Nontraumatic acute limb ischemia (ALI) may cause significant morbidity and death if not addressed in time and need to be promptly recognized and treated. Perfusion should be thoroughly assessed using available multiple methods, and patients should be considered for revascularization (endovascular or open surgery) to restore blood perfusion as soon as possible. Underlying conditions, which caused ALI, need to be assessed and treated accordingly.

**Keywords:** Acute limb ischemia, evaluation, treatment

### INTRODUCTION

Acute limb ischemia (ALI) occurs due to a sudden decrease in the blood flow to a limb, resulting in a potential threat to the viability of the extremity. Unfortunately, the threat is not only to the limb, but also these patients are also at high risk for death. Limb hypoperfusion, especially when left untreated, causes systemic acid-base and electrolyte abnormalities that impair cardiopulmonary and renal function. Successful reperfusion may result in the release of highly toxic free radicals, further compromising these critically ill patients.

Although it comes on suddenly, it does not imply that the patient has not had long-standing peripheral artery disease. It is important to determine what suddenly changed to cause the onset of symptoms. By convention, ALI usually refers to patients presenting with symptoms for <2 weeks, which ranges from the patient with a few hours history of a painful cold white leg, to the patient with a few days history of short distance claudication or the patient with a sudden increase in ischemic symptoms on a background of peripheral arterial disease.

In many ways, vascular disease in the leg is similar to that in the heart as the risk factors, underlying conditions, and pathogenetic processes are the same, and in many cases, patients have both conditions. Like in acute myocardial infarction, time is very precious in ALI and all same principle applies to ALI in management.

The incidence of acute limb ischemia is estimated at approximately 1/6000 populations per year in the west. Unfortunately, a similar estimate is not available for India. Estimates of mortality following acute limb ischemia range from 9% to 22%. Limb salvage following acute limb ischemia is estimated at 70%–90%.

### ETIOLOGY

ALI results from sudden occlusion of the arterial supply. This may be due to an embolus that originates at a distant site or thrombosis which generally occurs within the local arterial bed. Embolic events cause a greater degree of ischemia than thrombosis, as the embolus characteristically lodges in a “virgin” vascular bed with no prior collateral development. On the other hand, generally thrombosis occurs in vessels with prior, gradual atherosclerotic narrowing or intimal damage that has stimulated the formation of collateral channels. The presence of these collaterals lessens the severity and rapidity of symptom development when the atherosclerotic narrowing progresses to occlusion.

Emboli usually arise from plaque rupture in atherosclerotic arteries or a clot breaking off from an aneurysm or from within...
the heart in patients with atrial fibrillation or another underlying heart disease. Paradoxical embolism, caused by an embolus arising in the venous system and then crossing the heart through an opening such as a patent foramen ovale causing occlusion of the arterial tree is known but rare.

A thrombus contains the constituents of blood and is formed in situ within the blood vessel. Thrombosis may be influenced by any of the three factors described in Virchow’s triad, i.e., stasis, endothelial injury, and hypercoagulability.

Underlying causes of the thrombosis are atherosclerosis, aneurysm, trauma, vasculitis (e.g., in a rheumatologic disease such as lupus), and hypercoagulable states (particularly in patients with cancer).

Other rare causes of ALI can be vasculitis, compartment syndrome, popliteal entrapment syndrome, arterial dissection following trauma, iatrogenic, adventitial cystic disease, previous graft occlusion, etc.

There is also some evidence that the proportion of ALI caused by the embolic disease is falling, due to the decreased incidence of rheumatic heart disease and the improvement in the management of atrial fibrillation.[1] In this context, and with an ageing population, the presentation of acute on chronic limb ischemia is more common. This can be more difficult to diagnose since the classical signs of acute limb ischemia may be attenuated by the presence of collaterals.

**Figure 1: Etiology of ALI**

Time spent investigating and chasing this neurologic diagnosis can be critical as the window of time for successful revascularization of acute embolic origin ischemia is very limited. A proper clinical examination would prevent such disasters.

**History**

History should include the duration, location, intensity, and suddenness of the onset of pain and changes over time. Embolic occlusions are usually very sudden and of great intensity, such that patients often present within a few hours of onset. Pain can be either constant or elicited by passive movement of the involved extremity. The duration of symptoms is of prime importance in the planning of therapy.[2]

The history should include a history of intermittent claudication, previous leg bypass or other vascular procedures. A history suggestive of embolic sources, such as palpitations, cardiac arrhythmias, previous myocardial infarction, and cardiac surgery should also be elicited. A history of previous thrombotic episodes in either the venous or arterial system should also be elicited.

General cardiovascular risk factors (smoking, hypertension, diabetes, hyperlipidemia, amputations, other vascular procedures, and family history of cardiac or vascular events) should be recorded, as these can be predictors of periprocedural mortality.

It is also important to document the patient’s premorbid state of mobility and functionality both as a goal toward successful rehabilitation and to document any preexistent infirmities.

**Examination**

A thorough general and local examination can provide a wealth of information and can often be adequate to plan emergent surgical interventions. General examination should specifically record all pulses and any arrhythmias or pulse deficits.

Pallor and Poikilothermia (level of coldness) in the limb are important to record and to evaluate the level of ischemia and its progress over time. Propagation of thrombus after the initial occlusive event may convert a marginally ischemic limb into a severely threatened extremity. Occasionally, propagation may occur due to a decrease in blood flow secondary to low cardiac output resulting from congestive heart failure or myocardial infarction.

A focused neurologic examination comparing the limb to the other member of its pair for sensory and motor deficits will help to establish the extent of neurologic damage, a factor of significance if medico-legal complaints arise. Sensory capabilities, such as light touch, two-point tactile discrimination, proprioception, and vibratory perception, are lost early on. Profound paralysis with complete lack of sensation indicates an irreversible state of ischemia, and the patient may be best treated with primary amputation.

The muscles should be assessed for compartment syndrome—pain on passive or active movement and hardening of the muscle group are hallmarks and indicators that emergent treatment is required.
**Classification of Acute Limb Ischemia**

The purpose of the history and examination is to determine three things:

- Is the leg acutely ischemic? (or is there an alternative diagnosis?)
- Is the likely cause embolic or thrombotic?
- Is the leg viable, threatened or irreversibly ischemic?

The answers to these three questions will determine the immediate management. It is not always possible to distinguish between embolic and thrombotic etiology, since many patients with an embolic cause may also have some underlying peripheral arterial disease by their age (15%–20% of patients >70 years old have the peripheral arterial disease[8]). It is most important to decide whether the leg is viable, threatened or irreversibly ischemic [Table 1].

The category establishes the type and urgency of treatment. This classification system is simple and depends on factors that can be assessed easily by nonspecialists:

- **Pulses** – arterial and venous pulses/signals assessed by hand-held Doppler
- **Sensation** – the patient closes the eyes and answers if he or she can feel the examiner’s touch
- **Motor function** – can the patient move his or her toes/ankle?

**Investigations**

- **Electrocardiogram:** to diagnose atrial fibrillation or other cardiac arrhythmias or an acute cardiac event, which may be a source of emboli.
- **Two-dimensional Echocardiography:** if time permits, to rule out cardiac source of emboli.
- **Bloods:** routine blood tests relevant to a suspected acutely ischemic limb and for possible surgical intervention. A baseline complete blood count, creatinine, electrolytes, and coagulation profile would be a minimum. A pro-thrombotic workup can be done if feasible and considered essential.
- **Arterial blood gas analysis:** to look for acidosis secondary to ischemia. If the patient is acidic the most important initial management is rehydration.

Imaging: imaging is not essential for the management of every patient of ALI and should be requisitioned only if it is likely to change the management strategy and not going to delay the definitive treatment inordinately. The choice of imaging modality includes:

1. Conventional imaging includes a digital subtraction angiogram. This is an invasive procedure using intra-arterial contrast but has the potential for therapeutic intervention (thrombolysis and angioplasty)
2. Magnetic resonance angiography and computed tomography (CT) angiography are less invasive and should provide the same anatomical information. A CT angiogram is significantly quicker and more readily available
3. Arterial duplex is noninvasive but is operator dependent and iliac, and calf vessels can be difficult to image.

The choice of imaging is likely to depend on the local resources available.

**Management Options/Strategies**

Therapeutic choices are often few, and patient expectations are not always realistic. The management of acute limb ischemia requires a thorough understanding of the anatomy of the arterial occlusion and the open surgical and percutaneous options for restoring limb perfusion. It is very important to explain and document the degree of morbidity that has already occurred and also the likely prognosis for the patient and family.

**Initial management in the emergency department**

Initial management is consisted of following as shown in Figure 2.

- **Analgesia** - As with any painful condition there is no rationale to withhold analgesia to facilitate assessment
- **Anticoagulation** - Eighty-units/kg bolus intravenous (IV) heparin (unfractionated) should be given immediately to all patients with acute limb ischemia; even when they are likely to be undergoing surgery or angiography.[1] This is to prevent propagation of thrombosis. In patients in whom definitive treatment is deferred an intravenous heparin infusion (18U/kg/hr) should be prescribed or can be started on therapeutic low molecular weight heparin (LMWH)
- **IV fluids** - Patients with acute limb ischemia are often dehydrated. These patients are likely to be undergoing

| Table 1: Rutherford’s classification of acute limb ischemia |
|-----------------------------------------------|
| Capillary return | Motor | Sensory | Arterial Doppler signal | Venous Doppler signal |
|------------------|-------|---------|-------------------------|-----------------------|
| **I. Viable**    | Present | Present | Present | Present |
| **Ia. Threatened (salvageable if promptly treated)** | Intact/slow | Present | Partial (toes only) or none | Present |
| **Ib. Threatened (salvageable with immediate reconstruction)** | Slow/absent | Partial paralysis | Partial (more than toes) or complete | Absent (usually) |
| **II. Irreversible (major tissue loss or permanent nerve damage inevitable)** | Absent + staining | Absent profound paralysis (rigor) | Absent profound (anaesthetic) | Absent |
surgery or be given iodinated contrast that will be a further renal insult. Reperfusion of ischemic tissue releases toxic metabolites, potassium, creatinine kinase, and myoglobin, which can further damage the kidneys. Administration of potassium should be avoided. Aggressive rehydration should be initiated unless co-existent cardiac conditions are limiting.

- Refer - Refer to a vascular specialist urgently if not available. Any delay risks jeopardizing the limb, particularly if there is sensorimotor impairment or compartment syndrome.

**Definitive management**

This is based on Rutherford’s classification of ALI and should be considered simultaneously with initial management in the emergency department.

**Category I**

These patients have a viable limb. There is no good evidence to support the use of LMWH in this situation, and it is more difficult to adjust if interventions are required. Formal imaging (angiogram, MR angiogram, CT angiogram or arterial duplex depending on local resources) should then be arranged within normal working hours to plan definitive treatment.

**Category IIa**

These patients have a threatened limb. They should have immediate imaging, to guide operative (or endovascular) intervention. In some cases where there is a minimal sensory loss only, they may be managed conservatively until imaging can be obtained during normal working hours.

**Category IIb**

These patients have a threatened limb and cannot wait. If circumstances allow it may be possible to obtain imaging before theater, but this should not delay intervention. They need urgent revascularization, either operatively or with thrombolysis (see below). Imaging may be acquired while the patient is in theatre.

In a patient with a clear history for embolus (and a source of embolus) and a normal contralateral limb, an embolectomy may be performed under local anesthesia.

In all such patients, a fasciotomy should be considered. In those with established compartment syndrome always perform the fasciotomy before the embolectomy - this will limit the ongoing muscle damage and may also reduce the amount of reperfusion injury. In addition, on occasion, the muscle may be found to be completely nonviable in which case an amputation without revascularizing dead tissue would be appropriate. In those without a preexistent compartment syndrome, the limb should be reassessed at the end of revascularization for a possible fasciotomy. Maintain a low threshold for performing a fasciotomy.

The advantage of local anaesthesia is that elderly patients with cardiac comorbidity better tolerate local anesthesia. The disadvantage is that if a simple embolectomy is unsuccessful and a more extensive procedure is required it may be necessary to convert to general anesthesia. In all cases, an anesthetist should be present to manage the patient medically during the procedure. On-table imaging should be available and the whole limb prepared and draped.

**Category III**

These patients have irreversible ischemia, and the limb is not salvageable. Revascularization in this situation is likely to kill the patient, due to the massive release of potassium, creatine kinase, myoglobin, lactate, and oxygen free radicals from the ischemic tissue, which can cause renal failure, myocardial toxicity, and multi-organ failure. The options are either amputation or palliation.

In an acute scenario with evidence of infection a so-called guillotine amputation may be performed to allow a quick operation to remove necrotic/infected tissue, with a definitive amputation at a later date once the patient is more stable and infection has been treated.

It is vital to recognize those patients in whom an ischemic limb is part of the process of dying, and not subject them to unnecessary and futile interventions.

Special consideration should be given to acute renal failure due to myoglobinuria and limb compartment syndrome after revascularization, which can be of significant importance in ALI management. Any patient not receiving a fasciotomy should be monitored on an hourly basis for any sign of compartment syndrome.

**Treatment strategies**

**Endovascular techniques**

The development of noninvasive or minimally invasive treatment options for revascularization is ongoing. It aims to reduce the surgery-related morbidity without affecting the limb salvage rate. Thrombolysis is one such strategy. Available endovascular options are systemic thrombolysis, catheter-directed thrombolysis (CDT) [Figure 3] and more advanced percutaneous mechanical thrombolysis (PMT).

The introduction of CDT, locally-administered thrombolytic agents has challenged past few decades of dominance of
the Fogarty catheter thrombectomy. Thrombolytic agents are in widespread use for the dissolution of arterial and venous pathologic thrombi. Thrombolytic agents have been successfully employed to dissolve the occluding thrombus, reconstitute blood flow, and improve the status of the tissue bed supplied by the involved vascular segment. All thrombolytic agents in clinical use today are actually plasminogen activators. Following thrombolysis an angiogram should be performed to identify any underlying stenosis.

There have been five randomized controlled trials comparing surgery with thrombolysis in the acutely ischemic limb including 1283 patients, which have been analysed in a systematic review. Major complications were more common after thrombolysis with a 1.3% risk of stroke (versus 0% after surgery) and an 8.8% risk of major haemorrhage (versus 3.3% after surgery). While there was clinical heterogeneity between the studies the authors concluded that universal initial treatment with either surgery or thrombolysis cannot be advocated on the available evidence. There have been no further randomized controlled trials since.

Another option of endovascular treatment – PMT devices, is in evolution and at present contains various devices classified as hydrodynamic devices, rotational devices, and other mechanical adjuncts to CDT. All these new options have not yet proven their advantages or superiority over conventional options available.

**Open surgical techniques**

Open surgical techniques for salvage of an ischemic limb include [Figure 4]:

1) Balloon catheter thrombectomy
2) Bypass procedures to direct blood flow beyond the occlusion
3) Endarterectomy with or without patch angioplasty
4) Intraoperative isolated limb thrombolysis.

For many years, thrombo-embolectomy has been the mainstay of management of acute limb ischemia and it remains a very quick and effective procedure when used in the right situation. In the UK, thrombolysis use peaked in the late 1990s and most centres now use surgery as a first-line management in most patients, mainly due to concerns regarding efficacy and complication rates for thrombolysis.

All patients who undergo any intervention for acute limb ischemia should receive risk factor management as outlined in Figure 5.

**Conclusion**

In the acute setting, open operative revascularization, thrombolytic therapy, and PMT should not be viewed as competitive treatment modalities. The choice of therapy depends on the presentation, urgency, comorbidities, and available treatment options.

In the last decade, significant endovascular advances have been made. New devices and techniques have enhanced our ability to treat high-risk patients who have limb ischemia.

For the primary care physician, a low threshold for suspecting and assessing perfusion in patients with acute limb pain is important. These patients should promptly be referred to an appropriate unit for urgent treatment.
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