing blood onto a surface is followed by variable deposition of fibrin and platelets. Important evidence suggests that initial deposition of albumin may minimize subsequent blood element deposition,[95] whereas deposition of fibronectin appears to stimulate platelet, fibrin, and blood cell aggregation and deposition.[96] Platelet aggregation, stimulated by damage imparted by shear stress, is critical both for surface thrombosis and "healing" of synthetic grafts.

Other issues include graft porosity. Pore sizes less than 22 mm are considered to be optimal and rapidly increased pseudointimal ingrowth (and thrombotic potential) at larger pore sizes.[97] Furthermore, surface "roughness" affects deposition of proteins or even cells[98]; entrapped air is a stimulant of platelet and white cell aggregation in this setting.

Anastomotic neointimal hyperplasia contributes to 70% to 90% of failures in access biografts. The development of this process appears currently to be independent of the type of graft used: Controversy continues about whether compliance mismatch between the stiff graft and the flexible host vein or artery participates in this process.[99] Different grafts seem to have an equivalent prevalence of neointimal hyperplasia. Therefore, hydraulic mechanisms within arteriovenous flow (markedly increased shear forces, flow separation, and turbulence, with resultant damage to formed elements of the blood) may be of critical importance.[100] Again, platelets probably play a substantial role in the pathogenesis of anastomotic neointimal hyperplasia, with aggregation, deposition, and elaboration of various mitogens that stimulate smooth muscle cell proliferation, fibroblast, and proteoglycan migration and deposition characterizing junctional neointimal hyperplasia. The widespread use of erythropoietin and the concurrent anecdotal observation of apparently decreased access graft patency have raised the question of whether alterations in blood rheology or in the possible mitogenic capability of erythropoietin have contributed to this phenomenon.

Active areas of investigation related to grafts include the construction of various composite grafts: Dacron/silicone rubber to permit a "no leak," immediately puncturable graft; Dacron or ePTFE/polyglycolic acid "hybrids" to encourage orderly healing following biodegradation of a material filling graft pores; and plasma polymerization of Teflon grafts to improve thromboresistance.[101,102] Albumin coating of Dacron grafts permits their insertion without preclotting and may provide better graft healing.[95] Surface bonding of materials such as heparin or tissue plasminogen activator, if durable, could also provide a reliable nonclotting surface, and permanent bonding of carbon could make a truly nonwettable (and hence nonthrombogenic) surface.

Conclusions

Although the optimal vascular conduit for hemodialysis is undeniably an arterialized autogenous subcutaneous vein, only a minority of end-stage renal disease patients can count on such access. The remainder require implantation of artificial or biomaterial conduit. The majority of current arteriovenous grafts are made of PTFE. However, in view of all the problems associated with PTFE grafts on one side and no alternative biological materials on the other, this surgical success has created 2 untoward consequences: high rates of arteriovenous access thrombosis and infection. This alarming process has to be regarded as an interdisciplinary call to action. Thus, continuation of this clinical practice means further enormous costs and patients' morbidity and mortality. This outlook requires new concepts to improve vascular access materials.

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