Comparison of Surgical and Thrombolytic Treatment of Peripheral Arterial Disease

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Acute occlusion of a peripheral artery is a catastrophic event. Whether resulting from in situ thrombosis of a native artery, a bypass graft, or embolization, acute limb ischemia threatens both the patient's limb and life. Traditionally, open surgical intervention has been the "gold standard" for treatment of these patients. However, the multiplicity and complexity of medical comorbidities account for high rates of perioperative morbidity and mortality. Thus, a minimally invasive alternative to open surgery is desirable, provided that the rate of limb salvage remains similar and other untoward events are infrequent. Catheter-directed thrombolytic therapy has been studied in this regard, offering the potential to restore arterial perfusion without the need for open surgery in many cases. In addition, thrombolysis can clear thrombus from small arteries that are inaccessible to a balloon catheter. Lastly, successful thrombolysis may unmask the lesion responsible for the occlusion and allow a directed, sometimes less invasive treatment. Thrombolysis has been criticized, however, on the basis of associated hemorrhagic complications, a slow rate of thrombus dissolution, and a higher risk of rethrombosis. This article explores the available data and, in this manner, provides an analysis of open surgery and thrombolytic therapy as initial interventions in patients with lower limb ischemia.
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Peripheral arterial disease (PAD) comprises those entities that result in obstruction to blood flow in the arteries, exclusive of the coronary and intracranial vessels. Most obstructions are caused by the insidious development of atherosclerotic plaque buildup, and, terminally, by thrombotic occlusion of the remaining lumen. A minority of patients develops peripheral occlusions on the basis of nonatherosclerotic etiologies, most commonly embolism from the heart.

At first, patients with chronic PAD experience symptoms of claudication, with muscular pain that develops with ambulation. In the late stages, however, tissue hypoperfusion progresses to pain that occurs even at rest. Ischemic ulceration and gangrene can develop, and major amputation is eventually required in more than one third of these patients.[1] Alternatively, patients may present with a sudden onset of acute limb ischemia, usually when the occlusion occurs abruptly and without the establishment of preexisting collateral pathways. Mortality is closely linked with the presence of pain at rest or tissue-loss, so-called "critical limb ischemia," with a 1-year mortality rate that approximates 20% in several series.[2,3] Importantly, mortality is greatly increased when patients present with acute limb-threatening symptoms. In-hospital mortality rates have been reported in excess of 20% in this group of surgical patients.[4,5] These rather dismal results have prompted interest in a less invasive strategy for treating the arterial obstruction, namely, pharmacologic thrombolysis.

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Epidemiology

Intermittent claudication has been used as a marker of PAD in epidemiological studies to approximate the prevalence of lower extremity PAD in a particular patient population. The estimate is dependent, however, on demographic factors of the specific population under study, including age, sex, and geographic area. In addition, the methodology used to determine the prevalence of intermittent claudication affects the estimate.[6] For instance, studies based on questionnaires tend to overestimate the prevalence of symptomatic PAD, and patients with complaints that resemble claudication but are unrelated to the vascular system will be erroneously classified as having PAD. Studies that use an objective method of diagnosis, such as measurement of Doppler systolic ankle pressures, are most accurate.

An "ankle-brachial index" can be calculated by dividing the ankle systolic pressure measured with a blood pressure cuff at the malleolar level by the higher of the two brachial pressures. Defining PAD by an ankle-brachial index of < 0.95, one study observed a prevalence of 6.9% in patients aged 45 to 74 years, only 22.0% of whom were symptomatic.[7] The prevalence of intermittent claudication increases dramatically with advancing age, ranging from 0.6% in individuals aged 45 to 54, to 2.5% in those aged 55 to 64, to 8.8% in patients aged 65 to 74.[8] The Rotterdam study, a population-based analysis of 7715 patients, documented a prevalence of intermittent claudication ranging from approximately 1.0% in those between the ages of 55 to 60 years, to 4.6% in those between the ages of 80 to 85.9 Despite this rather low prevalence of intermittent claudication, fully 16.9% of males and 20.5% of females aged 55 and over had PAD as defined by an ankle-brachial index of < 0.90 in either leg. This observation confirms that the vast majority of patients with significant PAD are asymptomatic. Although the diagnosis of asymptomatic PAD is of lesser clinical significance with respect to the lower extremities, it is a strong marker for future cardiovascular events such as myocardial infarction.[10]

Lower-Extremity Peripheral Arterial Disease

The natural history of lower-extremity PAD has been evaluated in a variety of studies, both with regard to the progression of disease in the leg as well as to the long-term morbidity from concurrent generalized atherosclerotic disease. In the Rochester trial, described later, claudication symptoms were surprisingly benign; the risk of limb-loss was low and was greatly overshadowed by the risk of morbid cardiovascular events and death. Although arteriographic progression of atherosclerotic disease was found in one study in 63% of patients after 5 years,[11] Bloor's classic study of 1961 documented a rate of major amputation of only 7% after 5 years and 12% after 10 years of follow-up.[12] More recent data corroborate the finding that limb-loss is a relatively rare eventuality in patients with intermittent claudication, with a 5-year risk of major amputation of only 2%.[13] By contrast, limb-loss is much more frequent once the symptoms of rest-pain or tissue-loss become evident (critical limb ischemia). In a prospective study from Italy, the risk of major amputation after only 3 months was 12.2% in patients with rest-pain or ischemic ulceration.[3] The risk of limb-loss was also found to increase further when patients continued to smoke,[14] as well as in patients with diabetes.[11]

The long-term prospects for patients with lower-extremity PAD must be considered in the context of coexistent generalized atherosclerosis. In an early study from the

Cleveland Clinic, some degree of coronary atherosclerosis was present in 90% of patients undergoing routine coronary angiography prior to elective peripheral vascular surgery, and 28% of the patients had severe, three-vessel coronary disease.[15] Long-term survival in patients with lower extremity PAD is greatly diminished as a result of atherosclerotic complications in the coronary and cerebrovascular beds. In the classic study of Criqui, even asymptomatic patients with peripheral atherosclerosis had a risk of mortality that exceeded that of the nondiseased population,[10] a finding substantiated by other studies.[16] The mortality risk was incrementally higher in patients with symptomatic PAD and was further increased in patients with severely symptomatic disease.[10] The cause of death in patients with PAD, however, is rarely a direct result of the lower-extremity arterial disease itself. Approximately 55% of patients die from complications related to coronary artery disease, 10% succumb to complications of cerebrovascular disease, and 25% die of nonvascular causes.[13] Less than 10% succumb to vascular events, most commonly a ruptured aortic aneurysm.[13]

Diagnosis

The diagnosis of peripheral arterial occlusive disease begins with taking an accurate history. Intermittent claudication must be differentiated from lower-extremity pain resulting from nonvascular etiologies. True claudication begins after a reproducible length of ambulation and resolves within a few minutes after the patient stops walking, even if he or she remains standing. By contrast, pain from impingement on the nervous structures as a result of spinal stenosis does not resolve after ambulation ceases, and, in fact, may be worsened by prolonged sitting or standing. The location of the pain is the key to the site of arterial occlusion: claudication in the calf is typically a result of disease in the superficial femoral artery, whereas claudication in the hip, thigh, and buttock occurs with the narrowing of the aorta and iliac arteries.

The most efficient means of objectively documenting the presence and severity of lower-extremity PAD is the measurement of the Doppler ankle-brachial index. Normally, the ankle-brachial index is > 1.0. The index is decreased to 0.50 to 0.90 in patients with claudication and to lower levels in patients with pain at rest or tissue-loss.[17] The ankle-brachial index may be normal in some patients with mild arterial narrowing; treadmill exercise has been used in these cases to increase the sensitivity of the test. Patients with diabetes mellitus or renal failure may have calcific lower-leg arteries, rendering them incompressible and causing a falsely elevated ankle-brachial index. In these cases, a toe-brachial pressure index can be measured and is more predictive of significant arterial disease.[18]

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Contrast arteriography remains the "gold standard" with which all other tests must be compared. Even today, standard arteriography is the most accurate test for all but the occasional patient with such a slow flow in the tibial or foot vessels that digital subtraction imaging fails to demonstrate a patent artery. Arteriography is, however, a semi-invasive modality, and, as such, its use should be confined to those patients for whom a surgical or percutaneous intervention is contemplated. Patients with borderline renal function may experience contrast-induced nephrotoxicity, and in this subgroup the use of alternate contrast agents such as gadolinium or carbon dioxide have been employed.

Treatment

The management of patients with lower-extremity PAD is two-pronged: first, the risk factors important in the progression of generalized atherosclerosis are addressed, followed by interventions such as pharmacotherapy and endovascular therapy or surgery to relieve the lower-extremity symptoms. Treatment of the patient's lower-extremity symptoms should be chosen on the basis of the severity of the symptoms. Invasive intervention for asymptomatic disease is never appropriate, but the presence of even asymptomatic disease should serve as a marker of generalized atherosclerosis, and therapy should be directed at the primary prevention of systemic complications such as MI and stroke. Similarly, patients with mild or moderate claudication symptoms are best treated with conservative measures such as the institution of an exercise program. Pharmacotherapy for intermittent claudication can be added as adjunctive treatment to improve walking, although no agent has provided sufficient efficacy to gain widespread acceptance. Although statistically significant differences in such endpoints as the walking distance on a treadmill can be

demonstrated in clinical trials, the lack of a robust clinical impact that measures the benefit of these agents has limited their widespread use. Moreover, the use of pharmacotherapy for claudication varies from country to country, with a high rate of use in France and a relatively low rate in the United States.

Thrombolytic Therapy

Aggressive pharmacotherapy attains great importance in patients with acute limb ischemia resulting from in situ native artery thrombosis or thrombosis of a bypass graft. Early heparin anticoagulation may limit the propagation of thrombus and prevent clinical deterioration, although there is little objective data on which to base this practice.[4] Retrospective studies suggest that heparin decreases the risk of recurrent embolization in patients with embolic occlusions, and most surgeons continue heparin therapy through the perioperative period, until the patient can be adequately anticoagulated with oral agents.[19,20] Thrombolytic agents are of value in patients with acute limb ischemia, and some studies have suggested that their use reduces the high rate of morbidity and mortality associated with immediate surgical intervention.[21,22] Although thrombolytic therapy does not uniformly obviate the need for an endovascular or open surgical procedure to correct the underlying causative lesion, the use of these agents as initial therapy allows one to defer the more invasive modalities to an elective setting, when the patient can be better prepared for a major intervention.[23]

Surgical Intervention

Surgical revascularization is unquestioned as appropriate therapy for patients with chronic critical limb ischemia, directed at the prevention of limb-loss and its accompanying disability. By contrast, surgical intervention is rarely indicated in patients with intermittent claudication alone, because the risk of major amputation is exceedingly low. Only in the occasional patient whose symptoms interfere with the patient's lifestyle or performance of an occupation will the benefits of surgical revascularization outweigh the risks. There exist two basic choices when surgery is contemplated for chronic lower-extremity disease: endarterectomy and bypass grafting.

Open surgical procedures. Endarterectomy is an acceptable option when truly localized disease is present, for example, the narrowing of the aorta and common iliac arteries alone.[24] Otherwise, patency rates are unsatisfactory, and bypass grafting is more appropriate. The traditional operation for aortoiliac occlusive disease is an aortofemoral bypass, performed with a prosthetic graft because of the large caliber of the vessels. Infrainguinal bypass procedures are best performed with autogenous vein grafts, although the results of prosthetic bypasses are acceptable if the graft does not cross the knee joint.[25] The results of bypass procedures are correlated with the level of the disease; aortofemoral reconstructions are associated with higher patency rates than those for infrainguinal procedures. Nevertheless, with a nondiseased saphenous vein of adequate caliber, the long-term patency rate of a bypass to even the infrapopliteal (crural) vessels is quite satisfactory, approximating 70% to 80% at 5 years, irrespective of whether the vein is reversed or left in situ with the valves disrupted.[26,27] Considering the quite dismal results of percutaneous angioplasty and stenting for disease in the crural arteries, autogenous vein bypass to the distal vessels should be considered as first-line therapy in patients with limb-threatening ischemia and distal disease.[27]

Percutaneous catheter interventions. Percutaneous catheter interventions to treat occlusive lesions of the lower extremities, first described by Dotter and Judkins in 1964,[28] are attractive alternatives to open surgical procedures such as endarterectomy and bypass. Procedural indications have been liberalized compared to those for surgical procedures, based on the argument that the minimally invasive nature of percutaneous modalities warrants broadened application. Nevertheless, although devices and results have improved over time, the long-term patency of percutaneous interventions remains inferior to open surgical techniques. Moreover, the use of primary stenting compared to stenting only after inadequate balloon dilation has never been proved to be advantageous.[29,30]

Proponents of endovascular therapy cite two contentions to justify continued use of these modalities: first, the decrement in durability is offset by the less invasive nature of endovascular interventions and the resultant decreased morbidity; and second, a patient infrequently experiences clinical or angiographic worsening upon failure of an endovascular intervention, and the interventions can be repeatedly

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Table 1
In-Hospital or 30-Day Rates of Amputation and Death in Selected Series of Patients with Acute Peripheral Arterial Occlusion Treated with Open Surgical Intervention

Study	Year	Amputation Rate	Mortality Rate
Blaisdell et al[4]	1978	25%	30%
Jivegård et al[5]	1988	NA	20%
Rochester[34]	1994	14%	18%
STILE[40]	1994	5%	6%
TOPAS[35]	1998	2%	5%

NA, Amputation rate not part of the data from this trial.
STILE, Surgery or Thrombolysis for the Ischemic Lower Extremity; TOPAS, Thrombolysis or Peripheral Arterial Surgery.

performed after they fail. In a meta-analysis of 2116 patients who underwent aortoiliac percutaneous transluminal angioplasty (PTA) and stent placement, the 30-day mortality rate was less than 1%,[29] and the patency of PTA and stenting for aortoiliac stenoses averaged 86% at 3 years, falling to 62% when aortoiliac occlusions were treated.[30] The results of infrainguinal PTA and stenting were not as good, with 3-year patency rates below 60%.[30] Thus, the available data would suggest that long-term durability is greater with surgical revascularization than with endovascular therapy, but periprocedural complications are lower when percutaneous modalities are employed.

The risk-benefit ratio associated with endovascular versus open surgical revascularization can be ascertained only through the performance of well-designed comparative clinical trials. In patients with anatomically appropriate lesions, however, most practitioners preferentially employ endovascular interventions, a practice based on the presumption of lower risks to the patient. Treatment of patients presenting with acute limb ischemia was formerly relegated to open surgical revascularization. Such an approach was associated with a high rate of complications, including major amputation and death.[4,5] Today, many centers employ intra-arterial thrombolytic therapy as the initial intervention, infusing thrombolytic agents directly into the occluding thrombus. Agents such as urokinase,[31] alteplase,[32] and reteplase[33] provide a less invasive means of restoring adequate arterial perfusion, addressing the unmasked culprit lesion responsible for the occlusion. An endovascular or open surgical procedure is performed on an elective basis after adequate patient preparation.

The Risk of Morbidity and Mortality in Acute Limb Ischemia

The acute occlusion of a peripheral artery is a catastrophic event. Whether resulting from in situ thrombosis of a native artery, a bypass graft, or embolization, a series of studies have shown that acute limb ischemia threatens both the patient's limb and life (Table 1). A now classic study by Blaisdell and associates, published over 20 years ago, documented an amputation rate of 25% and a mortality rate of 30%, each following open surgical repair for acute leg ischemia.[4] Despite improvements in operative techniques and postoperative patient care, more recent series continue to verify unacceptably high rates of morbidity. Jivegård and colleagues, in 1988, reported a 20% mortality rate in these patients treated operatively.[5] Even the later prospective studies of selected patients with recent peripheral arterial occlusions observed rates of limb loss and death that exceeded desired targets.[22,34-36]

Thus, the risk of morbidity and mortality following open surgical intervention remains at an unacceptably high level. What factors explain this finding? Clearly, the baseline medical status of the patients that present with acute peripheral arterial occlusion underlies the observation. Patients are frequently elderly, with a high rate of cardiac and other comorbidities. They are ill-equipped to tolerate the insult of ischemia of an extremity, let alone an invasive surgical intervention to relieve the obstruction. A multivariable analysis of the data from the Rochester series uncovered several variables that were predictive of poor outcome, irrespective of the type of treatment instituted.[37] A summary of available literature would appear to confirm that individuals who present with acute, limb-threatening ischemia comprise one of the sickest subgroup of patients that the peripheral vascular practitioner is asked to treat.[38]

There is some evidence to confirm the impression that a less invasive intervention is better tolerated in this very ill group of patients who develop acute limb ischemia. Poor technique, inadequate devices, and inferior agents colored the initial experiences with catheter-directed thrombolytic therapy. For instance,

the now well-accepted principle of ensuring infusion of the thrombolytic agent directly into the substance of the occluding thrombus was not always ardently adhered to. Formerly, end-hole catheters were employed, and it was not until the late 1980s that multisided-hole catheters were available. Lastly, streptokinase was the most frequently used agent until the landmark article of McNamara in 1985 documented improved results with locally administered high-dose urokinase.[31]

These data suggest that thrombolysis may be of greatest benefit in patients with acute bypass graft occlusions of fewer than 14 days.

Comparison of Thrombolytic Therapy and Primary Operation

Three well-controlled, randomized comparisons of thrombolytic therapy versus primary operation in patients with recent peripheral arterial occlusion have been undertaken. From the start, one must realize that thrombolytic therapy alone is seldom sufficient therapy. Successful pharmacologic dissolution of thrombus must be followed by definitive therapy to address the underlying lesion that caused the occlusion. In fact, Sullivan and colleagues reported that when no such lesion can be found, the risk of early rethrombosis is unacceptably high.[39] These authors observed postthrombolytic, 2-year patency rates of 79.0% in bypass grafts with flow-limiting lesions identified and corrected by angioplasty or surgery versus only 9.8% in those without such lesions.

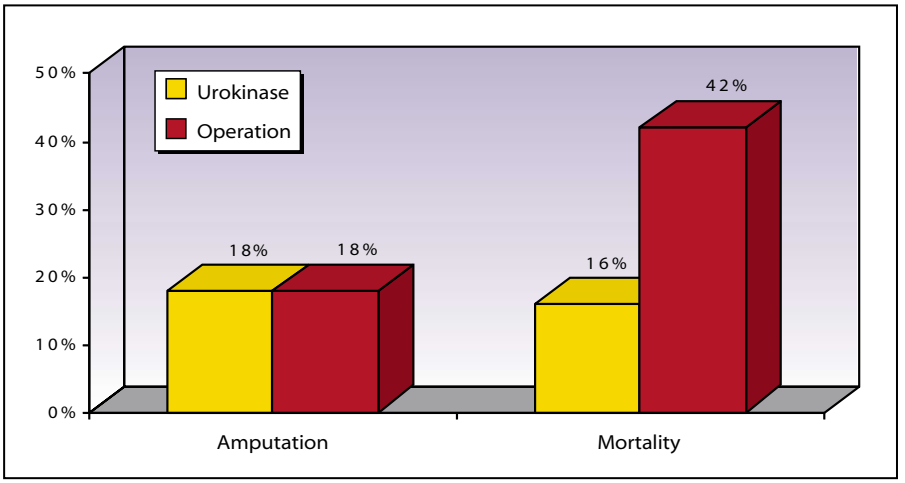
The Rochester Trial

The first study, the Rochester series,[34] compared urokinase to primary operation in 114 patients presenting with what has subsequently been called "hyperacute ischemia." All enrolled patients in this trial had severely threatened limbs (Rutherford Class IIb) with a mean duration of symptoms of approximately 2 days. This single-center trial was funded by the National Institutes of Health Thrombolysis and Thrombosis Program Project grant at the University of Rochester. After 12 months of follow-up, 84% of the patients randomized to urokinase were alive, compared to only 58% of the patients randomized to primary operation (Figure 1). By contrast, the rate of limb salvage was identical in the two groups at approximately 80%. A closer inspection of the raw data revealed that the defining variable for mortality differences was the development of cardiopulmonary complications during the periprocedural period. The long-term mortality rate was high when these periprocedural complications occurred but was relatively low when they did not occur. The occurrence of such complications more commonly in patients taken directly to the operating theatre explained the greater long-term mortality rate in the operative group.

The STILE Trial

The second prospective, randomized analysis of thrombolysis versus surgery was the Surgery or Thrombolysis for the Ischemic Lower Extremity (STILE) trial.[40] Genentech (South San Francisco CA), the manufacturer of the Activase® brand of recombinant tissue plasminogen activator (rt-PA), funded the study. At its termination, 393 patients were randomized to 1 of 3 treatment groups—rt-PA, urokinase, or primary operation. Subsequently, the two thrombolytic groups were combined for purposes of data analysis when their outcomes were found to be similar. Although the rate of the composite endpoint of untoward events was higher in the thrombolytic patients, the rates of the more relevant and objective endpoints of amputation and death were equivalent between treatment groups (Figure 2).

Figure 1. *At the 12-month follow-up in the Rochester Trial, the rate of amputation was identical in the two study groups, which were treated either by urokinase or by surgery; the mortality rate was, however, significantly lower in patients assigned to the thrombolytic arm. Data from Ouriel et al.[34]*



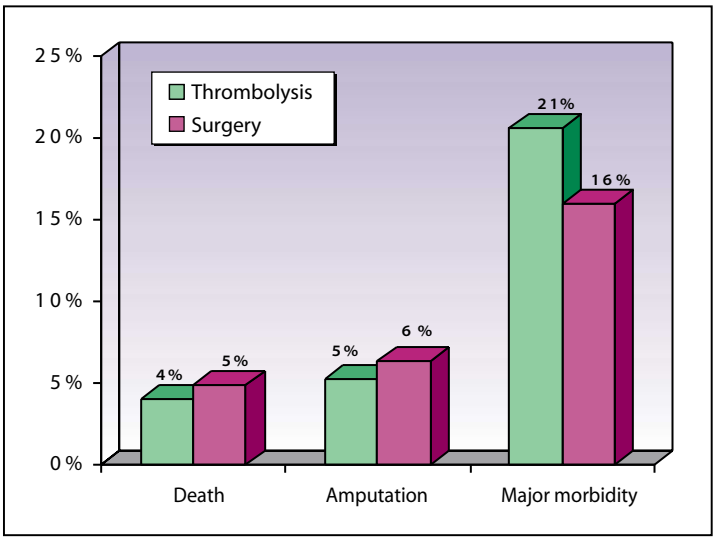


Figure 2. *Outcome measures from the STILE trial after 30 days of follow-up. Note that the rates of death and amputation are similar in the two treatment groups. Data from Anonymous.*[40]

Subgroup analyses of the STILE data appeared in two study reports, one relating to native artery occlusions[41] and one to bypass graft occlusions.[42] The results showed that thrombolysis appeared to be more effective in patients with graft occlusions. In addition, at 1 year, the rate of major amputation was higher in native arterial occlusions treated with thrombolysis (10%) than with surgery (0%; $P = .0024$). By contrast, the rate of amputation was lower in patients with acute graft occlusions treated with thrombolysis ($P = .026$). These data suggest that thrombolysis may be of greatest benefit in patients with acute bypass graft occlusions of fewer than 14 days.

The TOPAS Trial

The third and final randomized comparison of thrombolysis and surgery was the Thrombolysis or Peripheral Arterial Surgery (TOPAS) trial, funded by Abbott Laboratories (Abbott Park, IL). Following completion of a preliminary dose-ranging trial in 213 patients,[43] 544 patients were randomized to a recombinant form of urokinase or primary operative intervention. After a mean follow-up period of 1 year, the rate of amputation-free survival among patients with bypass graft occlusions was identical in the two treatment groups—68.2% and 68.8% in the urokinase and surgical patients, respectively (Table 2).[35] Although this

Table 2
TOPAS Trial† Results by Type of Treatment, Duration, Intervention, and Outcome

Parameter	Native Artery Occlusion (N = 242)			Bypass Graft Occlusion (N = 302)		
	Urokinase (N = 122)	Surgery (N = 120)	*P*-Value	Urokinase (N = 150)	Surgery (N = 152)	*P*-Value Intervention
Patients with complete dissolution of clot* (n/total N/ [%])	67/112 (60)	NA	NA	100/134 (75)	NA	NA
Increase in ankle-brachial index (mean ± SE)	0.44 ± 0.04	0.52 ± 0.04	0.15†	0.48 ± 0.03	0.50 ± 0.03	0.76†
Mortality (%)						
6 months	20.8	15.9	0.33‡	12.1	9.4	0.45‡
1 year	24.6	19.6	0.36‡	16.2	15.0	0.77‡
Amputation-free survival (%)						
6 months	67.6	76.1	0.15‡	75.2	73.9	0.79‡
1 year	61.2	71.4	0.10‡	68.2	68.8	0.91‡

NA, not applicable.
*On final angiogram.
†*P*-value is based on one-way analysis of variance.
‡*P*-value is based on Kaplan-Meier analysis.
Data from Ouriel et al.[35]

Table 3
TOPAS Trial† Results by Type of Treatment, Duration, Intervention, and Outcome

	Urokinase Group (N = 272)		Surgery Group (N = 272)	
	6 Months	1 Year	6 Months	1 Year
Intervention/Outcome	**Interventions (n)**			
Operative Intervention				
Amputation	48	58	41	51
Above the knee	22	25	19	26
Below the knee	26	33	22	25
Open surgical procedures	315	351	551	590
Major	102	116	177	193
Moderate	89	98	136	145
Minor	124	137	238	252
Percutaneous procedures	128	135	55	70
	Patients (%)			
Worst Outcome*				
Death	16.0	20.0	12.3	17.0
Amputation	12.2	15.0	12.9	13.1
Above the knee	5.6	6.5	6.1	7.5
Below the knee	6.6	8.5	6.8	5.6
Open surgical procedures	40.3	39.3	69.0	65.4
Major	23.6	24.3	39.3	39.3
Moderate	10.3	8.7	16.3	13.4
Minor	6.4	6.3	13.4	12.7
Endovascular procedures	16.9	15.4	2.1	1.7
Medical treatment alone	14.6	10.3	3.7	2.8

*Worst outcome represents the single most severe outcome experienced by the patient by the specified time point.
†Data from Ouriel et al.[35]

trial failed to document improvement in survival or limb salvage with thrombolysis, fully 31.5% of the thrombolytic patients were alive without amputation, having had nothing more than a percutaneous procedure after 6 months of follow-up (Table 3).[35] After 1 year, this number had decreased only slightly to 25.7% alive, without amputation and with only a percutaneous intervention. Thus, the original goal of the TOPAS trial—to generate data on which regulatory approval of recombinant urokinase would be based—was not achieved. Nevertheless, the findings confirmed that acute limb ischemia could be managed with catheter-directed thrombolysis, achieving similar amputation and mortality rates as those for surgery, but avoiding the need for open surgical procedures in a significant percentage of patients.

Although this trial failed to document improvement in survival or limb salvage with thrombolysis, fully 31.5% of the thrombolytic patients were alive without amputation, having had nothing more than a percutaneous procedure after 6 months of follow-up.

Summary

In summary, acute peripheral arterial occlusion is associated with an unexpectedly high rate of morbidity and mortality. Co-existing medical problems, most commonly coronary artery disease, compound the peripheral insult. Thrombolysis offers the opportunity to address the acute limb ischemia in a less invasive fashion, identifying the underlying lesion in many cases, with a potential to diminish morbidity and mortality. Thrombolysis should be considered as a treatment option in many patients who present with acute limb ischemia. ■

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Main Points

- Most obstructions in peripheral arterial disease are caused by atherosclerotic plaque buildup, and, terminally, by thrombotic occlusion of the remaining lumen.
- Patients with chronic peripheral arterial disease at first experience symptoms of claudication and pain with ambulation. In late stages, pain is felt even at rest. Ischemic ulceration and gangrene may develop, requiring a major amputation, or patients may present with a sudden onset of acute limb ischemia.
- The rates of amputation and death are higher than expected when patients with acute limb ischemia are treated by primary open surgical means.
- These rates remain high in spite of technical improvements in the conduct of operative procedures and advances in perioperative patient care.
- Mortality may be lower in medically compromised patients with very severe ischemia when treated with the thrombolytic agent urokinase (Rochester Trial).
- Patients with bypass graft thromboses fare better with thrombolysis than do patients who have native arterial occlusions (STILE Trial).
- Thrombolysis offers the opportunity to address acute limb ischemia in a less invasive fashion, identifying the underlying lesion in many cases, with a potential to diminish morbidity and mortality; it should be considered as a treatment option for many patients who present with acute limb ischemia.

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