

Quality Improvement Guidelines for Percutaneous Management of Acute Limb Ischemia

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Abbreviations: ALI = acute limb ischemia, MTD = mechanical thrombectomy device, STILE = Surgery versus Thrombolysis for Ischemia of the Lower Extremity (trial), TPA = tissue plasminogen activator, UK = urokinase

PREAMBLE

THE membership of the Society of Interventional Radiology (SIR) Stan-

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dards of Practice Committee represents experts in a broad spectrum of interventional procedures from the private and academic sectors of medicine. Generally, Standards of Practice Committee members dedicate the vast majority of their professional time to performing interventional procedures; as such, they represent a valid broad expert constituency of the subject matter under consideration for standards production.

Technical documents specifying the exact consensus and literature review methodologies as well as the institutional affiliations and professional credentials of the authors of this document are available upon request from SIR, 10201 Lee Highway, Suite 500, Fairfax, VA 22030.

METHODOLOGY

SIR produces its Standards of Practice documents with use of the following process. Standards documents of relevance and timeliness are conceptualized by the Standards of Practice Committee members. A recognized expert is identified to serve as the principal author for the standard. Additional authors may be assigned depending on the magnitude of the project.

An in-depth literature search is performed with use of electronic medical

literature databases. Then, a critical review of peer-reviewed articles is performed with regards to the study methodology, results, and conclusions. The qualitative weight of these articles is assembled into an evidence table (available online at www.jvir.org [1–37]), which is used to write the document such that it contains evidence-based data with respect to content, rates, and thresholds.

When the evidence of literature is weak, conflicting, or contradictory, consensus for the parameter is reached by a minimum of 12 Standards of Practice Committee members with use of a Modified Delphi Consensus Method (Appendix 2 [38]). For purposes of these documents, consensus is defined as 80% Delphi participant agreement on a value or parameter. In addition, for the specific purpose of this document, studies with fewer than 50 patients were not included for defining the parameters established herein. The nomenclature convention and abbreviations for this document are based on United States Adopted Names/United States Pharmacopeial Council accepted generic terms and are listed in **Table 1** (39).

The draft document is critically reviewed by the Standards of Practice Committee members by telephone conference calling or face-to-face meeting. The finalized draft from the

Table 1
United States Adopted Names/United States Pharmacopeial Council Accepted Generic Terms

Generic Name	Brand Name	Manufacturer	Abbreviation (39)
Alteplase (tissue plasminogen activator)	Activase	Genentech, South San Francisco, CA	tPA
Reteplase	Retavase	Centocor, Malvern, PA	RPA
Human-derived UK	Abbokinase	Abbott Laboratories, Abbott Park, IL	UK
Recombinant UK	Not available	—	r-UK
Prourokinase	Not available	Abbott Laboratories, Abbott Park, IL	Pro-UK
Tenecteplase	TNKase	Genentech, South San Francisco, CA	TNK

Committee is sent to the SIR membership for further input/criticism during a 30-day comment period. These comments are discussed by the Standards of Practice Committee, and appropriate revisions are made to create the finished Standards document. Before its publication, the document is endorsed by the SIR Executive Council.

ACUTE LIMB ISCHEMIA

Acute limb ischemia (ALI) is one sequela of peripheral arterial disease and one of the most common vascular emergencies interventional radiologists and vascular surgeons are asked to evaluate and treat. There are diverse etiologies for ALI, with the two most common etiologies being embolus and thrombosis in situ secondary to underlying disease such as atherosclerosis. Differentiation between the two can sometimes be difficult; the latter is far more common in occluded bypass grafts. ALI is usually caused by atherosclerotic disease but can also arise from other etiologies (eg, dissection, intimal hyperplasia, in situ thrombosis secondary to a hypercoagulable state, trauma, vasculitis, aneurysm thrombosis). Outcomes and prognosis of ALI largely depend on the rapid diagnosis and initiation of appropriate and effective therapy. The 30-day mortality rate is approximately 15% and there is a variable amputation rate of 10%–30% (40). For many years, primary surgical intervention was performed, but entailed significant morbidity and mortality (41–43).

In 1974, Dotter et al (44) reported the feasibility of the use of transcatheter streptokinase infusions for the treatment of arterial and graft occlusions. Since that time, there have been

a number of advances in catheter-directed thrombolytic therapy. Current methods include a variety of fibrin-specific thrombolytic agents and multiple methods for local delivery (eg, pulse-spray, intrathrombus bolus technique) as well as adjunctive use of mechanical thrombectomy devices (MTDs). Successful management of ALI requires optimal patient selection with astute and timely clinical assessment.

Randomized prospective trials have shown that patients with acute leg ischemia (<14 days) have improved survival and long-term benefit compared with those who undergo surgery when thrombolysis is used alone or to reduce the magnitude of surgery (8,17,45). Intraarterial catheter-directed administration of thrombolytic agents can achieve thrombolysis of the thrombosed segments and unmask a causative lesion in most cases. This lesion can then often be treated with endovascular techniques. In many patients, thrombolysis with adjunctive procedures can reduce the scope of or even eliminate the need for surgery. Surgical reperfusion therapy is a very high-risk procedure in elderly patients, with surgical mortality rates as high as 29% in high-risk populations (46).

Constructing a single uniform protocol from the numerous clinical studies is not possible because of the wide variability in reporting. Several independent variables have been identified, including (i) acute versus chronic limb ischemia; (ii) target site treated, ie, native vessel or graft; (iii) dosing regimen of the thrombolytic drug and duration of therapy; (iv) method of infusion, ie, continuous infusion versus bolus infusion or another method; (v) postthrombolytic anticoagulation therapy, eg, heparin or aspirin; and (vi) clinical endpoints, eg, successful

thrombolysis versus clinically useful thrombolysis versus amputation-free survival. For instance, the Rochester study used “event-free survival” (7), the Surgery versus Thrombolysis for Ischemia of the Lower Extremity (STILE) trial used “composite clinical outcome” (8), and the Thrombolysis or Peripheral Arterial Surgery (TOPAS) study used “arterial recanalization and extent of lysis” (17).

Although outcome measures in published studies focus on amputation-free survival, for the purposes of quality assurance, a definition of greater clinical relevance was sought. The outcome measures examined in this document are overall clinical success and major complications.

These guidelines are written to be used in quality improvement programs to assess the outcome of percutaneous management of ALI. The most important processes of care are (i) appropriate patient selection, (ii) performing the procedure, and (iii) monitoring the patient. Outcome measures are assigned threshold levels.

DEFINITIONS

Acute limb ischemia is defined as any sudden decrease in or worsening of limb perfusion causing a threat to extremity mobility and viability that has been present for less than 14 days (47–49).

Thrombolysis (47) is defined for the purposes of this document as the percutaneous treatment of thrombus with pharmacologic therapy, mechanical therapy, or a combination of both.

Guide Wire Traversal Test

In the guide wire traversal test, a guide wire is passed through the length of the thrombus before initia-

Table 2
Recommended Scale for Gauging Changes in Clinical Status in Acute Limb Ischemia after Thrombolysis (48)

Score	Description
-1	Ischemia is worse (by at least one major or minor category from SVS/ISCVS Clinical Categories of Acute Limb Ischemia)
0	No change (failure)
+1	Ischemia improved <ol style="list-style-type: none"> a. Revascularization with thrombolytic methods alone <ol style="list-style-type: none"> 1. amputation necessary but at a lesser level* b. Adjunctive surgical revascularization necessary but at a lesser level† <ol style="list-style-type: none"> 1. amputation necessary but at a lesser level* c. Adjunctive endovascular revascularization necessary (eg, angioplasty, stent, atherectomy) <ol style="list-style-type: none"> 1. amputation necessary but at a lesser level*

Note.—Categories a, b, and c do not imply greater or lesser degrees of success.
 * Levels of amputation: 1, above the knee; 2, below the knee; 3, transmetatarsal; and 4, toe.
 † Levels of surgical revascularization: 1, Major: insertion of new bypass graft, replacement of an existing bypass graft, or excision or repair of an aneurysm. 2, Moderate: graft revision, patch angioplasty, endarterectomy, or profundaplasty. 3, Minor: thrombectomy/embolectomy or fasciotomy.

tion of prolonged infusion. If a wire is passed, thrombolysis for acute occlusion (<7 days old) is thought to be more likely (1,42,50). McNamara and Fischer (1) showed that initial successful thrombolysis was more likely with positive guide wire traversal (100% vs 10%; $P < .01$), and this was also observed (89% vs 16%; $P = .003$) by Shortell and Ouriel (50). Failure to pass a guide wire is not an absolute contraindication to thrombolytic therapy, but rather a predictor of poorer outcome.

Regional Intraarterial Infusion

In nonselective regional intraarterial infusion, the catheter through which the thrombolytic agent is delivered is positioned proximal to the occluded vessel. In selective regional intraarterial infusion, the catheter shaft is positioned in the occluded artery segment, proximal to, distal to, or adjacent to the thrombus, with the catheter tip embedded in the thrombus.

Infusion Methods

Intrathrombus infusion.—In intrathrombus infusion, the thrombolytic agent is delivered by an intraarterial catheter embedded within the thrombus. This position maximizes the concentration of the drug within the

thrombus and delivers the drug to the region of thrombus-bound plasminogen.

Intrathrombus "bolusing" or "lacing."—The term "bolusing" has been used interchangeably with "lacing." These terms refer to the initial intrathrombotic delivery of a concentrated thrombolytic agent with a view toward saturating the thrombus with the plasminogen activator before infusion. During this portion of the procedure, a catheter (with an end hole or multiple side orifices with or without a tip-occluding wire) is positioned in the most distal part of the thrombus. It is retracted proximally as the thrombolytic agent is delivered along the entire length of the thrombus.

Stepwise infusion.—Stepwise infusion entails placing the tip of the catheter within the proximal thrombus and infusing a fixed dose of thrombolytic agent over a short period of time. As thrombus dissolves, the catheter is advanced.

Continuous infusion.—Continuous infusion is infusion of thrombolytic agent with use of a constant rate (ie, steady flow).

Graded infusion.—Graded infusion entails periodic tapering of the infusion rates, with the highest doses given within the first few hours.

Forced periodic infusion.—Forced periodic infusion (ie, pulse-spray) entails forcefully injecting the thrombolytic agent into the thrombus to fragment it and increase the surface area available for thrombolytic action.

Pharmacomechanical thrombolysis.—Pharmacomechanical thrombolysis is the combination of mechanical thrombus disruption with concomitant infiltration of a thrombolytic agent.

Technical success.—Technical success is defined as restoration of antegrade flow with greater than 95% thrombolysis of the thrombus or embolus.

Time to thrombolysis.—Time to thrombolysis (15) is measured from onset of thrombolytic infusion to complete recanalization or maximum radiologic thrombolysis.

Complete thrombolysis.—Complete thrombolysis (15) entails clearance of an occluded vessel by thrombolytic therapy with restoration of flow to the distal runoff and reestablishment of peripheral pulses, or complete angiographic clearance of thrombus from an occluded vessel by thrombolytic therapy as determined by follow-up angiography. The underlying lesion may still be present.

Thrombolysis failure.—Thrombolysis failure (15) is the absence of clinically useful thrombolysis.

Clinically useful thrombolysis.—Clinically useful thrombolysis (48) entails relief of the acute ischemic symptoms or reduction of the level of the subsequent surgical intervention or amputation needed (Table 2).

Overall clinical success.—Overall clinical success (48) entails relief of the acute ischemic symptoms and return of the patient to at least his/her preocclusive clinical baseline level after the removal of thrombus and performance of adjunctive procedures.

Major hemorrhage.—Major hemorrhage is a hemorrhage of sufficient magnitude that it leads to (i) extended or unexpected hospitalization, (ii) surgery to arrest the hemorrhage, or (iii) the need for blood transfusion. Intracranial hemorrhage of any size and hemorrhages that result in death are major by definition.

Although practicing physicians should strive to achieve perfect outcomes (eg, 100% success, no complications), in practice, all physicians will fall short of this ideal to a vari-

Table 3
Clinical Categories of Acute Limb Ischemia (51)

Category	Description	Findings		Doppler Signal	
		Sensory Loss	Muscle Weakness	Arterial	Venous
I. Viable	Not immediately threatened	None	None	Audible	Audible
II. Threatened					
a. marginal	Salvageable if promptly treated	Minimal (toe) or none	None	Often inaudible	Audible
b. immediate	Salvageable with immediate revascularization	More than toes, associated with rest pain	Mild, moderate	Usually inaudible	Audible
III. Irreversible*	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound, paralysis (rigor)	Inaudible	Inaudible

* When presenting early, the differentiation between category IIb and III may be difficult.
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able extent. Therefore, indicator thresholds may be used to assess the efficacy of ongoing quality improvement programs. For the purposes of these guidelines, a threshold is a specific level of an indicator which should prompt a review. "Procedure thresholds" or "overall thresholds" reference a group of indicators for a procedure, such as major complications. Individual complications may also be associated with complication-specific thresholds. When measures such as indications or success rates decrease below a (minimum) threshold, or when complication rates exceed a (maximum) threshold, a review should be performed to determine causes and to implement changes if necessary. For example, if the incidence of intracranial hemorrhage is one measure of the quality of pharmacologic thrombolysis, values in excess of the defined threshold, in this case 2%, should trigger a review of policies and procedures within the department to determine the causes and to implement changes to lower the incidence of the complication. Thresholds may vary from those listed here; for example, patient referral patterns and selection factors may dictate a different threshold value for a particular indicator at a particular institution. Therefore, setting universal thresholds is very difficult and each department is urged to alter the thresholds as needed to higher or lower values to meet its own quality improvement program needs.

Complications can be stratified on the basis of outcome. Major compli-

cations result in an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Minor complications result in no sequelae; they may require nominal therapy (see Appendix 1). The complication rates and thresholds described herein refer to major complications.

INDICATIONS AND PATIENT SELECTION

Patient selection is determined by a number of clinical findings, particularly the acute ischemia category of the limb in question (Table 3) (51). Patients can usually relate their deterioration of symptoms to a particular time period. An appropriate history, physical examination, and evaluation of the patient for absolute and relative contraindications should be recorded. The history should focus on when, where, and what events surrounded the ALI symptoms. The patient should be evaluated for pain, sensory deficit, numbness, paresthesia, decreased motor function, pallor, and decreased temperature. Laboratory tests should be obtained to assess for renal function, baseline hematocrit and coagulation profile, and evidence of hyperkalemia and acidosis. An electrocardiogram may be obtained to ascertain if any cardiac arrhythmias are present and to assess for a recent myocardial infarction. Doppler imaging examination of the limb should be performed when possible. Patients with ALI are considered candidates for thrombolysis when they present with Rutherford category 1 disease and cat-

egory IIa ischemia. Patients with category IIb ischemia may be candidates for thrombolysis. The treating physician must make this determination on a case-by-case basis. Patients with category III ischemia should not be treated percutaneously because catheter-based thrombolytic therapy often takes many hours and threatened ischemic changes may become irreversible over the course of treatment (Table 3). MTDs may reduce the time to restoration of flow, thereby allowing patients with more severe degrees of ischemia to undergo percutaneous thrombolysis. Intravenous heparin at full anticoagulation doses should be initiated as soon as possible and continued until thrombolysis is started. Prompt initiation of anticoagulation reduces or prevents clot propagation and reduces the chances of further embolization. In one study, the time from establishing diagnosis to initiation of therapy was correlated with amputation rates (52). The amputation rates were 6% if thrombolytic therapy was initiated within 12 hours of development of acute symptoms of ischemia, 12% if initiated within 13–24 hours, and 20% if initiated after 24 hours. It is very important to control pain and treat any underlying medical condition such as congestive heart failure and cardiac arrhythmias.

Important questions to consider before undertaking therapy include whether: (i) the patient can tolerate the anticipated time of treatment, (ii) the total clot burden is suitable for thrombolysis in a reasonable length of time, (iii) the clot location is within reach of the thrombolytic catheters/devices,

and (iv) the patient has risks of thrombolysis/anticoagulation that outweigh the benefits of the thrombolytic therapy.

Published studies indicate that patients with acute leg ischemia of less than 14 days duration and those with acute bypass graft occlusions benefit most from thrombolysis; the benefits reported were improved survival and improved long-term patency of the limb when thrombolysis was the initial therapeutic option (8,42,53). Subanalysis of the data showed that lower amputation and mortality rates occurred when patients were randomized to receive thrombolysis versus surgery when symptoms were less than 14 days in duration (8), whereas a higher rate was seen in patients with symptoms for longer than 14 days. Further analysis of the STILE trial (45) indicated that the 1-year amputation-free survival rate was significantly higher in patients with acute limb ischemia randomized to receive thrombolytic therapy compared with surgery (20% vs 48%; $P = .026$; failure of catheter placement in 28% of patients). In a study performed by Ouriel et al (7) in which patients were randomized between surgery and thrombolytic therapy, after 12 months, 84% of the patients randomized to receive thrombolytic therapy were alive whereas only 58% of those randomized to receive surgery were still alive ($P = .01$). Further subgroup analysis of the STILE trial data in two reports suggest that thrombolysis appears to be more effective for graft occlusions than for native artery occlusions (45,53). Based on the results of the TOPAS and STILE trials, a Working Group proposed that thrombolytic therapy should be considered appropriate initial management in patients with acute occlusion of the leg arteries or bypass grafts (47). These recommendations are not absolute, as they are based on subgroup analysis of patient populations within larger trials. Some studies have also indicated that the likelihood of limb salvage after thrombolytic therapy is greater when a greater number of patent vessels are present (5,10,11).

Contraindications for pharmacologic thrombolytic therapy are based on medical conditions thought to increase the risk of local and remote hemorrhage. In 1980, a National Insti-

tutes of Health panel discussed absolute and relative contraindications to systemic intravenous thrombolysis to treat pulmonary and venous thromboemboli (54). The recommendations were arrived at by consensus and were not evidence-based. These contraindications have been subsequently adopted for intraarterial catheter-directed thrombolytic procedures (47) without confirmatory evidence. It may be that risks of remote or systemic hemorrhage are lower with catheter-directed thrombolysis, which uses lower doses of drug compared with systemic doses, albeit over longer periods of time. Therefore, the listed contraindications should be used to weigh the relative risks and benefits of thrombolytic treatment in patients who may have conditions that also increase the risks posed by surgical therapy. Patients with relative contraindications may be appropriate to treat with thrombolysis. When clinically significant bleeding is recognized, continuation of thrombolytic therapy is dependent on the clinical status of the patient and the severity of bleeding. Attempts should be made to identify the site of bleeding and treat the cause appropriately. Contraindications that may exist for catheter-based angiography should also be considered.

Absolute Contraindications

Absolute contraindications include:
Active clinically significant bleeding;
Intracranial hemorrhage;
Presence or development of compartment syndrome.

Relative Contraindications (47)

Relative contraindications include:
Cardiopulmonary resuscitation within past 10 days;
Major nonvascular surgery or trauma within past 10 days;
Uncontrolled hypertension: >180 mm Hg systolic or >110 mm Hg diastolic blood pressure;
Puncture of noncompressible vessel;
Intracranial tumor;
Recent eye surgery;
Neurosurgery (intracranial, spinal) within past 3 months;
Intracranial trauma within 3 months;
Recent gastrointestinal bleeding (<10 days);

Established cerebrovascular event (including transient ischemic attacks within past 2 months);

Recent internal or noncompressible hemorrhage (55–57);

Hepatic failure, particularly in cases with coagulopathy;

Bacterial endocarditis;

Pregnancy and immediate postpartum status;

Diabetic hemorrhagic retinopathy;

Life expectancy < 1 year.

THROMBOLYTIC THERAPY

Agents

Streptokinase and anistreplase are not considered in this document because of their antigenicity and low efficacy in comparison with urokinase (UK), alteplase (tissue plasminogen activator; TPA), and reteplase (mtein of TPA) (58,59), the major thrombolytic agents in use today. Their mechanism of action involves conversion of plasminogen to an active thrombolytic enzyme, plasmin, which breaks down fibrin. Absolute recommendations on drugs and doses are not possible on the basis of available data.

Recombinant UK, despite having a higher molecular weight and a shorter half-life, is thought to have the same clinical efficacy and safety profile as UK. Recombinant pro-UK is a plasminogen activator with greater affinity for fibrin-bound plasminogen. Both these agents are not available commercially at the time this document was constructed.

Alteplase and its analogues have been used for catheter-directed thrombolysis. TPA works by cleaving fibrin-bound plasminogen into plasmin, which then causes enzymatic breakdown of cross-linked fibrin strands. TPA has a greater affinity for fibrin-bound plasminogen than free plasminogen.

Reteplase is a recombinantly derived mtein of TPA consisting of 355 of the 527 amino acids that form TPA that has less affinity for fibrin-bound plasminogen (60). Multiple small retrospective studies exist (61–63) but are insufficient to comment on the efficacy of this agent.

Tenecteplase is a third-generation plasminogen activator approved for acute myocardial infarction with an

enhanced safety profile compared with alteplase. It has a longer half-life, increased clot selectivity, and improved resistance to plasminogen activator inhibitor compared with alteplase (64).

Concomitant use of glycoprotein IIb/IIIa receptor antagonists for accelerated thrombolysis has shown promising results in small series (29,31, 63,65,66) but has yet to be validated in a large study. None of these agents are specifically approved for noncoronary thrombolysis.

Dosage

Urokinase.—The most commonly described protocol is a graded infusion regimen consisting of 240,000 U/h UK for 4 hours, then a lower dosage of 120,000 U/h for a maximum infusion time of 48 hours (14,17,67). The TOPAS phase I study appears to show that the dosage of UK associated with the lowest risk of hemorrhage (2%) that maximized thrombolytic efficacy (71%) was 4,000 IU/min (13). No significant differences between different dosages and surgery in terms of mortality and amputation were found in this study. In a study by Cragg et al (68), a comparison was made between high-dose and low-dose UK infusions for native arterial and graft occlusions. The high-dose regimen was 250,000 U/h for 4 hours, then 125,000 U/h. The low-dose regimen was 50,000 U/h. This small study suggested that both dose regimens were equally effective and there was a higher frequency of minor bleeding complications in the high-dose group.

Tissue plasminogen activator and reteplase.—Weight-adjusted doses of TPA have ranged from 0.02 to 0.1 mg/kg/h (69–71), whereas non-weight-based doses generally range from 0.25 to 1.0 mg/h, even though higher doses have been reported (14,15,25,72,73). In general, the lowest effective dose has not been determined. Braithwaite et al (15) performed a multicenter trial randomizing 100 patients with acute leg ischemia of less than 30 days duration. This study compared high-dose bolus TPA (3–5-mg bolus doses, then 3.5 mg/h for a maximum of 4 hours, then 0.5–1.0 mg/h) versus low-dose TPA (0.5–1.0 mg/h). There were no

statistically significant differences between the two groups in terms of 30-day limb salvage or complication rates. An advisory panel was convened in 1999 to provide guidelines for the use of alteplase. The suggested dosage regimens were (i) a weight adjusted dose of 0.001–0.02 mg/kg/h and (ii) a non-weight-adjusted dose of 0.12–2.0 mg/h. No formal recommendation was made on the use of weight-adjusted versus non-weight-adjusted dosing (57). The recommended maximum dosing was no greater than 40 mg for catheter-directed therapy.

For reteplase, a consensus document published in 2001 (74) suggested that the minimum dose should not be less than 0.25 U/h, with a dose range of 0.25–1.0 U/h. Maximum dose amount and infusion time suggested were 20 U and 24 hours, respectively. In a study examining different doses of reteplase for lower-extremity arterial occlusions, doses of 0.5 U/h, 0.25 U/h, and 0.125 U/h were found to be equally effective, with more bleeding complications with the highest dose (28).

Delivery

Intravenous administration of thrombolytic agents should not be performed for ALI. A randomized parallel group study showed that intravenous administration of TPA led to a higher incidence of hemorrhagic complications with less successful thrombolysis than with intraarterial delivery (75).

Treatment is usually initiated when the occluded segment is successfully traversed with a guide wire (ie, guide wire traversal test), a concept introduced by McNamara and Fischer (1). Attempts to pass a guide wire through the acute thrombus to initiate thrombolysis should be made. If unable to pass a wire, a short period of thrombolysis may be initiated. If a wire cannot be passed after this short period of time, consideration should be given to other methods of revascularization.

Multiple techniques for infusion of thrombolytic agents have been described, including (i) intrathrombus bolus administration followed by continuous low-dose infusion with use of an infusion wire or catheter with multiple side holes for maximum surface

area exposure (76,77); (ii) stepwise and graded infusions; and (iii) pulse-spray pharmacomechanical thrombolysis (78–80). Intrathrombus infusion is the current state of practice, with placement of an infusion wire or multiple-side hole delivery catheter completely along the length of the thrombus, as this is associated with a greater chance of complete thrombolysis (42). The delivery method that provides optimal thrombolysis has not been studied in a large prospective trial.

Bolus TPA administration appears to reduce the duration of treatment and may be of advantage in acutely ischemic limbs but with increased risk of hemorrhage compared with lower-dose continuous infusion. In a study by Braithwaite et al (15), the median duration of infusion was decreased by 80% from 20 hours to 4 hours, with almost 50% of the patients demonstrating complete or clinically useful thrombolysis by 4 hours. When bolus technique was compared with continuous infusion in a study by Ward et al (81), a 46% decrease in infusion time was observed, but with a greater incidence of major hemorrhage. Another prospective randomized study comparing high-dose bolus TPA plus infusion versus infusion without a bolus dose supports this approach (82).

Although intraoperative thrombolysis may have a role at the time of operative revascularization to dissolve clot in the distal vasculature, sufficient data are not available to render an opinion regarding efficacy and outcome. In a single study with 53 patients (83), limb salvage with the intraoperative technique was obtained in 70% of cases.

Heparin Use during Thrombolytic Infusions

The published literature shows varying doses from none to therapeutic anticoagulation with no dose identified that predicts adverse bleeding. Heparin should be used carefully during thrombolytic infusions because of the risk of bleeding. Generally, subtherapeutic doses of heparin are acceptable when used in conjunction with thrombolytic therapy, although therapeutic doses are recommended with UK infusion treatment. In the study by McNamara and Fischer (1), pericatheter thrombosis occurred in

two of seven infusions when heparin was not administered concurrently. In a study by Ouriel et al (17), therapeutic doses of heparin initially administered intravenously were associated with an intracranial hemorrhage rate of 4.8%. The protocol in this study was subsequently revised; the heparin dose was reduced to subtherapeutic doses and given through the arterial sheath instead of intravenously to prevent pericatheter thrombosis.

With fibrinogenolysis, the products of fibrinogen degradation increase the patient's sensitivity to heparin, possibly making them more prone to bleeding. Careful monitoring of partial thromboplastin time is recommended. Postthrombolysis anticoagulation is recommended until the underlying lesion, if any, is corrected.

Laboratory Monitoring

No clinical trials have been completed to support laboratory monitoring that may predict adverse bleeding during thrombolytic therapy. Although monitoring of serum fibrinogen levels is thought by some to predict adverse bleeding, no pivotal study has validated this belief. In the Prourokinase versus Urokinase for Recanalization of Peripheral Occlusions, Safety and Efficacy (PURPOSE) trial by Ouriel et al (20), 13 of 16 patients (81.3%) with a serum fibrinogen less than 100 mg/dL had a major or minor bleeding complication compared with 105 of 179 patients (58.7%) with serum fibrinogen levels greater than 100 mg/dL ($P = .108$). In the STILE trial (8), it was demonstrated that those with bleeding complications had a significantly lower plasma fibrinogen level at the end of infusion ($P = .01$). Another study (66) demonstrated that major complications were associated with a mean 72% decrease in fibrinogen, whereas minor complications were associated with a mean 46% decrease in fibrinogen. Routine monitoring of hemoglobin may allow for detection of significant occult bleeding before it becomes clinically apparent.

Adjunctive Techniques

It should be emphasized that thrombolytic therapy is almost always one component of a multidisciplinary, multimodality strategy aimed at estab-

lishing arterial patency. When flow in the vessel has been restored, repeat angiography should be performed to define the vascular anatomy and areas of disease that may require additional treatment. In most cases, a causative lesion will be identified, and this should be managed with the appropriate endovascular technique or conventional surgical procedure. Failure to detect and rectify an underlying lesion is associated with poor long-term patency.

The speed and long-term efficacy of intraarterial thrombolysis can be enhanced with use of adjunctive techniques. These techniques will help achieve two clinically important endpoints:

1. They may be used in conjunction with thrombolysis to remove insoluble material or debulk the thrombus to accelerate the restoration of flow.
2. They may be used to correct underlying lesions at the time of thrombolysis or in the periprocedural period.

Among the procedures that may be used in conjunction with or independent of pharmacologic thrombolysis are catheter suction thromboembolectomy and mechanical thromboembolectomy. The latter uses a variety of systems, including saline solution jet spray with an associated Venturi effect and an additional external suction or a high-speed rotating impeller. Simple catheter aspiration is well established in many centers as an important adjunct to thrombolysis. In patients in whom it is important to accelerate thrombolysis or remove residual clot, aspiration thrombectomy or the use of MTDs are alternatives.

Percutaneous Mechanical Thrombectomy Devices

Percutaneous MTDs mainly serve a role in patients with contraindications to thrombolytic therapy and can be used as an adjunctive procedure for incomplete thrombolysis/embolization. They are also used to debulk the thrombus mass before local lysis to shorten the lytic treatment period. As many as 20% of patients can have a contraindication to thrombolytic therapy (8). Rotational (eg, Helix; Microvena, White Bear Lake, MN) and hydraulic (eg, Hydrolyzer; Cordis, Miami,

FL, and AngioJet; Possis Medical, Minneapolis, MN) recirculation devices are available. Experience with some of these devices is limited and confined to small series (84–87). Many of these catheter devices allow concurrent pulse-spray administration of a thrombolytic agent. This technology has the potential to minimize the two main drawbacks of endovascular ALI therapy, the long duration of thrombolytic infusion that is needed to establish full arterial perfusion and hemorrhagic complications.

Although most of the aforementioned devices are approved by the Food and Drug Administration for use in occluded hemodialysis access grafts, only the AngioJet is approved for peripheral arterial applications. Limited population sizes in multiple retrospective studies with different definitions of success and outcomes limits critical interpretation of outcomes. The Oasis (Boston Scientific, Watertown, MA) and AngioJet devices examined in this document fragment and remove clot. Hemolysis and fluid overload are possible with these devices. Comparative randomized studies are needed to determine if MTDs are faster and safer and how effective they are compared with pharmacologic thrombolysis. Basic principles for use of these devices are to minimize endothelial damage and downstream embolization.

With the AngioJet, the manufacturer recommends that the pump be run less than 10 minutes in a flowing blood field to prevent excessive hemolysis. MTD complications include hemolysis and possible renal failure secondary to release of free hemoglobin. Use of MTDs may reduce thrombus burden, thereby reducing length of time and total dose of thrombolytic therapy and consequently possibly decreasing hemorrhagic complications and improving outcome. A recommendation based on current literature for the use of MTDs as a stand-alone method for thrombolysis cannot be made.

Percutaneous Aspiration Thrombectomy

The percutaneous aspiration thrombectomy technique uses a large-bore catheter connected to a syringe to aspirate clot from vessels. This tech-

Table 4
Published Complication Rates and Suggested Thresholds of Major and Minor Complications

Specific Major Complications for Thrombolysis of ALI	Reported Rate (%)	Suggested Threshold (%)
Pharmacologic		
Intracranial hemorrhage	0–2.5	2
Major bleeding requiring transfusion and/or surgery	1–20	10
Compartment syndrome	1–10	4*
Distal embolization not corrected with thrombolysis	1–5	5
Mechanical		
Distal embolization (mechanical thrombectomy/aspiration)	1.8	2

* Determined based on the weight of the majority of studies presented in the evidence table, excluding a single study in which the observed complication rate was 9.8%.

nique, first described by Sniderman et al (88), can be used alone or in conjunction with thrombolytic therapy. In a retrospective study of 102 patients with acute arterial embolic occlusions, primary angiographic success, defined as reperfusion in a previously completely occluded vascular segment, was obtained in 87.3% of cases (although thrombolytic agents may have been used in as many as 60% of the cases) (89). In another study with patients who had only acute embolic occlusions, percutaneous aspiration thrombectomy was successful in 77 of 90 limbs (86%); however, UK limited to 200,000 U was required in 74 cases (90). In another study, percutaneous aspiration thrombectomy alone was successful in 31% of cases of acute and subacute arterial occlusion (91). Analysis of cases that were successful showed that all were the result of embolic occlusion. Percutaneous aspiration thrombectomy is typically used as an adjunct to thrombolysis in acute arterial occlusion or can be used as salvage therapy to remove distal emboli.

The indication for percutaneous management of acute limb ischemia is presentation with acute symptoms with Rutherford category 1/2 ischemia determined by physical and Doppler examination (threshold, 99%).

SUCCESS RATES

Technical Success

Technical success is defined as restoration of antegrade flow with com-

plete or at least 95% thrombolysis of the thrombus or embolus (threshold, 70%).

Overall Clinical Success

Overall clinical success is defined as relief of the acute ischemic symptoms and return of the patient to at least his/her preocclusive clinical baseline level after the removal of thrombus and performance of adjunctive procedures (threshold, 75%).

COMPLICATIONS

Published rates for individual types of complications are highly dependent on patient selection and are based on series comprising several hundred patients, which is a volume larger than most individual practitioners are likely to treat. Generally, the complication-specific thresholds should be set higher than the complication-specific reported rates listed herein. It is also recognized that a single complication can cause a rate to cross above a complication-specific threshold when the complication occurs within a small patient volume (eg, early in a quality improvement program). In this situation, the overall procedure threshold is more appropriate for use in a quality improvement program. In **Table 4**, all values were supported by the weight of literature evidence and panel consensus.

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APPENDIX 1: SIR STANDARDS OF PRACTICE COMMITTEE CLASSIFICATION OF COMPLICATIONS BY OUTCOME

Minor Complications

- A. No therapy, no consequence, or
- B. Nominal therapy, no consequence; includes overnight admission for observation only.

Major Complications

- C. Require therapy, minor hospitalization (<48 h),
- D. Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h),
- E. Have permanent adverse sequelae, or
- F. Result in death.

APPENDIX 2: METHODOLOGY

Reported complication-specific rates in some cases reflect the aggregate of major and minor complications. Thresholds are derived from critical evaluation of the literature, evaluation of empirical data from Standards of Practice Committee member practices, and, when available, the SIR HI-IQ system national database.

Consensus on statements in this

document was obtained with use of a modified Delphi technique (1).

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The clinical practice guidelines of the Society of Interventional Radiology attempt to define practice principles that generally should assist in producing high-quality medical care. These guidelines are voluntary and are not rules. A physician may deviate from these guidelines as necessitated by the individual patient and available resources. These practice guidelines should not be deemed inclusive of all proper methods of care or exclusive of other methods of care that are reasonably directed toward the same result. Other sources of information may be used in conjunction with these principles to produce a process leading to high-quality medical care. The ultimate judgment regarding the conduct of any specific procedure or course of management must be made by the physician, who should consider all circumstances relevant to the individual clinical situation. Adherence to the SIR Quality Improvement Program will not assure a successful outcome in every situation. It is prudent to document the rationale for any deviation from the suggested practice guidelines in the department policies and procedure manual or in the patient's medical record.