Acute Limb Ischemia

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Abstract: Acute limb ischemia is a medical emergency with management options ranging from urgent revascularization to limb amputation. The best patient outcome requires tailoring the treatment to the individual patient. This article describes a step-by-step approach for diagnosis and management of patients presenting with acute limb ischemia.

Key Indexing Terms: Peripheral vascular disease; Ischemia; Embolism; Thrombosis; Thrombolysis. **[Am J Med Sci 2011;342(3):226–234.]**

Acute limb ischemia (ALI) is defined as the recent onset (<14 days) of decreased limb perfusion that endangers life and/or limb.[1] This is a medical emergency with management options ranging from urgent revascularization to limb amputation. The best patient outcome requires tailoring the treatment to the individual patient. The aim of this article is to guide physicians in the management of patients presenting with ALI.

ETIOLOGY

ALI is usually caused by arterial thrombosis in patients with underlying peripheral atherosclerosis, thrombosis of a lower extremity bypass graft or lower extremity embolism originating from the heart or a proximal arterial aneurysm. Other etiologies for ALI are embolism of air, fat, amniotic fluid or tumor and trauma. In patients without underlying atherosclerosis, extrinsic arterial compression, arterial dissection or an underlying hypercoagulable state can precipitate arterial thrombosis and result in ALI.

PATHOPHYSIOLOGY

With the onset of ALI, there is conversion of aerobic muscle metabolism to anaerobic metabolism with increased production of lactate.[2] Ischemic injury results in the loss of endothelial integrity, interstitial edema and a tense necrotic limb.[2] Systemically, there is release of inflammatory mediators (such as interleukins-1, 6, 8, tumor necrosis factor-α and monocyte chemotactic protein-1) and activation of the complement cascade. Multiorgan dysfunction may ensue, manifested by acute lung injury, acute renal failure and myocardial dysfunction.[3] Unchecked, these events become life threatening.

DIAGNOSIS

The clinical presentation of ALI depends on the location and duration of the arterial occlusion, the degree of collateral circulation, the extent of preexisting arterial disease (presence of collaterals) and the metabolic consequences of tissue ischemia.[4] Clinical classifications of stages of ALI as updated in 1997 are shown in Table 1.[5]

Patients with an embolic etiology of ALI typically present with sudden onset of symptoms.[6] In contrast, patients with ALI due to arterial thrombosis frequently have underlying peripheral arterial atherosclerosis and can have a more gradual or stuttering presentation. They often have developed a collateral circulation, which provides an alternate source of perfusion and reduces the severity of clinical ischemia.[6]

In patients with ALI and native arterial occlusion, signs of ischemia are most pronounced one joint distal to the level of occlusion. For example, if there is occlusion at the distal popliteal artery or tibial trifurcation (at the level of the knee joint), signs of ischemia will be seen at or below the ankle joint.[2,6] The presence of skin mottling, which does not blanch with pressure, the new onset of limb paresthesias and muscle weakness are signs of end-stage limb ischemia. A normal vascular examination in the contralateral limb suggests an embolic etiology for ALI. Physical findings suggesting underlying preexisting peripheral atherosclerosis are diminished extremity pulses, scant hair growth, atrophic skin, hypertrophied nails and ischemic ulcers. An arterial and venous Doppler ultrasound obtained at bedside is helpful in classifying severity of ischemia as outlined in Table 1.[5]

MANAGEMENT STRATEGY

For patients presenting with ALI and a viable or a marginally threatened limb (Rutherford class I and IIa), endovascular revascularization is the appropriate initial strategy with reported rates of 30-day limb salvage between 84% and 95%.[7] For patients presenting with a severely threatened limb (Rutherford class IIb), revascularization is required within 3 to 6 hours for limb salvage.[3] Clinical trials of endovascular revascularization in patients with ALI have included a broad range (28%–57%) of patient acuity and complexity presenting with a severely threatened limb.[8,9] Although clinical outcomes have not been analyzed separately, it would be prudent to consult a vascular surgeon to develop a collaborative approach to manage patients presenting with a severely threatened limb (Rutherford class IIb).

In patients presenting with irreversible ALI, revascularization is not appropriate. Because of extensive underlying muscle necrosis, the limb is not viable and revascularization may precipitate a reperfusion syndrome.[10] The reperfusion syndrome is characterized by the systemic release of inflammatory mediators, which may lead to multiorgan damage and death. Therefore, primary amputation is appropriate, and revascularization is contraindicated in patients presenting with "irreversible"/Rutherford class III ALI.[1] There is a role for endovascular revascularization to lower the level of amputation and to improve healing of the limb after amputation. A flowchart outlining the steps in management of a patient with ALI is shown in Figure 1.

Aspirin at a dose of 325 mg should be administered as soon as possible, unless contraindicated.[11] The patient should be immediately anticoagulated with therapeutic levels (goal partial thromboplastin time of 2.0–2.5 times normal) of intravenous unfractionated heparin to prevent further clot propagation. Others have suggested that if a diagnostic angiogram can be obtained immediately on presentation, delaying administration of unfrac-

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TABLE 1. Clinical categories of acute limb ischemia

Category	Description	Sensory loss	Muscle weakness	Arterial doppler signals	Venous doppler signals
I: Viable	Pain, pallor, pulselessness. Not immediately threatened	None	None	Audible	Audible
IIA: Marginally threatened	Pain, pallor, pulselessness. Salvageable if promptly treated	Minimal (toes) or none	None	Inaudible	Audible
IIB: Immediately threatened	Pain, pallor, pulselessness. Salvageable with immediate revascularization	More than toes; rest pain	Mild, moderate	Inaudible	Audible
III: Irreversible	Pain, pallor, pulselessness. Major tissue loss or permanent nerve damage	Profound, anesthetic	Profound paralysis (Rigor)	Inaudible	Inaudible

Adapted from Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg 1997;26:517–38.

tionated heparin until arterial access has been obtained in the cardiac catheterization laboratory is an acceptable treatment option.[3] There is no data regarding the administration of clopidogrel or a statin in patients presenting with ALI.

Although noninvasive modalities such as magnetic resonance angiography and computed tomography angiography allow for delineation of vascular anatomy, they have a limited role in ALI. If a noninvasive modality is chosen, one should make sure that it does not unduly delay subsequent therapeutic intervention. Urgent diagnostic angiography provides an objective assessment of the degree of ischemia, delineates etiology and guides management strategies.[6] For example, evidence of a crescent-shaped occlusion (meniscus sign) at the proximal edge of the embolus with otherwise normal-appearing arteries is evidence of an embolic origin. Intra-arterial vasodilators are appropriate to treat potential vasospasm in the vessel distal to the site of lodgment of the embolus. Arterial access should be obtained in the contralateral femoral artery with a 4-Fr sheath. A 4-Fr pigtail catheter is advanced and positioned in the descending aorta at the level of the renal arteries and an infrarenal abdominal aortogram with peripheral run-off is performed. The goal is to characterize the arterial inflow to visualize the occlusion and to determine number of occluded vascular segments along with outflow anatomy.

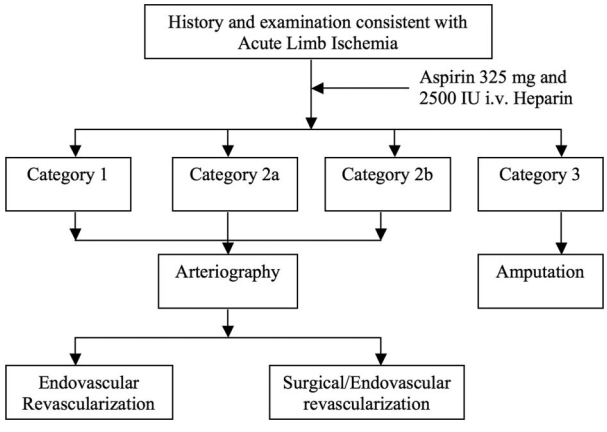

FIGURE 1. Approach to management of patients with acute limb ischemia.

APPROACH TO REVASCULARIZATION

Although early surgical strategies used catheter thromboembolectomy (Fogarty balloon) with patch angioplasty, contemporary surgical techniques involve placement of new bypass grafts or endarterectomy.[12] However, the mortality rate for open surgery in patients with ALI remains high (20%–25%).[13] The endovascular or catheter-based approach to ALI includes the use of intra-arterial thrombolytic agents, mechanical thrombectomy devices and balloon angioplasty with or without stent placement. The intravenous administration of thrombolytic agents has been abandoned because of excessive bleeding complications, and intra-arterial catheter-directed administration of thrombolytic agents or catheter-based thrombectomy is preferred as a first-line therapy for most patients presenting with ALI.[14]

Three randomized controlled trials have compared open surgical versus catheter-based endovascular revascularization for patients presenting with ALI (Table 2)[13,15,16] The Rochester trial randomized 114 patients with ALI of fewer than 7 days duration to intra-arterial urokinase (UK) or surgical intervention.[13] Successful thrombolysis (>80% thrombus removal) was achieved in 70% of those in the UK subgroup. Embolization occurred in 9%, all of which resolved with continued UK infusion. The mean time required for successful thrombolysis was 35.6 ± 2.1 hours. At 1 year, the cumulative risk of amputation (18%) was identical in both groups; however, the thrombolytic group had a lower all-cause mortality (84% versus 58%, relative risk reduction of 62%, $P = 0.01$). Intra-arterial thrombolysis was equally effective for both embolic and thrombotic occlusions, although the patient survival benefit was greater for patients with embolic occlusions (Figure 2).

The Surgery versus Thrombolysis for Ischemia of the Lower Extremity trial randomized 393 patients with nonembolic lower extremity ischemia of less than 6 months duration to intra-arterial UK, tissue plasminogen activator (tPA) or surgical revascularization.[16] The trial was prematurely terminated because patients assigned to thrombolysis more frequently had recurrent or ongoing ischemia (45% versus 24%, $P < 0.001$) at 30 days. Subsequent analysis, however, offered important insight. Patients presenting with symptoms ≤14 days and randomized to thrombolysis had better 6-month limb salvage (89% versus 70%, $P = 0.02$) rates. All-cause mortality was lower in patients in the thrombolytic arms; however, this did not reach statistical signifi-

TABLE 2. Summary of endovascular management in randomized controlled trials for patients presenting with ALI

Randomized controlled trial	No. patients	Duration of symptoms	Intra-arterial thrombolytic agent	Intravenous unfractionated heparin
Rochester 1994	114	<7 d	UK 4000 IU/min × 2 hr, 2000 IU/min × 4 hr, and 1000 IU/min × 42 hours	None
STILE 1994	393	<6 months	UK-Bolus 250,000 IU, 4000 IU/min × 4 hr, 2000 IU/min × 32 hr OR TPA 0.1 mg/kg/hr × 12 hr then reduced to 0.05 mg/kg/hr	5000 U bolus, 1000 U/hr to maintain PTT 1.5–2.5 times control
TOPAS 1996	544	<14 d	rUK 4000 IU/min × 4 hr, 2000 IU/min × 44 hr	Initially heparin was administered to maintain a PTT 1.5–2.5 times control. This was changed to small subtherapeutic doses given via the arterial sheath

ALI, acute limb ischemia; STILE, The Surgery versus Thrombolysis for Ischemia of the Lower Extremity trial; TOPAS, The Thrombolysis or Peripheral Arterial Surgery trial; UK, urokinase; rUK, recombinant urokinase; TPA, tissue plasminogen activator; PTT, partial thromboplastin time.

cance (5.6% versus 10%, $P = 0.45$). These outcomes were independent of the thrombolytic agent used.

The Thrombolysis or Peripheral Arterial Surgery trial randomized 213 patients with ALI secondary to native arterial or bypass graft occlusion of fewer than 14 days duration to recombinant UK (rUK) or surgery.[7] Survival and amputation-free survival at 1 year were similar in the thrombolytic and surgical groups. These results were confirmed in a larger multicenter randomized controlled trial of 544 patients with ALI of less than 14 days duration randomized to rUK or surgery.[15] Although at 6 months, survival and amputation-free survival were similar in thrombolytic and surgical groups, the surgical group had undergone more operative procedures (excluding amputations) compared with the thrombolytic treated group (551 versus 315). Major hemorrhagic complications (defined as blood loss ≥500 mL, blood loss requiring transfusion and blood loss resulting in hypotension or intracranial hemorrhage) were more frequent with thrombolysis (12.5% versus 5.5%, $P = 0.005$). Collectively, these trials have established the general strategy of attempting endovascular, catheter-based management first in patients presenting with ALI.

COMPARISON OF THROMBOLYTIC AGENTS

Currently available thrombolytic agents include (1) nonspecific plasminogen activators such as streptokinase (AstraZeneca, Wilmington, DE), UK (Abbott Laboratories, Chicago, IL), rUK (Abbott Laboratories) and proUK; (2) tissue-specific plasminogen activators such as alteplase (Genentech, San Francisco, CA), reteplase (rPA, Retavase, Centracor, Fremont, CA) and tenecteplase (TNK; Genentech, San Francisco, CA); and (3) a miscellaneous group consisting of novel agents such as fibrolase and plasmin.

Thrombolysis is indicated in patients presenting with ALI Rutherford class I or IIa. For patients presenting with ALI Rutherford class IIb, before initiating a thrombolytic agent, a vascular surgical consultation is encouraged. Contraindications to the use of a thrombolytic agent include active clinical bleeding, a prior hemorrhagic stroke and the presence of a compartment syndrome. Relative contraindications include conditions that increase the risk of hemorrhagic complications such as recent surgery or trauma within 10 days, cardiopulmonary resuscitation within 10 days and uncontrolled hypertension (>180 mm Hg systolic or >110 mm Hg diastolic). A complete list of indications and contraindication is provided in Table 3.[1] Although the use of intra-arterial thrombolysis is a "standard of care," the U.S. Food and Drug Administration has failed to approve the use of any thrombolytic agent for the treatment of ALI.

Comparisons of thrombolytic agents in patients with ALI have attempted to identify which agent is associated with the best clinical outcome. A Cochrane review pooled data from five randomized trials and 687 patients comparing intra-arterial UK to tPA for the management of ALI.[17] The review concluded

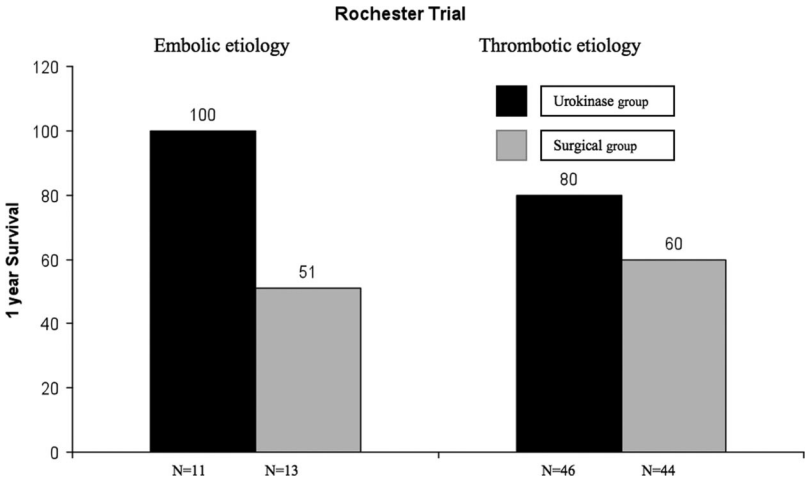

FIGURE 2. Clinical outcomes in patients with acute limb ischemia due to an embolic versus a thrombotic etiology.[13]

TABLE 3. Indication and contraindications to thrombolytic therapy in patients with acute limb ischemia[1]

Indications
Stage 1, IIa
Stage IIb after surgical consultation
Absolute contraindications
Active internal bleeding
Previous hemorrhagic stroke
Presence or development of compartment syndrome
Relative contraindications
Recent nonvascular surgery or trauma within 10 d
Cardiopulmonary resuscitation within 10 d
Uncontrolled hypertension >180 mm Hg systolic or >110 mm Hg diastolic
Puncture of a noncompressible vessel
Intracranial tumor
Recent eye surgery
Neurosurgery within past 3 months
Intracranial trauma within 3 months
Recent gastrointestinal bleed (<10 d)
Established cerebrovascular event (including transient ischemic attack within 2 months)
Hepatic failure with coagulopathy
Bacterial endocarditis
Pregnancy and immediate post-partum
Life expectancy <1 year
Diabetic hemorrhagic retinopathy
Recent internal or noncompressible hemorrhage

Adapted from Rajan DK, Patel NH, Valji K, et al. Quality improvement guidelines for percutaneous management of acute limb ischemia. J Vasc Interv Radiol 2009;20(7 suppl):S208–18.

that intra-arterial tPA and UK are equally effective in ALI. Although hemorrhagic complications (groin hematomas) were more prevalent (15% versus 8%) with high-dose intra-arterial tPA (5 mg/hr), the authors concluded that the quality of evidence was such that reliable conclusions about the superiority of any one thrombolytic agent cannot be made.

Different techniques of thrombolytic drug administration have also been studied. These include systemic intravenous administration, local intra-arterial continuous infusions and a "pulse spray" local infusion technique. Another Cochrane review of 336 patients with ALI studying the optimal infusion technique of thrombolytic agents concluded that local intra-arterial drug delivery was more effective than systemic intravenous therapy.[18] The actual method of intra-arterial delivery (pulse spray versus continuous infusion) did not affect limb salvage. This comparative analysis was limited by small numbers of patients studied, varying duration/etiology of symptoms and heterogeneous treatment strategies.

An advisory panel organized by the Society of Cardiovascular and Interventional Radiology recognized the off-label use of these drugs and recommended tPA be administered either as a weight-based dose of 0.001 to 0.02 mg/kg/hr or a non–weight-based dose of 0.12 to 2 mg/hr for treatment of patients with ALI of less than 14 days duration. A total limiting dose of 40 mg for catheter-directed therapy was recommended, with a maximum intra-arterial bolus not exceeding 10 mg.[19] The dose of rPA recommended was 0.25 1U/hr with or without an initial bolus of 2 to 5 U, up to a maximum dose of 20 U.[20] No formal dosing recommendation for TNK in peripheral thrombolysis has been made; however, doses of TNK used in clinical trials range from 0.25 to 0.5 mg/hr.[21]

ENDOVASCULAR THERAPIES

After completion of the diagnostic angiogram when a decision has been made to proceed with endovascular revascularization, the contralateral femoral system is entered and a 4-Fr angulated diagnostic catheter (eg, internal mammary artery) is placed at the aortic bifurcation. The catheter is manipulated so that the tip of the catheter "engages" the ostium of the contralateral common iliac artery. Angiography of the affected limb is then obtained to identify the culprit lesion. When the culprit lesion involves the femoral artery or lower, an 0.035-in angled hydrophilic guidewire (Glidewire, Terumo, Boston Scientific, Watertown, MA) is steered to the common femoral artery, and the diagnostic catheter is then advanced over this wire. The guidewire is exchanged for a stiff exchange 0.035-in guidewire (eg, Amplatz; Boston Scientific Corporation, Watertown, MA). The stiff guidewire facilitates the placement of a 6- to 8-Fr crossover sheath (Balkin, Cook, Bloomington, IN) as a platform for intervention. In patients with severe aortoiliac disease instead of contralateral femoral, a brachial approach can be used for vascular access. An attempt to traverse the occlusive thrombus with a 0.035-in hydrophilic guidewire (Glidewire, Terumo; Boston Scientific) is made. A multiside-hole infusion catheter is then placed distal to the thrombus and the intraluminal location is confirmed with a contrast injection. A thrombolytic agent may then be administered into the thrombus at the rate detailed above (Figure 3). These infusion catheters are available in various lengths, with multiple side-holes, allowing for adjustment for the extent of occlusion that is to be treated.

As an adjunct to thrombolysis, or as a standalone therapy, mechanical disruption/aspiration of the thrombus can be performed with mechanical thrombectomy devices (Figure 4). The actual sequence of pharmacologic versus mechanical lysis is a matter of personal preference. Proponents of the thrombolysis-first approach argue that initial thrombus lacing with a thrombolytic agent will result in better dissolution of downstream embolization and soften the thrombus for easier fragmentation. The thrombectomy-first proponents argue that thrombus aspiration as the initial modality re-establishes flow faster than thrombolysis and avoids unnecessary lytic exposure in some patients. A summary of the larger published reports on thrombectomy is provided in Table 4.

Devices used for mechanical disruption of the thrombus can be classified into rheolytic thrombectomy catheters, thromboaspiration catheters and microfragmentation catheters (Table 5).[31] Currently, AngioJet™ (Possis Medical, Minneapolis, MN), is the only Food and Drug Administration–approved device for mechanical thrombectomy in patients with ALI.[31] Newer types of devices being tested are ultrasonic and mixing devices. The OmniWave Endovascular System (OmniSonics, Wilmington, MA) system uses ultrasound (20 kHz) to dissolve occlusive thrombus without adjunctive thrombolytics. The EKOS system (Ekos Corporation, Bothell, WA) uses higher frequencies and lower energy ultrasound waves to hasten pharmacologic thrombolysis.[32] The Trellis (Bacchus Vascular, Santa Clara, CA) is a mixing device that uses pharmacologic thrombolysis to produce clot dissolution but does so using a double-balloon catheter system to confine the agent to a localized arterial segment. A rotating wire mixes the agent and dissolves the clot, which is aspirated through the sheath. Small

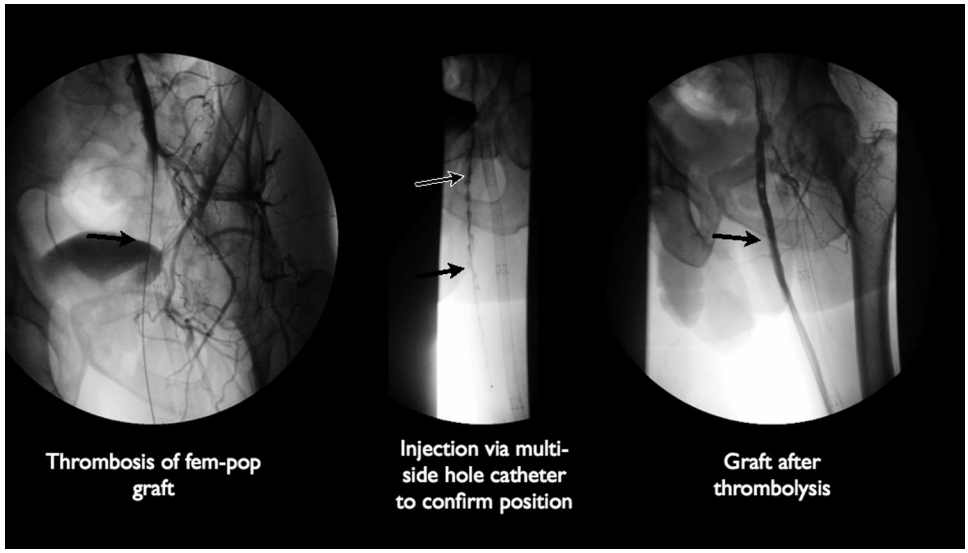

FIGURE 3. Pre- and post-angiograms of a thrombosed femoropopliteal graft treated with intra-arterial thrombolysis.

case series have demonstrated their use in patients with ALI,[33] and further data regarding the safety and efficacy of these devices are needed before they can be adopted for routine use.

OTHER ADJUNCTIVE THERAPIES

The published literature shows widely varying doses of heparin administered during thrombolytic infusions, from zero to therapeutic anticoagulation, with no dose identified that predicts bleeding.[13,15,16] Initial dose of heparin should be targeted to achieve therapeutic anticoagulation. When immediate angiography is planned, this can be delayed till vascular access is obtained. No weight-based regimes for ALI have been described; however, borrowing from the literature on acute venous thrombosis, a loading dose of 80 U/kg followed by an infusion of 18 U/kg achieves therapeutic anticoagulation.[34] As an adjunct to thrombolytics, the dose of heparin should be reduced. An expert advisory panel recommended a heparin bolus of 2500 U followed by a continuous drip of 500 U/hr to maintain the partial thromboplastin time between 1.25 and 1.5 times control as an adjunct to tPA for peripheral intra-arterial thrombolysis.[19] We currently lack sufficient data to recommend enoxaparin or bivalrudin for patients presenting with ALI.

Combination therapy with antiplatelet glycoprotein IIb/IIIa receptor inhibitors (GPIIb/Iia) and thrombolytic agents has been studied as a means to accelerate reperfusion, allow lower lytic doses, and perhaps improve clinical outcomes.[35] A single-centre randomized pilot trial, the Peripheral Artery Occlusion: Treatment with Abciximab plus Urokinase versus Urokinase Alone study, UK was compared with or without adjunctive abciximab (Reopro, Eli Lilly, Indianapolis, IN) in 70 patients with lower extremity arterial occlusions of ≤6 weeks in duration. The UK plus abciximab group achieved a significantly higher rate of amputation-free survival at 90 days than did UK alone albeit at a higher rate of bleeding events (Figure 5).[35]

POSTPROCEDURE MONITORING

After endovascular revascularization, all patients should be monitored carefully, usually in an intensive care unit. There is

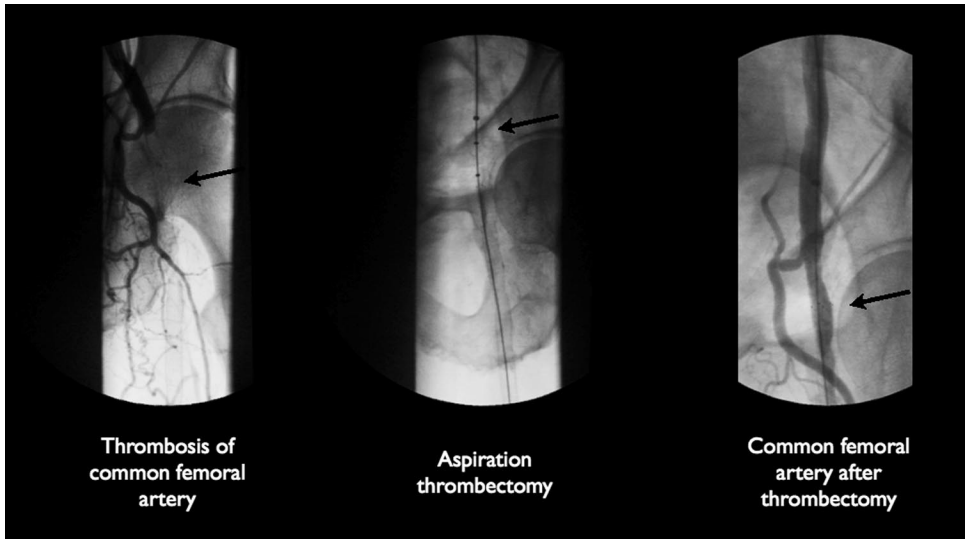

FIGURE 4. Pre- and post-angiograms of an occluded native superficial femoral artery treated with aspiration thrombectomy.

TABLE 4. Clinical reports on the use of mechanical thrombectomy devices

Study	No. patients/ conduit (%)	MTD success (%)[a]	Adjunctive lysis (%)	In-hospital complications
Oasis				
Höpfner[22]	51 Native, 44 (86) Grafts, 7 (14)	6 (11.8)	5 (9.8)	Embolization, 4.8% Hemorrhage, 8% Amputation, 17.7% Mortality, 8%
Angiojet				
Mũller-Hũlsbeck et al[23]	112 Native, 99 (86) Grafts, 16 (14)	84 (75)	20 (17.9)	Embolization, 9.8% Amputation, 1.8% Mortality, 7%
Silva et al[24]	22 Native, 13 (59) Grafts, 9 (41)	21 (95)	None	Embolization, 9% Hemorrhage, 10% Amputation, 5% Mortality, 14%
Wagner et al[25]	50 Native, 39 (78) Grafts, 11 (22)	26 (52)	15 (30)	Embolization, 6% Hemorrhage, 6% Amputation, 8% Mortality, 0%
Ansel et al[9]	57 Native, 42 (74) Grafts, 15 (26)	36 (64)	18 (31)	Hemorrhage, 12% Amputation, 3.5% Mortality, 3.5%
Hydrolyser				
Reekers et al[26]	28 Native, 11 (39) Grafts, 17 (61)	26 (58)	7 (25)	Embolization, 18% Hemorrhage, 0% Amputation, 11% Mortality, 0%
Henry et al[27]	41 Native, 28 (68) Grafts, 8 (20) Other (5)	34 (83)	10 (24)	Embolization, 2.4% Amputation, 0% Mortality, 0%
Amplatz				
Rilinger et al[28]	40 Native	30 (75)	10 (25)	Embolization, 0% Hemorrhage, 0% Amputation, 5% Mortality, 0%
Tadavarthy et al[29]	14 Native, 2 (14) Grafts, 10 (71) Other (2)	10 (71)	4 (28.6)	Embolization, 14% Hemorrhage, 14.3% Amputation, 0% Mortality, 0%
Gõrich et al[30]	18 Native	6 (33)	12 (66.7)	Hemorrhage, 6% Amputation, 6%

Adapted from Kasirajan K, Marek JM, Langsfeld M. Mechanical thrombectomy as a first-line treatment for arterial occlusion. Semin Vasc Surg 2001;14:123–31.

[a] Mechanical thrombectomy device success defined as restoration of flow by use of the device alone.

no role for laboratory monitoring during thrombolytic therapy.[1] Reperfusion manifests as improvement in limb temperature, improved capillary refill, reappearance of arterial pulses and alleviation of pain. It should be noted that a patient's symptoms may transiently worsen as the thrombus begins to disintegrate with distal embolization of the resulting smaller fragments.[3] The treatment for worsening symptoms is to continue, or at times increase the dose of the thrombolytic being infused.

The frequency of major hemorrhagic complications (intracranial, retroperitoneal or intraocular hemorrhage, clinical bleeding event associated with a hemoglobin decrease of 5 g/dL or requiring blood transfusion) ranges from 5% to 17%.[36] An emergent computed tomography scan should be obtained in all patients with suspected intracranial bleed. The thrombolytic agent should be stopped, anticoagulation reversed and a neurology consultation obtained. In patients with progression of ischemic symptoms or development of a compartment syndrome (manifested by a swollen tense limb), surgical consultation is required.

The time to repeat angiography to assess angiographic lysis depends on local practice. Studies have reported repeat

TABLE 5. Mechanical thrombectomy devices

Catheter	Company	Sheath size	Guidewire (inch)	Working length (cm)
RheolyticThrombectomy catheter				
Angioget	Possis Medical, Minneapolis, MN			
E-train		5F	0.018	110
LF-140		5F	0.018	140
CF-105		5F	0.018	105
Xpeedior		6F	0.035	110
Hydrolyser	Cordis, Miami, FL	6, 7F	0.025	65, 110
Oasis	Boston Scientific, Watertown, MA	6F	0.018	65, 110
ThromboAspiration catheter				
Gelbfish Endo Vac	Neo Vascular Technologies. Brooklyn, NY	6F	Incompatible	25
Microfragmentation catheter				
Amplatz	Microvena, White Bear Lake, MN	6, 8F	0.018	55, 90
Helix	Microvena, White Bear Lake, MN	7F	0.018	75, 120
Arrow-trerotola	Arrow International, Reading, PA	6F	0.025	65
Castańeda Brush	Micro Therapeutics, Aliso Viego, CA	6F	0.035	65
Cragg Brush	Micro Therapeutics, Aliso Viego, CA	6F	Incompatible	65
Ultrasonic devices				
Ekos	Ekos Corporation, Bothell, WA	5F	Incompatible	106, 135
Omniscience	Omnisonics, Wilmington, MA	6F	0.018	100
Mixing devices				
Trellis thrombectomy	Bacchus Vascular, Santa Clara, CA	6, 7, 8F	0.035	65, 140

Adapted from Kasirajan K, Marek JM, Langsfeld M. Mechanical thrombectomy as a first-line treatment for arterial occlusion. Semin Vasc Surg 2001;14:123–31.

angiography 4 to 12 hours after initiation of an intra-arterial thrombolytic agent.[7,16,37] Thrombolytic infusions longer than 48 hours without improvement in flow are associated with an increase in bleeding risk and are not recommended.[3,37]

Relook angiography not only serves to assess re-establishment of perfusion but also helps in identification and management of the underlying etiology. Identification and treatment of the culprit stenotic lesions (native vessels or grafts) in a patient with a thrombotic etiology for ALI will diminish recurrence and improve long-term clinical outcomes. There is no role for plaque debulking devices (directional atherectomy or LASER atherectomy) in patients with ALI. Whenever possible in patients with an identified embolic etiology for ALI, the underlying source should be addressed (for example, surgical or endovascular exclusion of a thrombosed popliteal aneurysm).[38] In patients in whom surgical or endo-

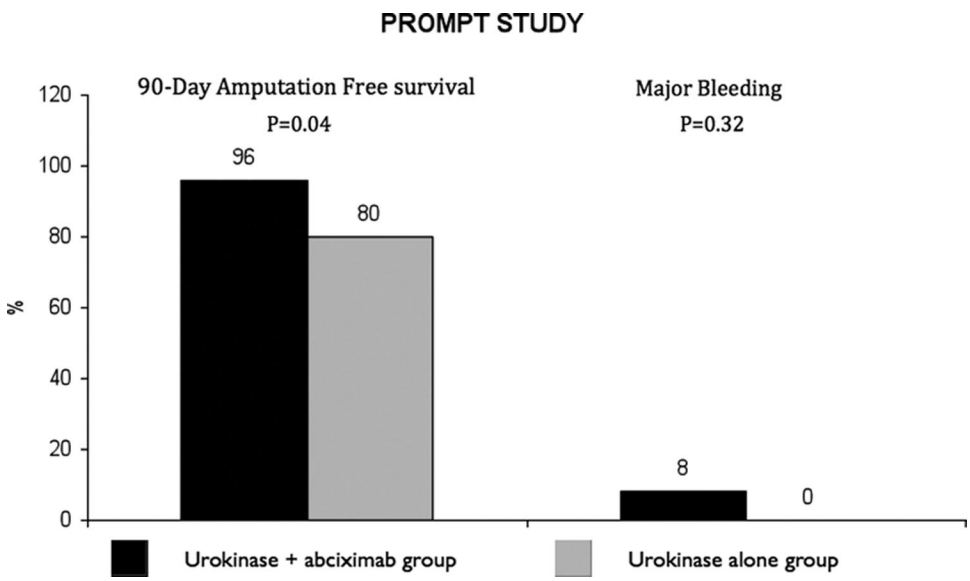

FIGURE 5. Peripheral Artery Occlusion: Treatment with abciximab plus urokinase versus with urokinase Alone-A Randomized Pilot Trial (the PROMPT Study).[26]

vascular treatment of the embolic source is not possible (atrial fibrillation or cardiomyopathy), long-term anticoagulation will decrease the recurrence rate.[14]

OUTCOMES

For patients with ALI, clinical success is defined by preservation of vessel patency, limb salvage and survival at 1 year. Several studies have looked at predictors of successful intra-arterial thrombolysis in patients presenting with ALI.[8,39] Angiographic success was defined as removal of ≥70% thrombus with establishment of antegrade flow in a previously occluded segment.

A history of previous successful thrombolysis, a shorter duration of symptoms (<14 days), the absence of motor dysfunction, an ankle-brachial index greater than 0.33 at presentation and guidewire traversal through the thrombus (positive guidewire test) all predict successful thrombolysis.[8,39] With regards to type of conduit, most (but not all) studies have shown that thrombolysis is more likely to be successful in an occluded surgical graft compared with native arteries.[8,39] Patients with synthetic graft occlusions have shown a higher success rate compared with those with saphenous vein grafts.[8]

Identification and treatment of the underlying etiology of ALI is imperative to decrease recurrence rates. [1]A number of comorbidities have been identified that decrease long-term clinical success, including advanced age, non-Caucasian race, history of stroke or a transient ischemic attack, malignancy, underlying peripheral arterial disease, congestive heart failure and low body weight.[39]

FOLLOW-UP

All patients with a history of ALI need long-term follow-up with a cardiovascular specialist. In those with identified peripheral arterial disease, appropriate secondary preventive measures such as daily exercise, smoking cessation, control of diabetes, blood pressure and treatment of hyperlipidemia should be instituted.[14] In addition, these patients need close monitoring early on and often for signs of impending recurrences.

SUMMARY

On the basis of the above data, for patients presenting with ALI and a clinically viable limb, endovascular revascularization is appropriate as a first-line therapy.[1] For patients with marginally threatened or immediately threatened limbs, choosing between surgical and endovascular revascularization is primarily based on time to revascularization with surgical revascularization often chosen for patients with advanced sensorimotor deficits.[3] In the late-presenting patient with irreversible ischemia, primary amputation is appropriate.[1] After establishment of blood flow by either a surgical or an endovascular approach, it is imperative to identify and treat the underlying etiology.

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