

# Identifying and treating intermittent claudication in people with diabetes

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## ARTICLE POINTS

**1** The most important risk factor for intermittent claudication (IC) is diabetes.

**2** IC has a significant effect on quality of life.

**3** IC can be identified by asking patients about any pain on walking and by checking foot pulses.

**4** Results of the ankle brachial pressure index will determine the most appropriate intervention.

**5** Medical treatment of cardiovascular risk factors and symptomatic treatment (with cilostazol) will improve quality of life and outcomes.

## KEY WORDS

- Intermittent claudication
- Peripheral arterial disease
- Ankle brachial pressure index

## Introduction

**Intermittent claudication (IC) – pain in the legs on walking that goes away with rest – is more common in people with diabetes than in those without. The appearance of IC symptoms is often the first indication of peripheral arterial disease (PAD; Jude, 2004) or peripheral vascular disease (PVD) in people with diabetes. Early diagnosis of IC, and therefore PAD/PVD, can reduce the substantial morbidity of the condition, which can culminate in limb loss for some patients. Members of the diabetes screening team should play a vital role in identifying people suffering from IC.**

The aching, cramping pain of intermittent claudication (IC) may be felt in the calves, feet, thighs or buttocks and is usually relieved by resting for a few minutes. IC occurs when atherosclerosis reduces arterial blood flow to the lower limbs, depriving the leg muscles of the extra oxygen needed during exercise. IC can therefore be seen as a marker for vascular and arterial disease.

The incidence of IC among people aged 55–74 years is 4.6% (Fowkes et al, 1991). People with diabetes are twice as likely to get IC compared with the general population, as they are more likely to have peripheral arterial disease (PAD) or peripheral vascular disease (PVD; TASC Working Group, 2000); and 20% of patients with PAD have diabetes (American Diabetes Association, 2003).

Risk factors for IC include dyslipidaemia and hypertension, but the most important risk factors are smoking and diabetes (Krentz et al, 2003). The longer a patient has diabetes and the longer the condition is poorly controlled, the more likely they are to have problems with their arteries and develop IC. Some diabetes patients with PAD will not have any IC symptoms because they will be masked by peripheral neuropathy (Jude et al, 2001). However, for those patients who do have symptoms the pain will prevent them

exercising, which will make their diabetes worse. IC has a significant adverse effect on health-related quality of life. Since patients can only walk short distances they are often unable to perform daily activities (Hiatt, 2001), which can lead to limitations on lifestyle, social isolation and unemployment (Binnie et al, 1999).

Around 10% of IC patients progress to critical limb ischaemia and 2% require amputation (Dormandy, 1991). However, IC patients with diabetes have a greater risk of progression (TASC Working Group, 2000). A Scandinavian study showed that the rate of progression to critical limb ischaemia over 6 years was 40% for those with diabetes versus 15% for those without diabetes (Jonason and Ringqvist, 1985).

## Importance of identifying patients with IC

Patients may only occasionally walk far enough to feel the pain of IC and even then they will often dismiss it as muscle cramp, a part of getting older, a part of their diabetes or arthritis. However, IC symptoms can indicate arterial disease elsewhere in the body, such as the coronary or carotid arteries, and the patient may be at risk of angina, a transient ischaemic attack or stroke (TASC Working Group, 2000). Furthermore, as the PAD progresses,

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**1** Peripheral circulation in the lower limb should be assessed by palpating the dorsalis pedis on the dorsum of the foot and the posterior tibial behind the medial malleolar.

**2** If intermittent claudication is suspected, and the correct equipment is available, a diagnosis can be confirmed by taking the ankle brachial pressure index.

patients can develop ischaemic leg pain or peripheral neuropathy. The main complication of peripheral neuropathy is foot ulcers, which can lead to increased morbidity and mortality and can be the leading cause of hospitalisation in people with diabetes (Boyko et al, 1996). Patients should be assessed for neuropathy by examining the foot, asking about symptoms and checking the sensation with a 10g monofilament and 128 Hz tuning fork (Boulton et al, 1998). The peripheral circulation in the lower limb should be assessed by palpating the dorsalis pedis on the dorsum of the foot and the posterior tibial behind the medial malleolar. Those with absent pulses have a higher risk of foot ulceration. Early detection and treatment of these ulcers can prevent amputation (Jude and Boulton, 1999).

**How to identify IC patients**

At the diabetes patient’s annual review it is worthwhile asking a few questions about pain on walking, possibly using the format of the Edinburgh Claudication Questionnaire (Table 1). If a patient has pain in his or her legs after a period of exercise which disappears after a short rest but reappears after the same period of exercise this will indicate the patient

has IC, particularly if foot pulses are not palpable. Foot pulses will often be weak or absent in patients with IC as well as those with non-symptomatic PAD.

If IC is suspected, and the correct equipment is available, a diagnosis can be confirmed by taking the ankle brachial pressure index (ABPI) – the ratio between Doppler-recorded systolic blood pressure in the lower and upper limb extremities (Table 2). An ABPI of <0.9 is taken to diagnose PAD (Table 3). However, in some people with diabetes the ABPI may be of limited value, as calcified, non-compressible arteries can give an ankle pressure much higher than the brachial pressure (Jude and Boulton, 1999). These patients should be referred to a vascular laboratory for alternative tests, such as toe systolic pressure. Toe digital arteries are less likely to be calcified, so pressure measurements more reliably reflect pressure within the digital artery. Transcutaneous oxygen pressure (TcPO<sub>2</sub>) can also be used to diagnose PAD and a pressure of <30 mmHg would be seen as abnormal (Jude and Boulton, 1999). The patient with occlusive disease has significantly reduced TcPO<sub>2</sub> measurements; this has been used to determine the possibility of ulcer healing and optimal amputation

**Table 1. The Edinburgh Claudication Questionnaire for diagnosing intermittent claudication (from Leng and Fowkes, 1992).**

<b>If a patient describes pain or discomfort in the legs when they walk, ask:</b>	<b>Reply and interpretation</b>
Does this pain ever begin when you are standing still or sitting?	No, patient has intermittent claudication (IC)
Do you get pain if you walk uphill or hurry?	Yes, patient has IC
Do you get pain if you walk at an ordinary pace on the level?	Yes, patient has IC
What happens if you stand still?	Pain goes away, patient has IC
Does the pain disappear within ten minutes or less if you stand still?	Yes, patient has IC
Where do you get the pain or discomfort?	Claudication pain occurs typically in the calf, atypically in the buttock or thigh. In the absence of calf pain, pain in the shins, hamstrings, feet or joints, or pain that appears to radiate, all suggest a diagnosis other than IC.

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**1** Mild to moderate claudication is best treated medically by managing risk factors such as stopping smoking, weight reduction, treating hyperlipidaemia and hypertension, and achieving good glycaemic control as well as an optimal exercise programme.

**2** Results of the ankle brachial pressure index measurement will determine where patients should be referred to and the most appropriate intervention.

## Table 2. Determining ankle brachial pressure index (ABPI) values.

Using blood pressure cuffs and a hand-held Doppler ultrasound machine:

- Measure systolic blood pressure in the brachial artery of each arm.
- Measure systolic blood pressure in both the posterior tibial and dorsalis pedis arteries in each leg.
- Divide the highest of the ankle pressure readings for each leg by the highest of the brachial pressure readings for the corresponding arm to give the right and left ABPIs, which will indicate the severity of the condition.

healing (Jude and Boulton, 1999).

### Who should identify these patients?

Ideally GPs who are already managing patients with diabetes should pick up IC. Diabetologists and podiatrists (community or diabetes clinic based) are the most likely members of the diabetes care team to screen for PAD and identify IC patients. A significant number of patients seen by diabetologists will probably already have progressed beyond IC to critical limb ischaemia. However, screening for IC should still be included

at the patient's annual review.

### Role of the podiatrist: An opportunity to identify IC patients

The podiatrist should ask patients about pain in their legs at regular foot checks. During foot screening, questions that will distinguish between ischaemic pain (claudication or rest pain) and neuropathic pain should be asked (Table 4).

### Referral to diabetologists and vascular surgeons

Mild to moderate claudication is best treated medically by managing risk factors such as stopping smoking, weight reduction, treating hyperlipidaemia and hypertension, and achieving good glycaemic control as well as an optimal exercise programme (see below). Good foot care education should also form part of the treatment package. Patients are therefore best managed by the diabetologists initially and referred to the vascular surgeon when symptoms worsen or complications set in. A patient would need referral to the surgeon if there is disabling claudication, ischaemic rest pain, ischaemic foot ulceration or gangrene. In all of the latter cases the patient should ideally be managed in a multidisciplinary diabetic foot clinic with the diabetologist, podiatrist and vascular surgeon. It is

**Table 3. Ankle brachial pressure index (ABPI) value and disease severity (from Olin, 1998).**

ABPI value	Disease severity
0.90–1.30	Normal
0.70–0.89	Mild
0.40–0.69	Moderate
≤0.40	Severe

important to distinguish between IC and painful neuropathy.

Results of the ABPI measurement will determine where patients should be referred to and the most appropriate intervention. If the ABPI value is >0.9 the patient does not have PAD. An ABPI value of 0.5–0.9 indicates moderate PAD and the patient should be given lifestyle advice by their GP and be followed up in the diabetic foot clinic. However, if the ABPI value is <0.5, severe PAD is indicated and the patient should be referred to a vascular surgeon.

For some patients with moderate PAD, lifestyle changes (with management of cardiovascular risk factors) will lead to an improvement in symptoms. However, as with many other conditions, patients find it hard to stick to such changes. If IC symptoms do not improve within a few

months the patient should be referred to the multidisciplinary diabetic foot clinic.

**Treatment**

**Reducing cardiovascular risk**

All patients with diabetes diagnosed with IC should be treated by the diabetologist with secondary prevention to reduce cardiovascular risk. Secondary prevention is often associated with an improvement in walking distance. Half of IC patients will improve or not get worse after following lifestyle advice, such as giving up smoking, weight loss, adhering to a proper diet, and regular exercise.

An antiplatelet agent such as aspirin, dipyridamole or clopidogrel will lower the risk of thrombotic vascular events, and has been shown to reduce vascular death in patients with IC by about 25% (Robless et al, 2001). Hypertension should be treated to target (130/80mmHg for people with diabetes; British Hypertensive Society guidelines, Williams et al, 2004), with an angiotensin-converting enzyme (ACE) inhibitor probably being the treatment of choice (Williams et al, 2004). The Heart Outcomes Prevention Evaluation (HOPE) study showed that the ACE inhibitor ramipril reduces cardiovascular related morbidity and mortality in patients with PAD by around 25% (HOPE Investigators, 2000).

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**1** For some patients with moderate peripheral arterial disease, lifestyle changes (with management of cardiovascular risk factors) will lead to an improvement in symptoms.

**2** All patients with diabetes diagnosed with intermittent claudication should be treated by the diabetologist with secondary prevention to reduce cardiovascular risk.

**Table 4. Diabetes foot screening: Comparison of ischaemic and neuropathic pain.**

Questions to ask the patient	Diagnosis		
	Ischaemic pain		Neuropathic pain
Do you get any pains in your legs? Do you get any pains in the back of your legs? If yes to any of these, then: What does the pain feel like?	Claudication	Rest pain	Painful neuropathy
What does the pain feel like?	Ache, tightening	Severe ache, burning	Burning, tingling, pins and needles, sharp pain, 'toothache'/deep pain
Show me where it hurts	Posterior calf, thigh, buttock	Often lower leg	Feet and legs
What brings the pain on and what makes it worse?	Walking/exercise, note location and distance	Constant, pedal pulses absent, visible atrophy	May come and go frequently, often worse in bed
What can you do to ease the pain?	Rest/stop walking	Cooling leg, hanging leg out of bed	Standing, walking around

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**1** Three indicated therapies are available to improve walking distance in intermittent claudication (IC) – naftidrofuryl, pentoxifylline and cilostazol. However, the only treatment proven to relieve the pain of IC is cilostazol (Pletal).

**2** Revascularising therapies, angioplasty, stenting and vascular surgery have a role to play in the management of patients for whom lifestyle changes and pharmacological treatment prove inadequate in controlling symptoms of IC.

**3** IC is twice as common in patients with diabetes and is a powerful marker of increased cardiovascular risk.

Patients with hyperlipidaemia should have their cholesterol levels lowered to target. The Heart Protection Study showed that lowering total and LDL-cholesterol by 25% with a statin reduces cardiovascular mortality and morbidity in PAD patients by around a quarter (Heart Protection Study Collaborative Group, 2002).

**Exercise**

The most effective exercise regimen for IC patients consists of walking sessions approximately 1 hour long, three times a week during which the patient walks to near maximal pain (preferably on a treadmill during supervised therapy), stops until the pain is relieved, and then resumes walking to near maximal pain again (TASC Working Group, 2000). Patients can also be encouraged to carry out foot exercises while sitting – point the toes, and rotate feet to keep calf muscles working. If IC patients adhere to an exercise programme a significant improvement in walking distance can be achieved. Unfortunately, only a minority of patients are able to attend supervised exercise classes and adherence with lifestyle advice is often poor. Many patients will therefore still experience high levels of pain on walking.

**Drug treatment**

Medication to relieve the pain of IC given in conjunction with lifestyle advice can have an additive effect – reducing the pain encourages adherence to the lifestyle changes. Treating the pain allows patients to walk further, which then acts as a stimulus to improve circulation in the legs, further improving walking distance.

Three indicated therapies are available to improve walking distance in IC – naftidrofuryl, pentoxifylline and cilostazol. However, the only treatment proven to relieve the pain of IC is cilostazol (Pletal). A recent review concluded that cilostazol represents the best evidence-based pharmacological therapy available for the symptoms of IC and should be the first-line treatment for symptom improvement in appropriate

patients (Barnett et al, 2004).

Cilostazol has been shown to significantly improve maximal and pain-free walking distance in people suffering from IC whether they have diabetes or not. In a pooled analysis of 436 people with IC who also had diabetes, those who received 100mg bd of cilostazol increased their maximal walking distances, initial claudication distance and absolute claudication distance significantly compared with placebo (Hittel and Donnelly, 2002; Rendell et al, 2002). People suffering from IC and with diabetes showed no significant differences compared with those without diabetes who had taken cilostazol in these trials with respect to improvements in walking distances and response rates. Mean percentage change in maximal walking distance from baseline was 53% for people with diabetes versus 60% for those without. However, increases in maximal walking distance were slightly lower in patients with diabetes, as these patients had a lower baseline walking distance and a higher incidence of concomitant cardiovascular disease.

Cilostazol is contraindicated in several subpopulations of patients, particularly those with congestive heart failure and severe hepatic or renal impairment.

**Interventional therapies**

Revascularising therapies, angioplasty, stenting and vascular surgery have a role to play in the management of patients for whom lifestyle changes and pharmacological treatment prove inadequate in controlling symptoms of IC. Surgery is required in those patients with non-healing foot ulcers, severe ischaemia and gangrene.

**Conclusion**

IC is twice as common in patients with diabetes and is a powerful marker of increased cardiovascular risk. It is therefore important to screen all diabetes patients for PAD, IC and foot ulceration, and also to check their feet regularly and educate them to look out for symptoms of these conditions. While reducing

**‘IC is twice as common in patients with diabetes and is a powerful marker of increased cardiovascular risk.’**

cardiovascular risk is a clinical priority, reducing the pain of IC is a priority for patients and can aid adherence with measures to improve lifestyles. Current data would appear to support the use of cilostazol as a promising therapy for patients with IC and diabetes, among the limited options available for these patients. ■

American Diabetes Association (2003) Peripheral arterial disease in people with diabetes. *Diabetes Care* **26**(12): 3333–41

Barnett AH, Bradbury AW, Brittenden J, Crichton B, Donnelly R, Homer-Vanniasinkam S et al (2004) The role of cilostazol in the treatment of intermittent claudication. *Current Medical Research and Opinion* **20**(10): 1661–70

Binnie A, Perkins J, Hands L (1999) Exercise and nursing therapy for patients with intermittent claudication. *Journal of Clinical Nursing* **8**(2): 190–200

Boulton AJ, Gries FA, Jervell JA (1998) Guidelines for the diagnosis and outpatient management of diabetic peripheral neuropathy. *Diabetic Medicine* **15**(6): 508–14

Boyko EJ, Ahroni JH, Smith DG, Davignon D (1996) Increased mortality associated with diabetic foot ulcer. *Diabetic Medicine* **13**(11): 967–72

Dormandy JA (1991) Natural history of intermittent claudication. *Hospital Update* **17**: 314–20

Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ (1991) Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. *International Journal of Epidemiology* **20**(2): 384–92

Hiatt WR (2001) Medical treatment of peripheral arterial disease and claudication. *The New England Journal of Medicine* **344**(21): 1608–21

Heart Outcomes Prevention Evaluation Study Investigators, The (2000) Effects of an angiotensin-converting-enzyme-inhibitor, ramipril, on cardiovascular events in high risk patients. *New England Journal of Medicine* **342**(3): 145–53

Heart Protection Study Collaborative Group (2002) MRC/BHF Heart protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet* **360**(9326): 7–22

Hittel N, Donnelly R (2002) Treating peripheral arterial disease in patients with diabetes. *Diabetes, Obesity and Metabolism* **4**(Suppl 2): S26–S31

Jonason T, Ringqvist I (1985). Factors of prognostic importance for subsequent rest pain in patients with intermittent claudication. *Acta medica Scandinavica* **218**(1): 27–33

Jude EB, Boulton AJM (1999) End stage complications of diabetic neuropathy. *Diabetes Reviews* **7**: 395–410

Jude EB, Oyibo SO, Chalmers N, Boulton AJ (2001) Peripheral arterial disease in diabetic and nondiabetic patients: A comparison of severity and outcome. *Diabetes Care* **24**(8): 1433–7

Jude EB (2004) Intermittent claudication in the patient with diabetes. *British Journal of Diabetes and Vascular Disease* **4**(4): 238–42

Krentz AJ, Mani R, Shearman CP (2003) Peripheral arterial disease in diabetes: Time for a coordinated approach to management. *British Journal of Diabetes and Vascular Disease* **3**(2): 92–6

Leng GC, Fowkes FG (1992) The Edinburgh Claudication Questionnaire: An improved version of the WHO/Rose questionnaire for use in epidemiological surveys. *Journal of Clinical Epidemiology* **45**(10): 1101–9

Olin JW (1998) Clinical evaluation and office based detection of peripheral arterial disease. In: AT Hirsch, FW Olin, eds. *An office-based approach to the diagnosis and treatment of peripheral arterial disease, I: The epidemiology and practical detection of peripheral arterial disease*. American Journal of Medicine Continuing Education Series: 10–17

Rendell M, Cariski AT, Hittel N, Zhang P (2002) Cilostazol treatment of claudication in diabetic patients. *Current Medical Research and Opinion* **18**(8): 479–87

Robless P, Mikhailidis DP, Stansby G (2001) Systematic review of antiplatelet therapy for the prevention of myocardial infarction, stroke or vascular death in patients with peripheral vascular disease. *British Journal of Surgery* **88**(6): 787–800

TASC Working Group (2000) Management of peripheral arterial disease: TransAtlantic Inter-Society Consensus (TASC). *European Journal of Vascular & Endovascular Surgery* **19**(Suppl A): S11–S244

Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF et al; The British Hypertension Society (2004) Guidelines for management of hypertension: Report of the fourth working party of the British Hypertension Society, 2004-BHS IV. *Journal of Human Hypertension* **18**(3): 139–85

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