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PRACTICE

EASILY MISSED?

# Chronic limb threatening ischaemia

Kevin Barraclough *general practitioner*[1], Andrew Bradbury *professor of vascular surgery*[2]

[1]Hoyland House, Painswick, UK; [2]University of Birmingham, Birmingham, UK

What you need to know

- Chronic limb threatening ischaemia (CLTI) is a more difficult diagnosis than acute limb ischaemia for the non-specialist because the clinical features can be more subtle and gradual in onset
- It can be easy to mistake CLTI for other conditions, such as cellulitis, gout, or plantar fasciitis
- The affected foot might appear pink or red as a result of reactive hyperaemia when the patient is sitting with the leg down. It is often necessary to elevate the foot on the examination couch to elicit the ischaemic pallor.

A 72 year old ex-smoker with diabetes presents to his general practitioner with a 4 week history of increasing pain in his right foot, worse at night. He finds hanging the leg down provides some relief and he now sleeps in a chair. His leg is increasingly swollen. A cut on his foot has failed to heal and is now red and discharging. On examination, there are no pulses below the femoral artery. The right foot is cold and pale on elevation, and hyperaemic upon dependency. The GP diagnoses chronic limb threatening ischaemia (CLTI) and the patient is seen in the vascular clinic on the same day and admitted. He undergoes imaging and vein bypass surgery. He is discharged a week later free of pain with a healing foot wound.

Peripheral arterial disease affects 10%-20% of patients over 60 and presents in several ways[1-3] (⇓). A quarter of patients have symptoms, typically intermittent claudication, of whom 1%-2% progress to CLTI each year.[2] However, many patients with CLTI do not have a history of intermittent claudication and present de novo with ischaemic rest (night) pain and/or a non-healing foot wound. This is either because they cannot, or choose not to, walk far enough to bring on the symptoms of intermittent claudication and/or because they have diabetic neuropathy. Patients with CLTI are at high risk of amputation and death, and all patients with suspected CLTI should be discussed immediately with a vascular surgeon.

How common is it?
A vascular surgical unit serving a population of one million will typically see up to 250 new patients with chronic limb threatening ischaemia each year; a full time GP might see one each year (on the basis of as yet unpublished data from National Institute for Health Research-Health Technology Assessment (NIHR-HTA) funded BASIL" and BASIL3 studies).

## Features of chronic limb threatening ischaemia

These are

- Ischaemic rest pain, typically worse at night and relieved by hanging the leg down, and/or
- Tissue loss; typically:

- ulceration, usually over pressure areas (toes, metatarsal heads, heel)
- gangrene, usually of the toes.

The pain of CLTI is often worse at night because when asleep, blood pressure falls and the beneficial effect of gravity on lower limb circulation is lost. Typically, the person will be woken in the early hours with pain in the affected foot. Patients usually find that hanging their foot down provides some relief and so might take to sleeping in a chair. But this often leads to dependent oedema, a further reduction in perfusion pressure, and more pain. Next, a minor foot injury (often unrecognised) might lead to a non-healing foot wound that becomes infected.

Of the patients who present to vascular surgeons with a new diagnosis of CLTI, typically 15% are offered primary amputation, 20% are treated conservatively with non-surgical therapy only, and 65% will undergo revascularisation either by means of bypass constructed with a vein usually taken from the leg (25%) or endovascular intervention (40%). Of those who undergo an initially successful revascularisation, approximately 50% have undergone major limb amputation or die within five years.[2]

Correspondence to K Barraclough k.barraclough@btinternet.com

## Why is it missed?

The diagnosis of acute limb ischaemia, which is characterised by the "six Ps" (pain, pallor, pulseless, paraesthesia, paralysis, perishing cold) is usually straightforward.[4] However, CLTI can be easily missed, leading to avoidable limb loss and, not infrequently, high value litigation. Indeed, the authors have been instructed in several hundred medicolegal cases where the central allegation of negligence has been a failure to diagnose, refer, and treat patients with chronic limb threatening ischaemia in timely fashion, leading to avoidable amputation.

It is important to maintain a high index of suspicion in any patient presenting with foot symptoms. This is especially so in patients who have risk factors such as smoking or diabetes and/or who have a history of vascular disease (intermittent claudication, heart attack, stroke).

Even then, CLTI can be missed because

- It can have a slow and insidious onset
- Symptoms can be confused with other commoner causes of foot pain such as plantar fasciitis, arthritis, cellulitis, and gout[5]
- There is often no history of intermittent claudication as patients do not walk and/ or they have diabetic neuropathy which obtunds the pain
- Even tissue loss can be painless due to neuropathy
- CLTI does not just affect older patients; for example, Buerger's disease and other vasculitides can present in people in their 20s and 30s[6]
- Most patients with CLTI have absent foot pulses; however they can be palpable, at least initially, in cases of distal embolisation. It is important to remember that patients can, albeit infrequently, have potentially limb threatening distal ischaemia in the presence of pulses, although there are usually other obvious features of ischaemia, such as coldness and discoloration.
- Palpation of foot pulses, even by vascular surgeons, is associated with a substantial false positive and negative rate.
- There is a failure to perform Buerger's test (the affected foot turns white on elevation as a result of ischaemia, and red on dependency because of reactive hyperaemia—the so called "sunset foot," see fig 1). For this reason, do not just examine the patient sitting in a chair, as the dependent foot can look reassuringly pink with an apparently normal capillary refill time.

## Why does this matter?

With prompt revascularisation through either vein bypass, angioplasty, or stenting, amputation can be avoided in most patients. It is our experience that if diagnosis is delayed and substantial tissue loss develops, the chances of limb salvage fall dramatically. Discuss all patients with suspected CLTI immediately with a vascular surgeon.

## How is chronic limb threatening ischaemia diagnosed?

A diagnosis of CLTI can usually be made or excluded based on a high index of suspicion, a careful vascular history, and an appropriate vascular examination.[7] If there is any doubt, err on the side of caution, and discuss the patient with a vascular surgeon. While measurement of the ankle to brachial pressure index (ABPI) can be useful in patients with intermittent claudication, it is much less useful in patients with suspected CLTI because:

- It is technically difficult; the signals are often difficult to hear and might be coming from collaterals rather than the main pedal (foot) arteries
- Pressure measurements will often be falsely elevated, especially in patients with diabetes, because of calcification of the arterial wall.

Measurement of ABPI is potentially unreliable in CLTI. It should not be used in primary care to determine referral in patients in whom CLTI cannot be confidently excluded by vascular history and clinical examination.

## How is it managed?

Management of CLTI involves urgent admission for:

- Medical optimisation including (for example) antiplatelet agents, statins, control of hypertension and diabetes, optimisation of cardiac and renal function
- Arterial imaging
- Revascularisation by means of vein bypass, typically using the great saphenous vein, or endovascular intervention (angioplasty, stenting).

Patients with CLTI usually have significant widespread vascular disease and multiple comorbidities, therefore their prognosis remains guarded. In the BASIL-1 trial, which was an NIHR-HTA funded UK multicentre randomised controlled trial of 452 patients treated in 27 NHS hospitals and which compared a "bypass surgery first" with a "balloon angioplasty first" revascularisation strategy for CLTI, about 50% of patients who presented with CLTI and underwent an initially successful revascularisation went on to require major limb amputation or died within five years.[8] It is important to educate patients who are at risk of CLTI because of lifestyle (smoking), comorbidity (diabetes), or a history of vascular disease (intermittent claudication, myocardial infarction, stroke), about the symptoms and signs of CLTI and to advise them to seek urgent medical assistance should they be concerned.

How patients were involved in this article
No patients were involved in the making of this article

Contributors: Kevin Barraclough, Andrew Bradbury

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# Table

**Table 1| Presentations of peripheral arterial disease**

| | Pathophysiology | Symptoms and signs | Management | Outcome |
|---|---|---|---|---|
| Acute limb ischaemia (onset ≤14 days) | | | | |
| Embolus | Sudden occlusion of a previously normal leg artery by an embolus, which usually comes from the heart and often develops as a result of atrial fibrillation | Very sudden onset of profound ischaemia (the six Ps: pain, pallor, pulseless, paraesthesia, paralysis, perishing cold) as there are no collaterals | Heparinisation and urgent embolectomy followed by long term anticoagulation to reduce risk of further embolisation | If blood supply is restored within 4-6 hours, the leg usually returns to normal |
| Thrombosis in situ | Sudden occlusion of a previously diseased artery due to disease progression, slow flow, or intercurrent illness that reduces blood pressure and/or increases the blood thrombogenicity | Onset of ischaemia is usually slower and the degree of ischaemia less profound due to pre-existing collaterals | Heparinisation. Revascularisation if leg fails to improve. Consider long term anticoagulation | Leg will often improve with medical therapy alone as thrombus resolves and further collaterals develop. Some patients will require urgent revascularisation |
| Chronic limb ischaemia (onset >14 days) | | | | |
| Intermittent claudication | Atherosclerotic narrowing of a leg artery; most commonly the superficial femoral artery in the thigh but can be iliac arteries in the pelvis | Gradual onset of pain in the leg upon walking which is relieved by rest. Pain returns when walking resumes. Pain is usually in the calf with superficial femoral artery disease but can affect the thigh with iliac artery disease | Lifestyle modification (stop smoking) and medical therapy (antiplatelets, statin) to reduce cardiovascular risk. Supervised exercise programmes. Diagnosis and management of comorbidities such as diabetes and hypertension | If patients are concordant with lifestyle modification, medical therapy, and supervised exercise, symptoms usually improve and very few require intervention. If patients are not concordant then the risks of progression to chronic limb threatening ischaemia greatly increase |
| Chronic limb threatening ischaemia (rest pain) | Atherosclerotic narrowing of multiple arteries above and below the knee. Below knee disease is especially common in patients with diabetes | Severe pain usually in the forefoot and toes that is present all the time and which is often worse with elevation leading to pain at night in bed | Some patients can be managed conservatively like those with intermittent claudication. Most will require revascularisation | If patients can be managed conservatively then the prognosis can be similar to intermittent claudication |
| Chronic limb threatening ischaemia (tissue loss) | | Ulceration and/or gangrene often affecting toes and pressure points | In addition to medical therapy, patients will require revascularisation by means of a bypass using a vein from the leg or endovascular intervention (angioplasty, stent) | More than 50% of patients will undergo an initially successful revascularisation. However, about 50% of those patients with chronic limb threatening ischaemia have lost their leg or die within 5 years |

## Figure

Reactive hyperaemia is seen when the patient is sitting down