Acute limb ischaemia

Introduction

Acute limb ischaemia can be a surgical emergency, defined as the sudden loss of perfusion of a limb. The incidence of acute limb ischaemia is thought to be 1–3 per 25 000 people per year (Clason et al, 1989).

Acute limb ischaemia may result in irreversible hypoxic damage and cell death, leading to amputation if not recognized and treated early.

Despite new technological advances in imaging and therapeutic modalities, acute limb ischaemia is associated with a high mortality (10–25%) and morbidity (amputation rate of 15–30%) and is best managed in specialist centres (Clason et al, 1989; Campbell et al, 1998; Norgren et al, 2007; Henke, 2009).

Presentation

Acute limb ischaemia is commonly associated with sudden onset of limb pain and classically presents with any of the '6 Ps' (*Figure 1*). Initially, arterial spasm produces a pale limb (white). After 4–8 hours, vasodilation allows deoxygenated blood to enter the limb, which then appears light purple or blue and mottled. On pressure the mottling may blanch. With further ischaemia, the leg will become darker and the mottling will become fixed. At this stage the acute limb ischaemia is irreversible (*Figure 2*).

Revascularization of a longstanding ischaemic limb allows oxygenated blood to enter the area, resulting in a release of oxygen free radicals into the systemic circulation. This may lead to acidosis, further tissue damage, renal failure and even death, and is known as reperfusion injury (Rutherford, 2009).

Figure 1. 6 Ps of acute limb ischaemia.

1. Pale
2. Pulseless
3. Painful
4. Paralysed
5. Paraesthesia
6. Perishingly cold

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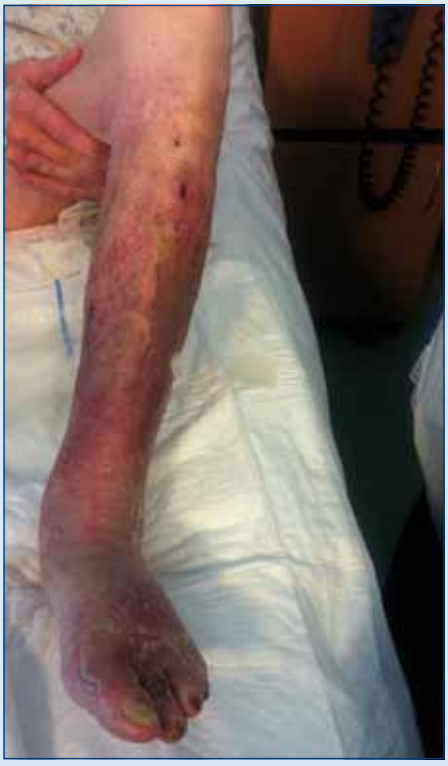
Pathogenesis

The underlying aetiology of acute limb ischaemia may be the result of arterial thrombosis in situ (85%) or embolic occlusion (15%) of grafts or native vessels (Walker, 2009).

Thrombosis in situ occurs as a result of rupture of an already present atherosclerotic plaque with subsequent aggregation of platelets, resulting in occlusion of a vessel. Atherosclerosis occurs most commonly at sites of turbulent flow, such as vessel bifurcations. Initially, a fatty streak is formed as lipid is taken up by intramural macrophages, which then become known as 'foam cells.' Death of these cells results in the deposition of their lipid stores into the intramural layer causing fibrosis and plaque formation. Thrombus formation over a plaque is usually asymptomatic but may narrow or occlude a vessel causing chronic ischaemia and infarction (Kumar et al, 2010). Atheroembolism may cause acute ischaemia downstream of the plaque. Aneurysms, e.g. abdominal aortic, femoral or popliteal, can occlude and cause ischaemia or send emboli distal into the foot.

Figure 2. Acute on chronic ischaemia.



Thrombo-emboli most often originate from the heart (80–90%) (Abbott et al, 1982). This may be a result of arrhythmia, most commonly atrial fibrillation, abnormal wall function or aneurysmal dilatation after myocardial infarction. These result in stagnation of blood and hence clot formation. Artificial valves and damaged native valves (following endocarditis or rheumatic fever) can also act as a nidus for vegetation formation, from which emboli can originate. Rarer embolic occlusion may result from an atrial myxoma or proximal aneurysm.

Differential diagnoses

Acute limb ischaemia is often easily diagnosed through detailed history taking and examination. However, it can be confused with other pathological entities if signs are atypical or examination is incomplete. The latter is common in medicolegal cases surrounding acute limb ischaemia, where complete examination of peripheral pulses was not performed or documented (Campbell et al, 2002). Other diagnoses that should be considered include deep venous thrombosis, compressive neuropathy, vasospasm (e.g. after medication use) and spinal cord pathology.

The National Patient Safety Agency have highlighted an incident where acute limb ischaemia was misdiagnosed as a 'spinal disc problem' and the patient was wrongfully referred to neurosurgery, leading to a 27-hour delay to revascularization and finally amputation (National Patient Safety Agency, 2011). The National Reporting and Learning Service also report 51 incidents in the UK between April

2010 and March 2011 relating to delays in the diagnosis and treatment of acute limb ischaemia (National Patient Safety Agency, 2011).

Diagnosis of acute limb ischaemia

Acute limb ischaemia is a clinical diagnosis based on history and examination of the affected limb. The history should elucidate: time since onset, current and prior functional capability of the affected limbs, any sensory or motor disturbance, background of peripheral vascular disease (claudication, previous ischaemia and surgery), trauma, comorbid disease (diabetes, hypertension, malignancy, arrhythmia and aneurysm), other risk factors for acute limb ischaemia (*Table 1*) and any contraindications to thrombolysis.

The history of the events leading up to the presentation is very important to allow the correct diagnosis. As can be seen from *Table 2* a short history with no preceding claudication would suggest an acute embolus, whereas a long history of claudication in the affected limb would suggest an acute thrombosis in situ. This is very important as subsequent treatment options may differ depending on the diagnosis.

The severity of acute limb ischaemia is based on the findings from physical examination, namely rest pain, sensory disturbance or loss, and muscle weakness. The Rutherford criteria classes acute limb ischaemia into four categories (*Table 3*) (Rutherford, 2009). Complete physical assessment should include examination of the cardiovascular system (e.g. for arrhythmia or murmur), gastrointestinal system (e.g. for aneurysm or bruit), peripheral pulses (including Doppler ultrasound assessment) and a neurological examination (for sensory disturbance or sensory level in cases of spinal cord pathology).

Table 1. Risk factors for acute limb ischaemia

Diabetes
Hypertension
Hypercholesterolaemia
Smoking
Pre-existing peripheral vascular disease
Abdominal aortic aneurysm or popliteal aneurysm
Atrial fibrillation

Table 2. Cause of acute limb ischaemia based on history

Cause	History
Acute embolus	Sudden onset of leg pain
	No history of claudication
	Source of embolus, e.g. atrial fibrillation, recent myocardial infarction
	Palpable pulses in contralateral limb
	Proximal aneurysm
Acute thrombosis	Pre-existing claudication with sudden deterioration
	No source of embolus
	Absent pulses in contralateral limb
	Widespread vascular disease

Management

As for all emergencies, management should start with resuscitation using an 'ABC' approach by providing appropriate oxygen, venous access and intravenous fluids. In all cases unless contraindicated, anticoagulation with 5000 units unfractionated heparin bolus should be administered without delay (Norgren et al, 2007) (*Table 4*). This is done to prevent further ischaemia through thrombus propagation and collateral occlusion (Walker, 2009). An infusion should then be started at 1000 units/hr. The activated partial thromboplastin time should be monitored and the infusion adjusted to maintain an activated partial thromboplastin time ratio of 2–2.5 (Clagett and Krupski, 1995). Adequate analgesia should also be provided.

Further management depends on the cause of the acute limb ischaemia. An acute embolic event requires either invasive exploration with an embolectomy in the operating theatre or thrombolysis in the interventional suite. An acute thrombosis requires an angiogram with or without thrombolysis and an angioplasty. Both may require bypass surgery.

Timing of further management will be dictated by whether the limb is viable (I), threatened (IIA and IIB) or non-viable (III) (*Table 3*).

Table 4. Absolute contraindications to thrombolysis*

Intracranial neoplasm
Haemorrhagic stroke
Active bleeding (e.g. varices)
Bleeding diathesis
Aortic dissection

*this is not an exhaustive list and clinical judgement (i.e. risks vs benefits) should be used in conjunction when considering contraindications to thrombolysis

Table 3. Classification of acute limb ischaemia based on the Rutherford criteria

Category	Limb	Foot colour	Sensory loss	Motor weakness	Arterial Doppler	Prognosis
I	Viable	Blue/white	None	None	Present	Not immediately threatened
IIA	Threatened	Blue/white	Minimal	None	Occasional	Salvageable with prompt treatment
IIB	Severely threatened	Blue/white/mottling	Rest pain	Mild to moderate	Absent	Salvageable with immediate treatment
III	Irreversible ischaemia	Fixed mottling	Anaesthetic	Paralysis	Absent	May require primary amputation

From Rutherford (2009)

Patients in categories I and IIA are felt to be stable enough to undergo imaging investigation before revascularization (*Figure 3*). Arteriography will allow further clarification of the site of occlusion, the aetiology or confirm a suspected diagnosis. The distal circulation can also be visualized. These findings will help choose the most effective mode of revascularization.

Revascularization is the end goal in the treatment of acute limb ischaemia and can be either endovascular or surgical. The method of revascularization will depend on the site, severity and cause of vessel occlusion as well as the patient's performance status. A Cochrane review found that with the current evidence base, surgery and thrombolysis (recombinant tissue plasminogen activator and urokinase) are equally effective in treating acute limb ischaemia (Berridge et al, 2002). No difference was seen in limb salvage rates at 1 year. However, thrombolysis was associated with an increased risk of ongoing limb ischaemia and bleeding (e.g. stroke – 1.3% *vs* 0%, and major haemorrhage – 8% *vs* 3.3%).

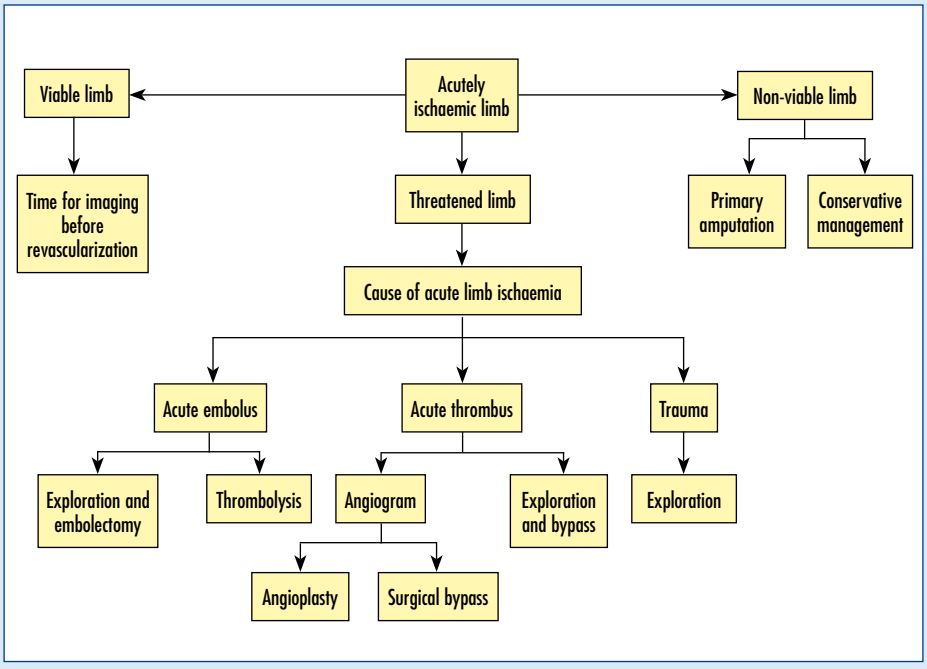
Endovascular management includes thrombolysis and percutaneous mechanical thrombectomy (Lyden, 2010). Catheter-directed thrombolysis is often used in mild ischaemia (I and IIA). Reperfusion occurs at a lower pressure, which may reduce the incidence or severity of reperfusion injury when compared to open surgery. Percutaneous mechanical thrombectomy is often used with catheter-directed thrombolysis to hasten clot breakdown. There are a number of variations on the technique (catheter suction thrombectomy, thrombus fragmentation, isolated pharmacomechanical thrombolysis and ultrasound-accelerated thrombolysis) (Walker, 2009; Lyden, 2010), but the evidence for their use in acute limb ischaemia is limited.

Surgical management includes embolectomy, bypass procedures and amputation. An exploration of the brachial or femoral artery with embolectomy can be performed quickly under local or general anaesthesia. This rapidly allows reperfusion of the limb. Postoperatively the patient should remain on a heparin infusion unless contraindicated.

Bypass with autologous vein harvest graft (commonly the long saphenous vein) or synthetic polytetrafluoroethylene graft is usually undertaken when occlusion is proximal and there is sufficient distal run-off. Long-term patency is better with vein grafts (5-year patency 76% *vs* 52%) (Klinkert et al, 2003; Norgren et al, 2007).

Amputation is indicated in non-viable limb ischaemia (III) and can be life-saving. Up to a third of patients with acute limb ischaemia will require amputation. There are a number of factors that should be considered before embarking on limb salvage or amputation (*Table 5*).

Figure 3. Algorithm of management of a patient with acute limb ischaemia.



Whichever mode of revascularization is used the acute and long-term success will be dictated by clinical factors (comorbid disease – diabetes and renal disease, smoking and degree of systemic disease) and anatomical factors (proximal or distal lesions, number of lesions treated, and quality of inflow and outflow vessels). Discussion should take place regarding the likelihood of successful therapy and long-term outcome.

Complications

Vigilance should be maintained following the acute management of acute limb ischaemia for progression of ischaemia and also complications of treatment. The latter can be as devastating as the acute limb ischaemia itself.

Reperfusion injury is the term given to the further damage to ischaemic tissues on reintroduction of perfusion (Girn et al, 2007). This occurs when oxygen free radicals are released that cause an inflammatory response resulting in cell breakdown and exacerbation of ischaemia. This can cause limb swelling locally and can systemically result in hyperkalaemia, systemic inflammatory response syndrome and multiorgan failure.

In the early period following revascularization, compartment syndrome may also develop (Tiwari et al, 2002). Here, increased vascular permeability causes increased interstitial oedema, which overcomes perfusion pressures within an anatomical compartment. It should be suspected when a patient complains of pain disproportionate to the clinical signs, abnormal sensation and swelling. Intracompartmental pressure monitoring may help diagnosis, with fasciotomy indicated when compartment pressures exceed 20 mmHg.

Table 5. Factors that should be considered in amputation for acute limb ischaemia

Likely success of revascularization
Prior functional status or performance status
Poor wound healing or chronic ulceration
Co-morbid illness
Level of amputation (e.g. above or below knee)

Compartment syndrome is an emergency and a fasciotomy must be performed immediately. Occasionally if the limb has been underperfused for a long time a fasciotomy may be performed at the time of revascularization. Fasciotomy is performed in 5–25% of patients with acute limb ischaemia (Eliason et al, 2003; Norgren et al, 2007). With prolonged compartment syndrome there may be infarction of muscle and myoglobinuria may cause acute kidney injury. Aggressive fluid resuscitation is advised in this instance to provide renal protection. Measurement of serum creatinine kinase levels may also act as a marker for impending renal failure (Brow et al, 1999).

Following the acute management of acute limb ischaemia and prevention of acute complications the focus should shift to determining a cause and secondary prevention. *Table 6* outlines possible investigations that can be used to find the cause for the acute limb ischaemia.

Conclusions

Acute limb ischaemia is a surgical emergency that relies on early recognition and management in a specialist centre for best outcomes. Treatment modalities of choice remain surgery, thrombolysis and angioplasty. The ideal modality is based on the history of the preceding events. **BJHM**

Conflict of interest: none.

Abbott WM, Maloney RD, McCabe CC, Lee CE, Wirthlin LS (1982) Arterial embolism: a 44 year perspective. *Am J Surg* **143**(4): 460–4

Berridge DC, Kessel DO, Robertson I (2002) Surgery versus thrombolysis for initial management of acute limb ischaemia. *Cochrane Database Syst Rev* **1**: CD002784

Brow TD, Kakkar VV, Das SK (1999) The significance of creatine kinase in cardiac patients with acute limb ischaemia. *J Cardiovasc Surg (Torino)* **40**(5): 637–44

Campbell WB, Ridler BM, Szymanska TH (1998) Current management of acute leg ischaemia: results of an audit by the Vascular Surgical Society of Great Britain and Ireland. *Br J Surg* **85**(11): 1498–503

Campbell WB, France F, Goodwin HM; Research and Audit Committee of the Vascular Surgical Society of Great Britain and Ireland (2002) Medicolegal claims in vascular surgery. *Ann R Coll Surg Engl* **84**(3): 181–4

Clagett GP, Krupski WC (1995) Antithrombotic therapy in peripheral arterial occlusive disease. *Chest* **108:** 431s–443s

Clason AE, Stonebridge PA, Duncan AJ, Nolan B, Jenkins AM, Ruckley CV (1989) Morbidity and mortality in acute lower limb ischaemia: a 5-year review. *Eur J Vasc Surg* **3**(4): 339–43

Eliason JL, Wainess RM, Proctor MC et al (2003) A national and single institutional experience in the contemporary treatment of acute lower extremity ischemia. *Ann Surg* **238**(3): 382–90

Girn HR, Ahilathirunayagam S, Mavor AI, Homer-Vanniasinkam S (2007) Reperfusion syndrome: cellular mechanisms of microvascular dysfunction and potential therapeutic strategies. *Vasc Endovascular Surg* **41**(4): 277–93

Henke PK (2009) Contemporary management of acute limb ischemia: factors associated with amputation and in-hospital mortality. *Semin Vasc Surg* **22**(1): 34–40

Klinkert P, van Dijk PJ, Breslau PJ (2003) Polytetrafluoroethylene femorotibial bypass grafting: 5-year patency and limb salvage. *Ann Vasc Surg* **17**(5): 486–91

Kumar V, Fausto N, Abbas A (2010) *Robbins & Cotran Pathologic Basis of Disease.* 7th edn. WB Saunders Company, Philadelphia

Lyden SP (2010) Endovascular treatment of acute limb ischemia: review of current plasminogen activators and mechanical thrombectomy devices. *Perspect Vasc Surg Endovasc Ther* **22**(4): 219–22

National Patient Safety Agency (2011) Early detection and treatment of acute limb ischaemia. www.nrls.npsa.nhs.uk/resources/?entryid45=130172 (accessed 5 February 2012)

Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group (2007) Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg* **45**(Suppl S): S5–67

Rutherford RB (2009) Clinical staging of acute limb ischemia as the basis for choice of revascularization method: when and how to intervene. *Semin Vasc Surg* **22**(1): 5–9

Tiwari A, Haq AI, Myint F, Hamilton G (2002) Acute compartment syndromes. *Br J Surg* **89**(4): 397–412

Walker TG (2009) Acute limb ischemia. *Tech Vasc Interv Radiol* **12**(2): 117–29

Table 6. Investigating the cause of acute limb ischaemia

Embolic	Electrocardiograph – arrhythmia, previous myocardial infarction
	24-hour electrocardiograph – paroxysmal arrhythmia
	Echocardiogram – ventricle wall dysfunction, damaged valves
	Abdominal ultrasound scan – abdominal aortic aneurysm
	Abdominal computed tomography – abdominal aortic aneurysm
Thrombosis in situ	Coagulopathy screen – thrombophilia
	Tumour markers
	Carotid Doppler
	Angiogram
	Glucose, glycated haemoglobin

TOP TIPS

- The 6 Ps act as a memory aid to diagnosing acute limb ischemia but do not all have to feature in the presentation.
- Pain does not always accompany an ischaemic limb. Patients with diabetic neuropathy are at a high risk for painless acute limb ischaemia.
- If you are unsure about the presence of a pulse use a handheld Doppler (often available on surgical wards).
- If in doubt, it is safer to inform a senior or refer the patient to the vascular team who can appropriately assess and categorize the status of the limb.

KEY POINTS

- A thorough examination of the peripheral vascular system is the most important part of the assessment of a patient with possible acute limb ischaemia.
- Acute limb ischaemia is best treated in a specialist centre and referrals should be made as soon as possible, minimizing the time to reperfusion.
- The overall management of the patient will depend on the viability of the limb at presentation and whether the cause is embolic occlusion or thrombosis in situ.
- Resulting complications are rare but life threatening and regular review is important to ensure a safe recovery after reperfusion.