

Clinical Diagnosis and Prognosis of Acute Limb Ischemia

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Acute limb ischemia (ALI) is a serious condition that can threaten the limb's viability and the patient's life. It is usually caused by atherosclerotic disease but can also arise from nonatherosclerotic causes. It has numerous clinical manifestations, the most common of which is pain. Proper diagnosis involves history, physical examination, and techniques such as Doppler assessment, contrast-enhanced magnetic resonance angiography, or catheter-based angiography. Differential diagnosis is important, as many other conditions can mimic ALI. Ischemia severity can be classified into three levels: viable; threatened, either marginally or immediately; and irreversible. Treatment options include surgical and less invasive endovascular techniques. Prognosis can be excellent, and early diagnosis and prompt initiation of therapy are essential to achieving a good outcome.

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Lower-extremity ischemia results from occlusion of the circulation to the limb either proximally or distally in the circulatory tree. Signs and symptoms may be acute, resulting in a medical emergency, or more moderate, resulting in a less urgent situation. Acute limb ischemia (ALI) is defined as *any sudden decrease or worsening in limb perfusion causing a threat to extremity mobility*.¹ Acute changes in perfusion, when occurring in patients with prior occlusive disease, can also result in deterioration in clinical status, with worsening claudication a frequent complaint. Chronic ischemia is generally viewed to be a stable disease process; however, patients with chronic symptoms may still develop accelerated worsening of their symptoms, representing a hybrid clinical problem.

ALI poses numerous risks, including risks associated with therapy, risks of limb loss associated with the underlying pathology, and, importantly, a significant risk of mortality. Mortality risks associated with surgical reperfusion have been reported at 9.7%–17% with a risk as high as 42% reported in the elderly.^{2,3} The most important variables in producing a good outcome are early diagnosis and implementation of prompt therapy. The following discussion is intended to familiarize the reader with basic diagnostic concepts of ALI and acceleration of chronic ischemic symptoms, as well as the most common therapeutic options currently available.

Etiology

Most ALI seen in clinical practice is caused by atherosclerotic disease.⁴ In these cases, the condition results from thrombosis of an underlying stenosis of an artery due to atherosclerotic plaque, thrombosis of indwelling bypass grafts or other vascular procedures, embolism from the heart, proximal plaque or aneurysm, an endovascular procedure, or thrombosed aneurysm.

ALI can also be caused by a host of diseases that are nonatherosclerotic.^{5,6,7} Nonatherosclerotic causes of ALI include arterial trauma (including iatrogenic), aortic or arterial dissection, arteritis with thrombosis, spontaneous thrombosis associated with hypercoagulable states,⁸ popliteal cysts causing thrombosis, popliteal entrapment with thrombosis,^{9,10} and vasospasm with thrombosis. In patients with this last condition, the thrombosis precipitates the acute ischemia.

Clinical Manifestations

The most common symptom associated with sudden deterioration of lower-extremity circulation is pain.

The pain is typically in the most distal part of the circulation, that is, the foot or toes, regardless of the level of ischemia, but this is not always the case. The rate of onset and duration of pain are important in determining potential etiologies of ischemia. Pain associated with arterial emboli will generally be of sudden onset, whereas that associated with thrombosis of an underlying stenosis may be sudden but preceded by a period of increasing claudication symptoms. Classically, the five Ps of

In patients with diabetes mellitus, coincidental neuropathy may confound the physical findings. Motor deficits are associated with more advanced and limb-threatening levels of anesthesia.

Diagnostic Methods

The history and physical examination are critical in the assessment of patients with lower-extremity ischemia and should answer three fundamental questions that will direct therapy: 1) Is the limb viable

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ALI include pain, pulselessness, pallor, paresthesias, and paralysis. Reduction in temperature may also be present. The limb manifesting these symptoms and signs should always be compared to the limb on the opposite side, and these manifestations should serve as baseline for the physical examination.

Pulses should be examined carefully at all levels, because level of occlusion can generally be detected by careful examination. Hand-held Doppler devices are also quite helpful in locating and analyzing pulses. Coolness, particularly relative to that of the contralateral limb, is an important finding, frequently asso-

ciated with no further progression occurs? 2) Is the limb viability threatened if perfusion is not immediately provided? 3) Have irreversible changes occurred that preclude salvage of the extremity? In patients with advanced peripheral vascular disease, one may also be confronted with the question of whether partial limb salvage can be accomplished if reperfusion is successful.

Although history and physical examination remain crucial elements of the diagnosis of ALI, a number of other diagnostic modalities may be of value. Simple Doppler assessment, more specifically, ankle brachial indices, which can be performed at

The five Ps of acute limb ischemia include pain, pulselessness, pallor, paresthesias, and paralysis.

ciated with pallor in the affected extremity. Capillary refill should also be assessed in addition to the presence of venous return. Sensory deficits can manifest themselves as paresthesias or numbness, but these signs may not be present in all cases.

the bedside, can be quite useful. More sophisticated techniques, such as pulse volume recordings, and more complete noninvasive assessment can also be valuable in assessing the anatomic level of disease. Color-flow duplex angiography has been very

Table 1
Clinical Categories of Acute Limb Ischemia

Category	Description/Prognosis	Sensory Loss	Muscle Weakness	Arterial Doppler Signals	Venous Doppler Signals
Viable	Not immediately threatened	None	None	Audible	Audible
Threatened					
Marginally	Salvageable if promptly treated	Minimal (toes) or none	None	(Often) inaudible	Audible
Immediately	Salvageable with immediate revascularization	More than toes Associated with rest pain	Mild, moderate	(Usually) inaudible	Audible
Irreversible	Major tissue loss or permanent nerve damage inevitable	Profound, anesthetic	Profound paralysis (rigor)	Inaudible	Inaudible

successful as an adjunct in demonstrating both etiology and level of occlusive disease.^{11,12}

Recently, contrast-enhanced magnetic resonance angiography (MRA) has become very useful in diagnosis of peripheral vascular disease. Although this technique may be more valuable in patients with chronic limb ischemia, its use in ALI may also be important, particularly as procedure times continue to decrease. The use of contrast, high radiofrequency gradients, and specific sequencing has allowed peripheral MRA procedures to become quite short, and they can frequently be tolerated by patients who are in pain.¹³⁻¹⁵

Catheter-based diagnostic angiography also has considerable value in the diagnosis of ALI, in large part because it allows initial therapy to be initiated if the clinical condition warrants it. These procedures are generally performed at our own institution by accessing the unaffected artery, which gives the interventionist a number of options regarding approach to subsequent occluded segments.

Differential Diagnosis

Symptoms of ALI can be produced

by a variety of vascular disorders and can be mimicked by some non-vascular diseases or conditions. The clinician needs to be aware of these conditions and be able to discriminate among them and make a definitive diagnosis.

Conditions that can mimic ALI include cardiac failure, particularly when superimposed on underlying chronic occlusive disease. Low-output heart failure can functionally worsen the stage of peripheral vascular disease in the absence of progressive occlusive change. On rare occasions, severe deep venous thrombosis can exhibit ALI symptoms, including reduction in pulses. Like ALI, this condition, known as phlegmasia cerulea dolens, is limb threatening without aggressive intervention, generally with thrombolytic agents. Acute neural entrapment syndromes, including spinal canal, herniated disc pathology can mimic ALI. Acute vasospasm, generally associated with ergotism, can also produce signs and symptoms of ALI, without true occlusions.

Classification

Classification of ALI based on level of risk to the extremity has several practical clinical benefits. Stratifying

severity of ischemia facilitates decision making and establishes a basis for individual outcomes analysis. Stratification also facilitates communication with the patient and family by providing an objective rationale for determining prognosis and for use of various treatment options. Recently the TransAtlantic Inter-Society Consensus (TASC) writing group reviewed the Society for Vascular Surgery/International Society for Cardiovascular Surgery classification and made recommendations and slight modifications.¹⁶ This revised classification system is described below and summarized in Table 1.

Viable

At this level of severity, the limb is not immediately threatened. The patient experiences no continuing ischemic pain or neurological deficit. Skin capillary circulation is adequate, and Doppler signals in a pedal artery are clearly audible.

Threatened

This level of severity implies reversible ischemia in a limb that is salvageable; major amputation can be avoided if arterial obstruction is relieved quickly. Two levels within

this category have been defined: *marginally threatened* and *immediately threatened*. Doppler signals are frequently inaudible in both, and symptoms of pain and sensation vary in severity. Any patient with motor loss is in the more severe category.

This group of patients is traditionally associated with surgical therapy. However, the patients in the marginally threatened group may benefit

TASC document: "Rapid diagnosis of the severity of acute limb ischemia and its probable cause is an urgent matter. Time to diagnosis and successful outcome of treatment are inversely related." Most importantly, rapid initiation of therapy will improve long-term outcome. In one study, the time from establishing the diagnosis to initiation of therapy was evaluated and correlated

to injection. Endovascular approaches include catheter-directed therapy with thrombolytic agents and/or mechanical thrombectomy devices or other pharmacologic agents. Both approaches offer advantages and disadvantages, and preference for one approach or the other may depend on local site preferences and availability of local resources for thrombolytic therapy and skilled practitioners. In single-center studies, limb salvage rates as high as 92% have been reported. In the few comparative trials of surgery versus catheter-directed therapy, 6- and 12-month limb-salvage rates seemed to average in the 80%–90% range. Mortality rates were similar for both procedures, although the Rochester study¹⁹ showed significantly lower mortality rates in patients treated with thrombolytic therapy.^{20–24} Most acknowledge the need for a prospective randomized trial comparing surgery and catheter-directed therapy, but economic, regulatory, and clerical barriers may be too considerable to overcome.

Conclusions

ALI is an important clinical problem that can result from both atherosclerotic and nonatherosclerotic causes. Clinical skills in both diagnosis and management of this condition can help save both life and limb. Treatment options for acute lower-extremity ischemia may include both surgical and less invasive endovascular techniques, including

Surgical treatments include thrombectomy, embolectomy, and bypass grafting, all of which may involve adjunctive intraoperative use of thrombolytic agents by direct injection.

from thrombolytic therapy, if the thrombolytic therapy can be initiated promptly. In patients who are immediately threatened, surgical therapy remains a treatment of choice.

Irreversible

This level of ischemia generally requires major amputation or results in permanent neuromuscular damage, regardless of promptness or nature of therapy. We have noted, as have the TASC authors, that a small proportion of limbs in this category may be salvaged by prompt, effective intervention.

Prognosis and Treatment

Outcomes and prognosis of ALI largely depend on the rapid diagnosis and initiation of appropriate and effective therapy. As stated in the

ed to amputation rates. Specifically, the amputation rate was 6% if therapy was initiated within 12 hours, 12% if initiated within 13–24 hours, and 20% if initiated after 24 hours.¹⁷

Treatment options for ALI include general patient management and reperfusion methods, including surgical or endovascular techniques. Initial medical therapy should include use of anticoagulation to reduce or prevent clot propagation and mitigate against further embolization. Pain control is important, as well as therapy of any underlying condition, such as congestive heart failure or arrhythmia.

Surgical treatments include thrombectomy, embolectomy, and bypass grafting,^{18,19} all of which may involve adjunctive intraoperative use of thrombolytic agents by direct

Main Points

- Acute limb ischemia (ALI) is a serious condition whose risks include loss of the affected limb and mortality.
- Most ALI is caused by atherosclerotic disease.
- Clinical manifestations of ALI include pain, pulselessness, pallor, paresthesias, and paralysis.
- Classification of ALI into levels of severity offers several clinical benefits.
- The most important variables in producing a good outcome are early diagnosis and prompt initiation of therapy.

thrombolytic therapy. Historically, catheter-directed urokinase, and more recently other agents, have been widely used to establish prompt reperfusion, as well as to achieve total clot lysis. The benefits of thrombolysis allow elimination of residual thrombus, identification of the underlying lesion, and application of other endovascular techniques, such as balloon angioplasty and stenting. When applied promptly and skillfully, endovascular techniques can result in great clinical benefit. The prognosis of acute limb ischemia can be excellent but depends on the physician's rapid diagnosis and prompt initiation of therapy directed at reperfusion. In patients undergoing angiographic evaluation, this can be rapidly accomplished by the interventionalist. ■

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