OPEN ACCESS TEXTBOOK OF GENERAL SURGERY

CLAUDICATION OF THE LOWER LIMB

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INTRODUCTION

Peripheral arterial disease (PAD) is a chronic atherothrombotic occlusive disorder of the peripheral circulation that predominantly affects the large, medium-sized and small arteries of the lower limbs. The prevalence of PAD ranges from 3% to 10% overall, increasing to 15 - 20% in patients over 70 years.

Classic risk factors for PAD include age over 55 years, smoking, diabetes mellitus, hypercholesterolaemia, hypertension, obesity and sedentary lifestyle.

Patients with PAD may be asymptomatic or can present with intermittent claudication (IC) and/or critical limb ischaemia (CLI). Patients with CLI have ankle pressures below 50 mmHg and/or toe pressures below 30 mmHg, ischaemic rest pain and/or tissue necrosis (skin ulcer or gangrene).

PAD may be classified into 3 segmental types depending on the distribution of the occlusive disease (Table I).

TABLE 1 : CLINICAL CATEGORISATION OF PAD

Clinical Category	Femoral	Popliteal	Pedal
Aorto-iliac disease	+ / 0	**0**	**0**
Femoro-popliteal disease	**++**	**0**	**0**
Tibio-peroneal disease	**++**	**++**	**0**

++ Good bounding pulses

+ Weak diminished pulses

0 Absent pulses

Patients with CLI have multi-segment disease as a rule. PAD is not a benign disease; the risk of mortality in patients with established PAD secondary to cardiovascular and cerebrovascular events far outweighs the 4% risk of a major amputation over 10 years. Asymptomatic patients with PAD have an approximately 10-year shorter life expectancy than patients without PAD. Patients with IC have a 10-year mortality rate approaching 50%. Patients with CLI have 1- and 5-year mortality rates approaching 25% and 50% respectively.

The modern evidence-based approach to treatment of PAD therefore emphasises lifestyle modification, control of risk factors, antiplatelet therapy, lipid-lowering agents and foot care. Patients with CLI will, in addition, need some form of surgical therapy: amputation, percutaneous transluminal angioplasty (PTA), peripheral stent or bypass procedure.

INTERMITTENT CLAUDICATION OF THE LOWER LIMBS

IC is defined as an exertional symptom affecting muscles of the lower limb secondary to PAD (Tables II and III). IC may rarely be associated with chronic exertional syndromes (such as entrapment syndromes, anterior compartment syndromes, etc.) in young patients.

Table 2. Classification of claudication

- Intermittent claudication (associated with PAD)
- Spinal claudication
- Venous claudication
- 'Atypical' claudication

Table 3: Stratification of PAD			
Fontaine		**Rutherford**	
Stage	**Clinical**	**Category**	**Clinical**
I	Asymptomatic	**0**	Asymptomatic
IIa	Mild claudication (CD >50 meters)	**1**	Mild claudication (completes treadmill test/ankle pressures >50 mmHg post treadmill test)
IIb	Moderate to severe claudication	**2**	2 Moderate claudication (between category 1 and 3) (CD <50 meters)
III	Ischaemic rest pain	**3**	Severe claudication (unable to complete treadmill test/ankle pressures <50 mmHg post treadmill test)
IV	Ulceration / gangrene	**4**	Ischaemic rest pain
CD = claudication distance.		**5**	Minor tissue loss
		6	Major tissue loss

Patients may describe pain, lameness, discomfort, cramping or stiffness involving the ipsilateral calf muscles and, to a lesser extent, the thigh muscles and buttocks. Diabetic patients with PAD may rarely report foot claudication. The combination of aorto-iliac disease, impotence and buttock claudication is known as the Leriche syndrome.

Patients with IC typically have no problems getting up from a recumbent position, but experience claudication on walking, especially up inclines. Relief of symptoms typically follows 3 - 5 minutes of resting (standing). The claudication distance (walking distance at which severe claudication occurs) can be used to assess the severity of claudication. Only 1 in 10 patients with PAD will give an accurate description of IC. Spinal claudication in this elderly cohort may confound the evaluation of patients with PAD. Patients with spinal claudication, typically associated with spinal stenosis, have pain on getting up, have unusually long claudication distances, may actually improve when walking up inclines and generally improve after 20 – 30 minutes of rest only in a customary seated or lying-down position. Patients with chronic venous disorders may also describe venous claudication (typically in patients with significant venous reflux and occlusive disease). Patients may occasionally present with 'atypical' claudication due to a host of other pathologies (Table IV).

There is a fourfold increase in the risk of IC in smokers, compared with non-smokers with PAD. In patients with PAD there is a twofold increase in IC in diabetic patients compared with non-diabetic patients.

The natural history of IC is generally benign. Approximately 50% of patients with PAD will have stable claudication and only 25% of patients will report progressive claudication. Progression in approximately 7 - 9% will be seen in the first year following diagnosis, stabilising to an annual rate of 2 - 3% thereafter. Only 1 - 3 % of these patients will progress to CLI. The risk of amputation in patients with IC is small and ranges from 1% to 3.3% over a 5-year period. A higher risk of amputation is generally applicable to diabetic patients. The best predictor of progressive IC (i.e. those needing revascularisation or amputation) is an ankle-brachial index (ABI = ratio of ankle pressure over best brachial blood pressure) of less than 0.50. Patients with IC and ankle pressures of 40 - 60 mmHg have an 8.5% annual risk of progression to CLI or limb loss.

Table 4: Differential diagnosis of the painful lower limb
Spinal stenosis
Sciatica
Lumbar spondylosis
Arthropathy (osteo, rheumatoid, gout, etc.)
Varicose veins
Deep-vein thrombosis/post-phlebitic syndrome
Peripheral neuropathy (diabetic, alcohol- associated, etc.)
Chronic regional pain syndromes
Chronic exertional syndromes (anterior compartment syndrome, etc.)
Restless leg syndrome
Infections (cellulitis, tinea pedis, etc.)
Other vascular pathologies (popliteal aneurysms, iliac artery syndrome of the cyclist, etc.)

INVESTIGATIONS

Investigations that may be requested at baseline aimed at facilitating management decisions are listed in Table V. Diagnostic investigations are generally informed by the patient's history of classic or 'atypical' IC, stable or progressive IC, lifestyle-limiting nature of the IC, modifiable risk factors, extent of co-morbidities and level of mobility and effort tolerance. Patients with 'atypical' claudication may require skeletal X-rays, an arthritis screen, venous Duplex ultrasound, etc., where appropriate.

Table 5: Baseline evaluation of the claudicant
Full blood count
Fasting lipid profile
Fasting blood glucose/HbA1C (glycosylated haemoglobin)
Serum urea, creatinine and electrolytes
Blood clotting profile
Additional tests to be based on clinical suspicion, e.g. a thrombophilia profile in young patients with PAD, etc.

Lower-limb exercise arterial Doppler test

Hand-held arterial Doppler testing at rest is inappropriate for exertional symptoms such as IC. Exercise arterial Dopplers are indicated for the appraisal of claudication. The arterial Doppler testing measures brachial, popliteal and ankle pressures and is used to calculate the ankle-brachial index (ABI = ankle pressure/best brachial pressure). This should be performed at rest (after a minimum of 10 minutes of rest) and following a period of exercise (standard treadmill test at a speed of 3.2 kph and an incline of 10 degrees for up to 5 minutes). Exercise tests are clearly not possible or appropriate in patients with poor cardiopulmonary function, arthritis, etc. and these patients should therefore be medically optimised or treated in other ways before proceeding to further investigations for IC.

Patients with IC generally have a resting ABI of between 0.5 and 0.9. These patients generally have a significant drop in ankle pressures (more than 15 mmHg decrease) or of ABIs (over 15 - 20% decrease) on exercise testing. Toe pressure measurements may be appropriate in patients with extensively calcified crural arteries (diabetic patients, patients with chronic renal failure, etc.)

Duplex Doppler arteriography

Duplex ultrasound evaluation of the abdominal aorta, iliac and infrainguinal arteries is only appropriate in patients who are candidates for revascularisation. Duplex arteriography is a non-invasive investigation providing a wealth of anatomical and functional data. This includes femoral waveform analyses (at rest and after exercise) to evaluate suprainguinal disease, seeing the anatomical location and extent of arterial stenosis and occlusions, recording any associated aneurysmal

disease, reporting the degree of vascular calcification and grading the severity of stenotic lesions. This test is fairly accurate for the femoro-popliteal segments but often suffers in imaging the aorto-iliac segments in obese patients or patients with extensive intra-abdominal gas. For the latter, a fasting Duplex arteriography may be more fruitful. This modality is also less accurate in imaging extensively calcified
crural arteries, especially in diabetic patients. This modality also offers other benefits at the same time, such as venous imaging in patients with suspected venous claudication and stigmata of chronic venous disorders, and also for evaluating the suitability of the greater saphenous vein for bypass surgery.

Multi-detector computed tomography angiography (MDCTA)

In patients with an equivocal Duplex arteriography, the MDCTA is a useful non-invasive imaging modality, especially for the aorto-iliac segment. It is fairly accurate compared with Duplex arteriography and conventional angiography. Disadvantages include cost, ionising radiation and contrast-related complications such as contrast nephropathy. The time required to create meaningful images by reconstruction on costly computer workstations is also an issue.

Magnetic resonance angiography (MRA)

Contrast-enhanced MRA (CEMRA) is a reasonable alternative non-invasive imaging modality, especially where evaluation of runoff (crural arteries) is required. Disadvantages include cost, limited availability, over-estimation of stenotic lesions and venous contamination of images. It is contraindicated in claustrophobic patients and in patients with additional hardware (pacemaker, prosthetic valves, etc.), but it has also recently been implicated in causing nephrogenic systemic fibrosis when certain gadolinium-based contract agents are used in patients with renal failure.

Peripheral angiography

Conventional digital subtraction peripheral angiography as a primary imaging modality has largely been superceded by Duplex Doppler arteriography and, to a lesser extent, MDCTA and MRA. Conventional angiography currently is reserved for interventional procedures (peripheral balloon angioplasty, stents, etc.) in patients with IC or where the other techniques fail or are contraindicated.

MANAGEMENT

The management of the patient with PAD and IC involves a two-pronged approach: risk factor management and relief of symptoms of IC.

Evidence-based risk factor management is mandatory in all patients to reduce cardiovascular and cerebrovascular events, to improve life expectancy and to improve quality of life.

Lifestyle modifications include weight loss, dietary manipulation, exercise and smoking cessation strategies.

Pharmacological interventions include optimisation of blood pressure and diabetic glucose control, antiplatelet therapy and lipid-lowering agents. Patients with IC are physically impaired; the treatment goals therefore include providing symptomatic relief, improving exercise performance and facilitating daily function. A structured approach currently should focus on structured exercise, with pharmacotherapy in selected cases. Revascularisation options should be reserved for medically refractory, lifestylelimiting IC.

Medical management

Smoking cessation

The time-honoured advice to 'stop smoking and keep on walking' remains true in current practice. Strategies include behaviour modification, nicotine replacement therapy and buproprion (an antidepressant).

Exercise therapy

There is a considerable body of evidence supporting the clinical benefits of structured exercise programmes in improving pain-free walking distance and maximum walking distance. Exercise training beyond 6 months has been associated with good outcomes. The improvement may relate to better cardiopulmonary profile, improved calf blood flow, metabolic adaptations in muscle and corrections in endothelial dysfunction. The best exercise modality to date remains walking, but other alternatives are also useful (cycling, swimming, upper extremity exercises, etc.). An exercise programme should incorporate approximately 30 minutes of exercise at least 3 times weekly at baseline, progressing to increasing durations. Endurance exercises have been found to be superior to strength training regimens. Supervised centre-based exercise programmes may be superior to unsupervised home-based exercise, but confounding issues affecting compliance exist, including need to travel, distance from home, lack of institutional rehabilitation programmes, cost, etc. Diabetic patients also need appropriate or customised footwear to prevent the development of foot ulcers. Currently a supervised exercise programme remains the standard of care for improving claudication in patients.

Pharmacotherapy

Cilostazol

Cilostazol (Pletal) is a phospodiesterase type III inhibitor with vasodilating, metabolic and antiplatelet properties. It is the only drug, when given at 50 - 100 mg twice daily, that has clinically proven benefits in improving claudication distance to date. It is superior to pentoxifylline (Trental) in efficacy. Sideeffects include headache, diarrhoea and palpitations. It should not be used in patients with congestive cardiac failure.

Naftidrofuryl

Naftidrofuryl, 600 mg daily, is a 5-hydroxytryptamine type II inhibitor that improves muscle metabolism and prevents red-cell and platelet aggregation. It has been used in several European countries for over 20 years and has consistently been shown to be superior to placebo in improving claudication.

Drugs with some supporting evidence for clinical utility include lipid-lowering statin therapy.
Statins have non-lipidlowering mechanisms including improved endothelial function, antiplatelet activity, anti-inflammatory activity, etc. accounting for its efficacy.

Revascularisation

Revascularisation is indicated for lifestylelimiting, medically refractory severe or progressive claudication. Younger patients with occupationally disabling claudication and aorto-iliac (large-vessel) disease, for example, are ideal candidates for revascularisation. Patients with stable mild to moderate claudication, especially associated with infrainguinal PAD, who are not limited by their symptoms, do not warrant an aggressive approach to revascularisation.

Therapeutic modalities include minimally invasive interventional techniques such as balloon PTA, peripheral bare-metal stents, peripheral stentgrafts (stents covered with fabric material) and, rarely, plaquedebulking techniques. Operative modalities include endarterectomy (removing the plaque from occluded or severely stenotic

segments, e.g. aorto-iliac endarterectomy) and bypass surgery utilising vein or prosthetic conduits.

In general, revascularisation procedures have better outcomes in claudicants compared with patients with CLI (with those patients with tissue necrosis having the worst results), and also in patients with suprainguinal PAD as opposed to infrainguinal PAD, and in patients with good vascular run-off.

Balloon angioplasty is indicated for focal stenoses (generally under 5 cm in length) or short occlusions (Figs 1a and 1b). Complications include haematoma, pseudoaneurysm, dissection, vessel perforation, embolisation, thrombotic occlusion and contrast-related problems. Balloon angioplasty is ineffective for ostial or heavily calcified lesions. The older randomised controlled studies, comparing PTA to exercise programmes in patients with mild to moderate claudication, found PTA to be more effective than exercise training in the early stages of the study, but long-term efficacy and durability remained elusive.

The recent MIMIC study reported improved 2-year outcomes in patients treated with supervised exercise and best medical therapy together with iliac and infrainguinal PTA, versus those without PTA. Results were also better for the iliac PTA subgroup.

Peripheral stenting or stentgrafting is generally reserved for 'bailout' salvage of PTA-related complications, sub-optimal PTA results, restenoses, iliac occlusions or long-segment lesions (Fig. 2 a - c). Stents appear to be more durable for suprainguinal lesions compared with infrainguinal lesions. Complications include in-stent stenoses, stent thrombosis and stent fractures.

Surgery is generally reserved for PAD profiles not suitable for interventional techniques, e.g. occluded common and external iliac arteries, long-segment occlusion of the superficial femoral artery, etc. Procedure related complications of surgery include haematoma, wound necrosis, wound sepsis, graft occlusion, graft sepsis, iatrogenic injuries and pseudoaneurysms.

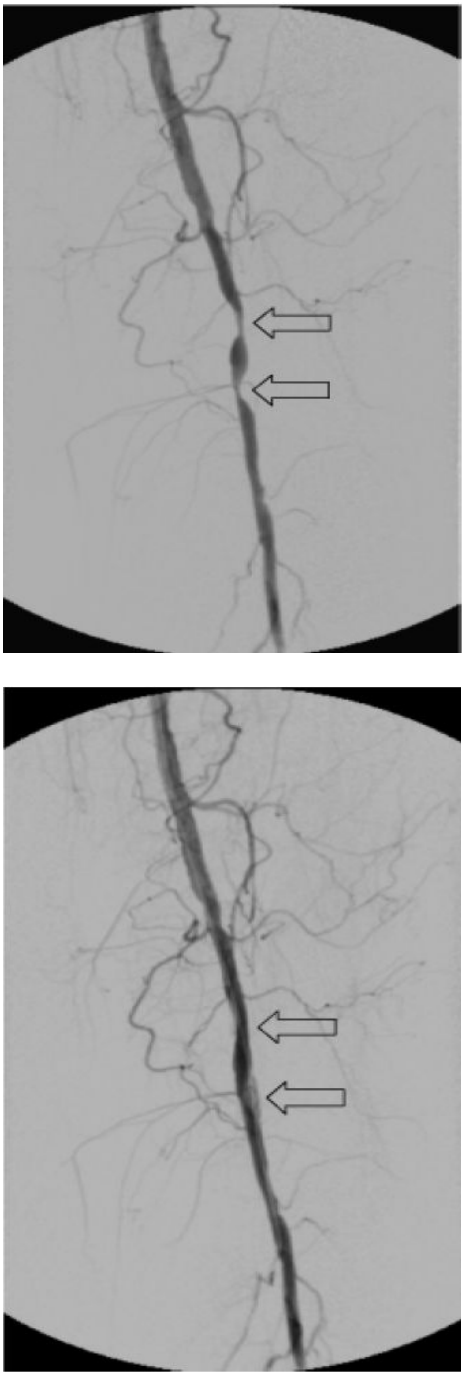

Fig 1 *Distal superficial femoral artery stenoses (a) (arrows) and (b)*

improved lumen (arrows) following angioplasty.

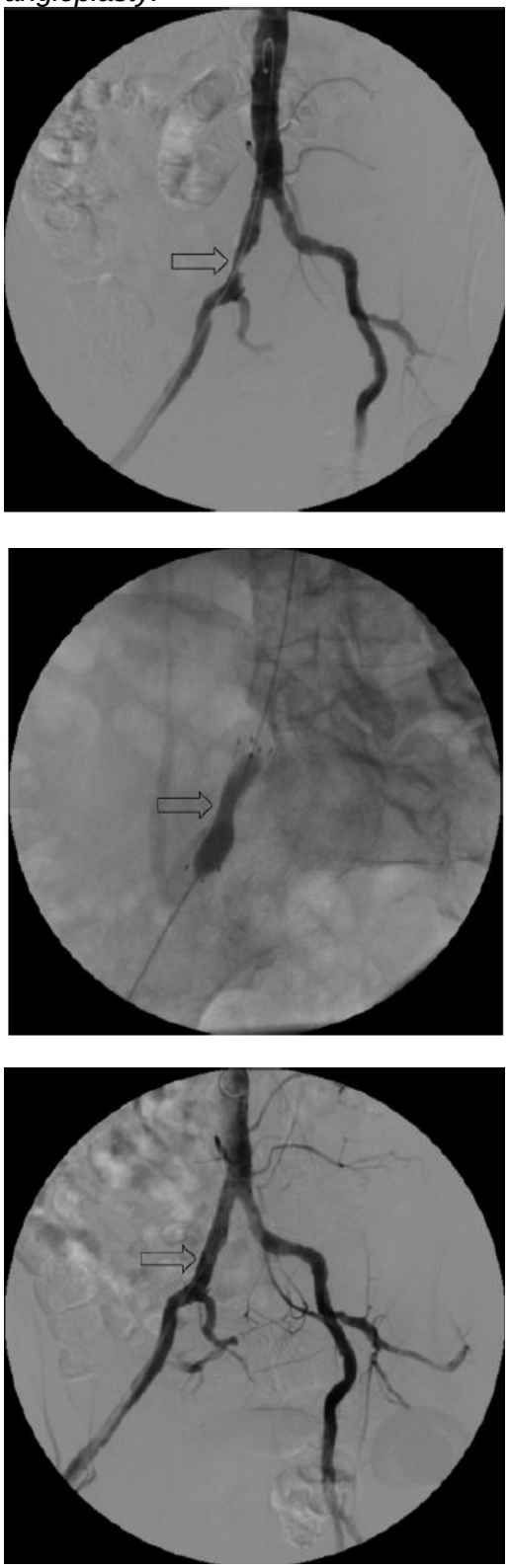

Fig. 2. *Right common iliac artery stenosis (a) (arrow), during balloon expansion of stent (b) (arrow) and after stent improvement (c) (arrow).*