Acute and chronic limb ischaemia

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Abstract

Acute (ALI) and chronic limb ischaemic (CLI) make up a major part of the workload of vascular surgeons and carry considerable morbidity and mortality. Peripheral artery disease (PAD) is the major cause of these conditions. Diagnosis of these conditions involves proper use of imaging including duplex ultrasound, computed tomography angiography (CTA), magnetic resonance angiography (MRA), as well as invasive techniques like digital subtraction angiography (DSA). Management ranges from conservative techniques, the mainstay of management in intermittent claudication (IC), with medical optimization, through to endovascular and open revascularization techniques in CLI and ALI. Finally where no revascularization options exist, primary amputation or palliation must be considered.

Keywords Acute limb ischaemia; angioplasty; arterial bypass; chronic limb ischaemia; limb ischaemia; peripheral artery disease

Chronic limb ischaemia

Chronic lower limb ischaemia can exist as a continuum from asymptomatic atherosclerotic peripheral arterial disease (PAD), through intermittent claudication (IC) to limb threatening critical limb ischaemia (CLI). Worldwide prevalence of PVD has been estimated to be approximately 10%, with incidence increasing to 15–20% in the over 70s.[1]

The cost of CLI to the individual and society can be great with an annual cost estimated within the UK in 1995 to be 200 million.[2] This will only rise with the increase in diabetes (Figure 1) and an ageing population.

Risk factors

Risk factors for chronic limb ischaemic can be divided into modifiable and non-modifiable, these are listed in Table 1.

Although there is good evidence that raised homocysteine levels are an independent risk factor for PAD, a large Cochrane systematic review found that treatment of homocysteinaemia in kidney transplant patients led to no decrease in cardiovascular mortality. The early management of PAD in patients with both end-stage renal disease and diabetes is critical, with high amputation rates. Early treatment is important as the presence of a foot ulcer itself, may contribute to the development or progression of CKD.[3]

Increased risk of PAD is also seen with raised haemocrit, high plasma fibrinogen levels and chronic renal insufficiency, though there is limited evidence this is causal.

Intermittent claudication

Intermittent claudication is a cramping muscular pain in the lower limbs induced by exercise, which is relieved by rest. The pain is normally induced after walking a defined distance, unless tissue oxygen demand is increased due to an incline or increased walking speed. The pain is caused by insufficient oxygen delivery to the tissues, and the location of the pain is dictated by the distribution of the disease. The most frequent site affected is the SFA, and claudication pain is often reported in the calf, as this is the area immediately distal to the disease. Pain can also be reported in the thighs and buttocks from aorto-iliac disease, or foot from crural vessel disease.

The symptoms of intermittent claudication only tend to progress in 20–25% of patients, with an overall amputation risk of only 1–3%.[4]

Management

Conservative management of IC is the mainstay of treatment, and this usually consists of lifestyle changes and medical interventions.

Evidence suggests that supervised exercise programs yield better functional outcomes then unsupervised programs,[5] although this does not appear to confer any change to quality of life in these patients. NICE recommends that all patients with IC should be offered a supervised exercise program. Intermittent pneumatic compression of the lower limbs, namely foot and calf, may also be of some limited benefit.

The medical management of most patients with IC involves antiplatelet drugs and statins. Antiplatelets have not been shown to improve symptoms in these patients, but due to the high risk of concomitant cardiovascular and cerebrovascular events, aspirin or clopidogrel are recommended. Clopidogrel has been shown to be superior to aspirin in IC patients. The concept of antiplatelet resistance has been raised in some studies, showing that 75% of patients are resistant to the effects of clopidogrel and 28.5% to aspirin.[6] This knowledge may lead to more bespoke antiplatelet drug treatments of PAD patients in the future. Statins have also been shown to result in an 18% reduction in rates of adverse limb outcomes in patients with PAD.[7]

Symptomatic treatment of IC can involve the use of cilostazol, a phosphodiesterase type 3 inhibitor, licenced in the UK and USA. It has been shown to improve maximum and pain-free treadmill walking distances and quality of life. Naftidrofuryl is a serotonin 5-hydroxytrytamine 2 receptor antagonist, and has also been shown, in meta-analysis, to have provide symptomatic improvement without serious complications. The use of both these drugs is limited due to restricted follow up and cost effectiveness.

The surgical management of IC patients is limited only to those who have failed conservative treatment. This surgical management can be further divided into open and endovascular.

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Figure 1 (**a**) Acute presentation of a ischaemic and infected foot in a patient with diabetes. (**b**) Outcome after amputation in a similar patient to that described in (**a**).

Endovascular strategies are used in iliac disease, whereas surgical techniques have been shown to be more durable in the infrainguinal region in patients that are fit for this. Though it should be noted that endovascular approaches appear superior to bypass surgery with prosthetic material.[8] There is a 1.9—2.9% risk of major complications with endovascular surgery in PAD patients.

Critical limb ischaemia

Critical limb ischaemia has been defined as ulcers, gangrene or ischaemic rest pain for more than 2 weeks, attributed to objectively proven arterial occlusive disease.[4]

The importance of diagnosis and treatment of critical limb ischaemia is clear, given the 2-year mortality rate of between 26% and 31%.[9]

Causes and clinical features

As with all forms of PAD, CLI is usually caused by atherosclerosis. Patients with diabetes are four times more likely to develop disease requiring amputation (Figure 1). Patients with CLI often have longer, multiple stenoses or occlusive segments of arterial inflow, when compared to IC patients.

Physical examination in these patients allows the presence or absence of pulses to dictate the anticipated level of obstructions. It may also reveal a positive Buerger's test (pallor on elevation, with rubor on dependency, secondary to reactive hyperaemia), skin changes at the extremes of disease, tissue loss and necrosis (Figure 2).

Risk factors for chronic limb ischaemia

Modifiable risk factors	Non-modifiable risk factors
Smoking	Age
Diabetes mellitus control	Gender
Hypertension	Ethnicity
Hyperlipidaemia	
Hypercoagulability	

Table 1

Investigation and imaging

Investigation should focus on two main areas: medical optimization of the patient with diabetic control, antiplatelets, and statins, and determination of the level of disease and suitability for endovascular or open intervention. The main diagnostic modalities are duplex ultrasound, digital subtraction angiography (DSA) (Figure 3), computerized tomographic angiography (CTA) and magnetic resonance angiography (MRA).

Management

As with IC, management can be divided in to conservative, medical and surgical, although in patients with CLI, conservative management is usually only reserved for those patients who cannot tolerate an intervention.

The medical management of CLI is for the most part similar to IC. Intravenous administration of iloprost or prostaglandin E-1 for 7—28 days may allow ulcer healing or reduction in ischaemic pain.[10]

The role of surgical management is to reestablish in-line flow to the affected areas. Once again this can be achieved using either endovascular or open means. The BASIL trial showed that in patients who have infrainguinal disease and a life expectancy greater then 2 years, bypass surgery is recommended over endovascular treatment. It should be noted, however, that this trial was performed in the era before drug-eluting technology and the development of dedicated stents. The PARADISE trial was a prospective non-randomized trial that investigated the efficacy and safety of drug eluting stents and showed a 6% major amputation rate, which is better then rates reported in balloon angioplasty and bypass surgery (18% was reported in BASIL). The clinical equipoise that is seen in some of these patients will