

Limb embolism and ischaemia

See the separate [Peripheral arterial disease](#) related article.

What is limb ischaemia?

Critical limb ischaemia is a condition with chronic ischaemic at-rest pain, ulcers, or gangrene in one or both legs, attributable to objectively proven arterial occlusive disease. Critical limb ischaemia implies chronicity and should be distinguished from acute limb ischaemia.^[1]

Acute limb ischaemia is most often due to either acute thrombotic occlusion of a previously partially occluded, thrombosed arterial segment, or to embolus from a distant site.

Without surgical revascularisation, complete acute ischaemia leads to extensive tissue necrosis within six hours. The effects of sudden arterial occlusion depend on the state of collateral supply.

- The collateral supply in the leg is usually inadequate unless there has been pre-existing occlusive disease.
- The subclavian artery has many collateral vessels so that occlusion of a major artery does not necessarily make an upper limb non-viable.

Causes of limb ischaemia (aetiology)^[1]

- Embolism: for example, left atrial thrombus in patients in atrial fibrillation, mural thrombus after myocardial infarction, prosthetic and abnormal heart valves, aneurysm (aorta, femoral, or popliteal), proximal atheromatous stenosis, malignant tumour, or foreign body.

- Thrombosis: most cases of leg ischaemia result from the presence of thrombus at sites of atherosclerotic narrowing; presentation of ischaemia may be:
 - Acute, as a result of emboli from rupture of proximal atherosclerotic plaque or thrombus.
 - Chronic, usually resulting from gradual extension of thrombus with development of collateral vessels.
- Trauma.
- Raynaud's syndrome.
- Compartment syndrome: this occurs when perfusion pressure falls below tissue pressure in a closed anatomical space; causes include:
 - Orthopaedic (tibial or forearm fractures).
 - Vascular: haemorrhage, phlegmasia caerulea dolens (massive thrombosis in the major veins of the limbs, causing gross swelling that obstructs arterial flow).
 - Soft tissue injury (prolonged limb compression, crush injury, burns).
- Congenital causes of early-onset leg ischaemia - eg, aortic hypoplasia.
- Ischaemia of the arm is most often embolism of cardiac origin, but may also be due to damage to the subclavian artery or thoracic outlet syndrome.

Prevalence

A 2019 literature review found the worldwide prevalence of peripheral arterial disease to be between 10–20%, varying with age, gender and region. [2]

Symptoms of limb ischaemia (presentation)

- History and examination should identify the severity of ischaemia and whether it is likely to be embolic or thrombotic. [1]

- Important features to differentiate include rapidity of onset of symptoms, features of pre-existing chronic arterial disease, potential source of embolus and the state of pulses in the contralateral limb.
- The affected part becomes pale, pulseless, painful, paralysed, paraesthetic and 'perishing with cold' ('the 6 Ps').^[1] ^[3]
- The onset of fixed mottling of the skin implies irreversible changes.
- The limb may be red when dependent, leading to a misdiagnosis of inflammation - eg, gout or cellulitis.

Diagnosing limb ischaemia (investigations)^[1]

- Duplex Doppler ultrasound scan may help demonstrate any residual arterial flow.
- Blood tests
 - FBC (ischaemia is aggravated by anaemia).
 - ESR (inflammatory disease - eg, giant cell arteritis, other connective tissue disorders).
 - Glucose (diabetes).
 - Lipids.
 - Thrombophilia screen.
- If diagnosis is in doubt, perform urgent arteriography - CT angiography, MR angiography or digital subtraction angiography.
- Investigations to identify the source of embolus:
 - Electrocardiogram (ECG).
 - Echocardiogram.
 - Aortic ultrasound.
 - Popliteal and femoral artery ultrasound.

Management of limb ischaemia^[4] ^[5]

- Urgent admission – this is an emergency and often requires urgent open surgery or angioplasty. Objective sensory loss requires urgent treatment. Heparinisation is needed immediately (this may double the limb salvage rate), and provide analgesia.
- Ischaemia following trauma and acute thrombosis may require urgent reconstruction.
- The limb must be checked for evidence of compartment syndrome and, if necessary, a fasciotomy should be performed.
- If the occlusion is embolic, the options are surgical embolectomy (Fogarty balloon embolectomy catheter) or local intra-arterial thrombolysis:
 - If embolectomy with a Fogarty catheter fails, an on-table angiogram is performed and bypass graft or intraoperative thrombolysis considered. Routine intraoperative angiography for arterial thromboembolectomy has been shown to be beneficial. ^[6]
 - After successful embolectomy, anticoagulation with heparin is needed to prevent recurrence. Many surgeons postpone heparin for six hours after surgery to reduce the risk of a haematoma. ^[7]
- If the occlusion is due to thrombotic disease the options are intra-arterial thrombolysis, angioplasty or bypass surgery. If due to thrombosis of an arterial graft, then thrombolysis is the first step.

- Intra-arterial thrombolysis:
[8]
 - For patients with acute arterial emboli or thrombosis, treatment with immediate systemic anticoagulation with unfractionated heparin has been recommended. This should be followed by long-term [oral anticoagulation](#) in patients with embolism.^[9]
 - An arteriogram is performed and the catheter advanced into the thrombus. A second or third generation thrombolytic agent (alteplase or reteplase) are used. These should be combined with heparin and thrombolysis continued for 48 hours or until clot lysis.
 - Streptokinase and urokinase are no longer used due to the increased risk of haemorrhagic complications.^[4]
 - Fibrinolysis usually takes between 6 and 72 hours to achieve clot lysis and so patients with limb-threatening ischaemia are not candidates for local fibrinolysis, and require emergent embolectomy.
 - Local thrombolytic therapy is therefore reserved for patients with non-life-threatening limb ischaemia.
 - Thrombolysis can be accelerated by using pulse spray through a multiple side-hole catheter, aspiration thrombectomy (debulking thrombus aspiration) and by using a high dose over a shorter time.
 - Complications of thrombolysis are haemorrhage, pericatheter thrombosis, haemorrhagic stroke and distal embolisation.
 - The contra-indications are critical ischaemia with neurological deficit, and irreversible ischaemic changes.
 - Recombinant tissue plasminogen activator (the preferred agent): up to 60–90% of thromboses will show clinically useful lysis. However, there is a high rate of reocclusion.
 - Thrombolysis is more successful when combined with target lesion endovascular/surgical correction to improve long-term patency rates and to decrease the amputation rate.^[10]

- Following successful lysis, correction of the underlying problem, possibly including angioplasty or operation, may be required.
- If a limb is irreversibly ischaemic, amputation will be required.

Other management^[3]

- Reduction in the rate of deterioration of underlying cardiovascular disease includes regular exercise, smoking cessation, treating hypertension and hyperlipidaemia, and improving diabetes control.
- Management of associated and underlying problems: treat anaemia or polycythaemia, cardiac disease.
- Low-dose aspirin or clopidogrel. Warfarin if otherwise indicated.
- Angiotensin-converting enzyme (ACE) inhibitors have been shown to reduce morbidity and mortality due to cardiovascular disease in patients with peripheral arterial disease by 25%.
- Statins to reduce total and low-density lipoprotein (LDL) cholesterol.

Complications of limb ischaemia^[11] ^[12]

- Reperfusion injury may cause more damage than the initial ischaemia:
 - Neutrophils migrate into the reperfused tissue, causing injury.
 - Limb swelling due to increased capillary permeability may cause a [compartment syndrome](#).
 - Leakage from damaged cells may cause acidosis and hyperkalaemia (leading to cardiac arrhythmias) and myoglobinaemia (leading to acute tubular necrosis).
- Chronic pain syndromes: acute complete ischaemia can lead to peripheral nerve injury.

Prognosis

- Complete acute ischaemia will lead to extensive tissue necrosis within six hours unless the limb is surgically revascularised.^[7]

- The mortality associated with acute ischaemia remains high, as thrombosis or embolism is not infrequently a pre-terminal event in patients dying from other causes, such as heart failure.
- A Cochrane review of surgery versus thrombolysis found no overall difference in limb salvage or death at one year between initial surgery and initial thrombolysis. Thrombolysis may be associated with a higher risk of ongoing limb ischaemia and haemorrhagic complications including stroke. The higher risk of complications must be balanced against risks of surgery in each person. ^[13]
- Quality of life (QoL) after open surgery or endovascular intervention appears to be similar. Revascularisation may provide modest benefits and amputation or conservative management maintain QoL. ^[14] However, certainty of evidence is generally low or very low, and interpretation is hampered by significant heterogeneity .
- Surgical treatment of acute limb ischaemia has a 30-day mortality rate of 15–25%, mainly because of related complications. ^[15]

Prevention of limb ischaemia

- Long-term anticoagulation for potential causes of thromboembolism.
- Primary prevention of cardiovascular disease; secondary prevention of cardiovascular disease.

Dr Mary Lowth is an author or the original author of this leaflet.

Further reading

- [Zemaitis MR, Boll JM, Dreyer MA](#); Peripheral Arterial Disease.
- [Smith DA, Lilie CJ](#); Acute Arterial Occlusion.
- [Adams CT, Lakra A](#); Below-Knee Amputation.
- [Martinez-Singh K, Chandra V](#); How to build a limb salvage program. *Semin Vasc Surg.* 2022 Jun;35(2):228–233. doi: 10.1053/j.semvascsurg.2022.04.011. Epub 2022 Apr 26.

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