Hypothesis: Thrombolysis is an accepted technique to salvage a failed infrainguinal bypass graft. Careful case selection, including consideration of the native arterial runoff and the type and location of the graft, will portend a better clinical outcome and prolonged graft patency.

Design: Retrospective study of an inception cohort of 91 acutely thrombosed grafts.

Setting: Academic tertiary care center.

Patients: We analyzed 91 consecutive occluded grafts in 69 patients for secondary graft patency and clinical outcome.

Intervention: Regional transcatheter thrombolysis.

Main Outcome Measures: Technical success, secondary graft patency, and the need for major limb amputation.

Results: Immediate technical success resulting in restoration of flow was achieved in 80 (88%) of 91 cases. Angioplasty or additional surgical intervention (eg, patch, interposition graft, or jump graft to a more distal site) was performed in 44 subjects (64%). Longer duration of secondary patency was associated with synthetic vs vein grafts ($P=0.03$), popliteal vs distal (tibial/pedal) insertion of the anastomosis ($P=0.008$), and intact native arterial outflow ($P=0.003$). Twenty-three cases required major limb amputation in the follow-up period, but 17 (74%) of these had reocclusion within 30 days of thrombolysis. Only 43 grafts (47%) were found to be patent at 1-year follow-up.

Conclusions: In carefully selected cases, thrombolytic therapy is an effective means to restore limb viability in patients with occluded infrainguinal grafts. Long-term patency rates, although similar to those of surgical series, remain poor.

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Thrombosis of infrainguinal bypass grafts remains a troublesome problem for the vascular surgeon and interventional radiologist. Aside from placement of a new graft, the 2 current therapeutic options are traditional surgical thrombectomy and transcatheter delivery of thrombolytic therapy with or without an adjunctive surgical or percutaneous intervention.

Unfortunately, the clinical data of patients who are treated with thrombolytic therapy can be confusing because many studies combine suprainguinal and infringuinal grafts or native arteries and bypass grafts, lack long-term follow-up, or have a relatively small sample size. With this series, we analyze our experience and the long-term results of thrombolytic therapy of infrainguinal grafts, evaluate potential predictors of outcome, and offer some prognostications as to what the physician and patient can expect.

METHODS

From January 28, 1992, through June 27, 1995, 91 thrombosed infrainguinal bypass grafts were treated with local thrombolytic therapy delivered by means of a percutaneous transcatheter approach. Sixty-nine subjects were included in the study; of these, 16 patients presented with reocclusion of the same graft and were treated 2 ($n=10$) or 3 times ($n=6$) after the initial hospital discharge. These additional events of thrombosis in the same graft were analyzed separately on their own merit. Demographics of our patient population are listed in the Table. Thrombolytic therapy was...
not instituted in patients presenting with advanced or irreversible acute limb ischemia manifesting as neuromuscular compromise (ie, category III ischemia according to the classification of Rutherford et al) or in patients who had a clinical contraindication to thrombolysis. We collected the data in a retrospective fashion, through a combination of inpatient and outpatient medical chart review, examination of the pertinent arteriograms, and direct contact with the patient. Approval by the institutional review board was obtained. Information retrieved included age, composition (polytet[PTFE] vs autologous vein) and location of the graft, duration of thrombosis (determined by development of acute symptoms), and medical comorbidities. We also recorded the initial technical success and complication rate, presence and location of any underlying graft pathologic characteristics, integrity of native arterial runoff from the graft, and type (if any) of adjunctive procedures (percutaneous or surgical). Although all patients presenting to the interventional radiology service for thrombolysis of occluded grafts were entered in the database, only those who had successful restoration of antegrade flow through the graft were considered in the follow-up analysis. A positive thrombolytic outcome (PTO) was defined according to the criteria outlined by McNamara et al as a successful lysis of a previously occluded vascular segment, with restoration of flow (augmented by adjunctive percutaneous or surgical means) such that the presenting symptoms and signs of vascular occlusion were relieved for at least 30 days. Variables studied in the follow-up period included relief from symptoms related to vascular disease. This was defined as the absence of claudication, rest pain, and paresthesia, and/or the healing of ulceration and infection. When available, the results of noninvasive monitoring examinations were reviewed. Successful limb salvage was defined as the lack of need for a major amputation (below or above the knee), but not a minor amputation (toes, ray, or transmetatarsal), because only the former was thought to result in serious limitation of patient lifestyle.

Thrombolytic therapy was performed immediately subsequent to diagnostic arteriography in those patients without contraindications. This group included those who were at increased risk for urokinase or heparin-induced hemorrhage and those who had advanced grade III ischemia according to the criteria of the Society for Vascular Surgery and the International Society for Cardiovascular Surgery. After placement of a vascular sheath and negotiation of a guide wire into the occluded graft, a single-injection catheter or coaxial system was used to deliver urokinase directly into the thrombus. In all cases, urokinase was the thrombolytic agent of choice. It was delivered through a multiside-hole infusion catheter(s) that was positioned directly into the occluded graft after initial diagnostic arteriography. Initial lacing of the thrombus was at the discretion of the individual radiologist. Infusion rates varied from 50000 to 240000 U/h. All patients received systemic heparin sodium during the infusion of the thrombolytic agent and were observed in a special surgical observation unit of the hospital until they returned to the angiography suite for follow-up arteriography and other percutaneous intervention (eg, angioplasty) if deemed appropriate.

Clinical follow-up, directed by the vascular surgeon (G.A.S.), consisted of routine scheduled office visits and noninvasive vascular examinations (eg, pulse volume recordings and duplex ultrasonography) to document graft patency or occlusion. Arteriography was not performed unless warranted by a change in the patient's symptoms, and additional therapeutic procedures were considered. Duration of follow-up ranged up to 4.4 years with a mean of 10.4 months.

We examined associations between categorical variables by constructing contingency tables. Statistical significance of the patterns was tested with the \( \chi^2 \) test. We examined duration of patency with Kaplan-Meier product-limit survival analysis. We tested statistical significance of survival differences between groups with the log-rank and Wilcoxon tests. All analyses were performed using JMP software (SAS Institute Inc, Cary, NC).

**RESULTS**

Immediate technical success, ie, the ability to lyse the thrombus and restore graft patency, occurred in 80 (88%) of the 91 grafts. The synthetic grafts composed of PTFE were more likely than autologous vein or composite grafts to respond to thrombolysis (98% [39/40] vs 78% [40/51] or 79%). Of the 80 grafts that underwent successful graft thrombolysis, the graft was abandoned and a new graft placed in 9 (11%) because of extensive intragraft disease (ie, neointimal hyperplasia) or distal native arterial disease thought likely to result in imminent graft occlusion. The graft was abandoned in an additional 11 (14%) with no further attempt at revascularization because of inadequate distal arterial runoff or unavailability of suitable conduit material (autologous vein) with which to construct a new graft.

In 26 cases (29%, including those in which a technical success was not achieved), adjunctive transluminal angioplasty was performed, and in 20 (22%), no other interventions were performed. Angioplasty was used to dilate anastomotic, native arterial, or intragraft stenoses and was technically successful in 23 (88%) of 26 subjects. In this subgroup of patients, mean duration of patency was 10.6 months. An additional 31 subjects (34%) required some surgical procedure, including patch angioplasty, interposition graft, or jump graft to a more distal site in the lower extremity to salvage the recently lyzed graft.
A PTO was achieved in 53 (58%) of the 91 grafts. We found a lesser likelihood of a PTO in patients who were being treated for occlusion of a femoral-distal bypass graft (ie, a distal anastomosis inferior to the popliteal artery) ($P$ = .001) and in those who did not have intact distal runoff ($P$ = .04). Although we found a trend toward more recent graft occlusion relative to presentation resulting in a PTO (4.8 days in the PTO group vs 8.6 days in the non-PTO group), the difference was not statistically significant ($P$ = .22). We also found no difference in the occurrence of a PTO with PTFE grafts compared with autologous vein grafts ($P$ = .13). We analyzed those cases in which a PTO was achieved, and the 1- and 2-year secondary patency rates, without additional intervention, were 52% (21/40) and 24% (12/51), respectively. Patients who had a PTO were also more likely to have long-term improvement in symptoms related to limb ischemia ($P$ = .002).

POSITIVE THROMBOLYTIC OUTCOME

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SECONDARY PATENCY

Secondary patency was defined as documented patency (determined by results of physical examination or non-invasive vascular monitoring) from the time of thrombolysis until the end of the follow-up period. For those cases with a PTO, the mean length of patency was 387.3 days (SD, 42.4 days). Life-table analysis of these cases, which shows a 1-year patency rate of 47% (25 of 53 cases), is displayed in Figure 1. Significant differences were found in subsets of patients. For example, patients with intact peripheral runoff had a mean length of patency of 287.0 days (SD, 2.3 days) compared with 125.4 days (SD, 35.8 days) in those without at least 1 identified artery to the distal extremity ($P$ = .003) (Figure 2). Femoral-popliteal grafts remained patent longer than femoral-distal grafts (mean, 290.5 vs 140.9 days) ($P$ = .008) (Figure 3). Synthetic grafts remained patent longer than vein or composite grafts (mean, 274.0 vs 192.9 days) ($P$ = .03) (Figure 4). Also, those patients who had adjunctive procedures performed at the time of thrombolysis (eg, angioplasty, surgical revision) had a greater duration of patency (mean, 406.7 vs 200.3 [SD, 57.6 vs 41.3 days]) ($P$ = .003) (Figure 5).

MAJOR LIMB AMPUTATION

In the follow-up period, 23 subjects (25% of grafts) required a below-knee or an above-knee amputation for end-stage ischemia of a limb. Initial failure of thrombolytic therapy, as defined by inability to achieve a PTO, was a predictor of early limb loss. Only 6 patients requiring amputation were in the group who had a PTO, compared with 17 who did not. This difference was statistically significant ($P$ < .001). Also, those patients without intact runoff distal to the graft had a significantly higher rate of limb loss ($P$ = .04). Type 1 diabetes mellitus was not a predictor of amputation in our study population.

COMMENT

Infrainguinal graft thrombosis is not an infrequent event. Because surgical bypass of occluded lower extremity arteries is one of the more frequent vascular surgery procedures, and combined surgical series indicate an ap-
proximately 70% 5-year patency rate for autologous vein grafts and a 40% to 50% 5-year patency rate for PTFE grafts, it is inevitable that a significant number of patients will present for some form of secondary reconstruction. Although thrombolytic therapy has been well described, its role remains somewhat controversial, in part because of the wide range of results reported. This may be related to the paucity of pure series in the literature of infrainguinal graft failures treated by means of thrombolysis. Our study reports a large series of infrainguinal grafts in a uniform group of patients and attempts to stratify subjects according to variables that may help predict a favorable outcome.

One factor that influenced a favorable long-term outcome was a relatively proximal anastomosis. Success of thrombolysis of femoral-popliteal grafts resulted in a longer duration of patency than in grafts that inserted distally onto a tibial or pedal vessel ($P = .008$). This is to be expected for several reasons. The first reason relates to the size of the conduit. Most grafts that insert distally were composed of autologous saphenous vein, usually in an in situ position. When neointimal hyperplasia occurs in the body of the autologous graft, as tends to happen, it can result in a greater loss of cross-sectional area in the distal, or narrower, part of the graft that predisposes to restenosis. However, we do not necessarily advocate abandoning these distal grafts when they present with their initial event of thrombosis. Rather, the role of thrombolysis is not to salvage all grafts, but to provide key anatomic information to the surgeon considering graft revision or a jump graft to a more distal site in the extremity. The benefit of thrombolytic therapy in treatment of the acute ischemic event is also helpful in preserving neuromuscular viability by opening thrombosed collateral vessels and restoring flow through the graft. The second reason that more distal grafts tend to do less well is that progressive atherosclerotic disease of the distal, especially pedal, arterial runoff (a common cause of graft failure) limits surgical options. There is often no viable vessel that may be used for a more distal anastomosis to preserve patency of the recently lysed primary graft. This results in a wait-and-see approach on the part of the vascular surgeon who will allow the graft to take its own course, intervening with surgery only when the patient’s symptoms mandate more aggressive surgical management, such as amputation. Only 25% of our study population required a major amputation in the follow-up period, although the 1-year patency rate overall was only 47%. Obviously many patients will maintain viable, functional, and pain-free limbs, although their grafts have reoccluded.

One of the key determinants of achieving long-term clinical success in our patients was the ability to achieve a PTO. Our 58% PTO rate, which includes all patients treated with lytic therapy (whether or not an initial technical success was achieved) is slightly superior to that reported at 30 days in the multicenter trial for evaluating surgery vs thrombolysis for ischemia of the lower extremity, which had a 47% ischemia-free outcome in their patients undergoing bypass graft at 1 month. Potentially magnifying this difference is the uncertainty as to what proportion of patients in that trial had infringuinal grafts. This factor must be taken into consideration, given the greater expected success rate in those with suprainguinal grafts. Significantly, 17 (45%) of the 38 subjects in whom a PTO did not occur required major limb amputation in their follow-up period. Thus, PTO may be a crude predictor of subsequent limb salvage.

In a series of 61 occluded infrainguinal grafts treated with thrombolysis, Berkowitz and Kcep reported that graft age of less than 10 months resulted in a relative increase in reocclusion. We found no discriminating factor related to graft age in our series to predict outcome. A 45% 5-year patency rate for saphenous vein grafts in that series was found in the conduits older than 10 months. This finding compared favorably with a 23% 5-year patency rate for all grafts and a 21% 5-year patency rate for recently placed (<10 months) saphenous vein grafts. Our 23% 2-year patency rate achieved in patients with a PTO is substantially poorer. However, in that series, documentation of graft patency or occlusion was not described, which rendered their data potentially unreliable.

Our results are similar to those reported by Mewissen et al, who reported thrombolytic therapy to be an
We were unable to identify the diabetic subgroup of patients as those who responded less well to thrombolytic therapy. This finding contradicts the results of a study that examined the response to lytic therapy of a population of patients with arterial occlusions.10 Nackman et al7 found that the highest rate of limb salvage after thrombolysis of occluded synthetic grafts occurred in patients with intact distal runoff. By comparison, our patient population fared somewhat better than that of Lacroix et al,9 who reported only a 19% patency rate and 64% limb salvage rate at 6 months after thrombolysis of 50 recently occluded grafts, most of which were infrainguinal.

Despite the poor 1-year graft patency rates after thrombolysis (47%), we point to the mean patency in those patients who had a secondary intervention at 13 months as evidence that thrombolytic therapy, as a part of the strategy in the management of infrainguinal graft occlusions, can result in success, especially if patients are carefully selected. Twenty of the 80 patients in whom the graft was successfully lysed required only a transcatheater angioplasty to maintain graft patency and limb salvage. Thirty-one additional patients required only a relatively minor surgical procedure (patch angioplasty, interposition, or jump graft) rather than placement of an entirely new graft. Thrombolysis was critical in depicting the distal native arterial anatomy and, often, the underlying cause of the graft thrombosis. This is a critical point when contemplating a secondary surgical revascularization. Furthermore, some patients will continue to maintain a viable, functional extremity long after a graft has reocluded. Therefore, graft patency rates should be tempered by the more clinically relevant variables of limb salvage and quality of life. We maintain that thrombolysis will continue to play an important role in the management of infrainguinal graft thrombosis.

CONCLUSIONS

Our review, to our knowledge the largest to date of infrainguinal graft thrombolysis, supports the use of regional thrombolytic therapy as the initial treatment for acute lower extremity ischemia due to infrainguinal graft thrombosis, as we were reliably able to restore patency to the graft and improve clinical symptoms with low complication rates. We found several factors that were predictive of a better outcome, including patency of the runoff vessels, a more proximal graft location, and achievement of a PTO. Finally, despite the encouraging high technical success rate for regional thrombolysis, more than 40% had recurrence of their clinical symptoms within 30 days, and one quarter of patients required a major amputation during the follow-up period. This finding reflects the advanced state of disease in patients requiring treatment of thrombosed lower extremity grafts and the progressive nature of atherosclerotic disease. It also accentuates the need to continue looking for ways to identify which patients will receive long-term benefit from medical procedures that have become technically feasible even in patients with end-stage disease.

However, we believe that in the setting of acute thrombosis of an infrainguinal graft, thrombolysis is effective in reestablishing vascular integrity and provides important information regarding the underlying cause of the thrombotic event. This is particularly important in the patient with a saphenous vein graft, which may be salvaged, avoiding the need to place a new conduit.

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