10 STEPS Before you refer for: Peripheral arterial disease

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Introduction

Peripheral arterial disease (PAD) is a condition that is frequently underdiagnosed and often the subject of suboptimal care. It can present with rest pain or gangrene (critical ischaemia), but this is not common. Intermittent claudication (IC), leg pain on walking, is its most common manifestation. Leg pain on walking is a presentation commonly seen in general practice, and has several potential causes other than PAD. IC has been shown to affect 4.5% of subjects between the ages of 45 and 65 years and is a marker for increased cardiovascular risk.[1] In respect of the leg itself, IC is a relatively benign condition with most patients improving or stabilising and fewer than 5% progressing to major amputation. However, patients with IC are at increased risk of death, especially due to vascular events in the coronary and cerebral territories.[2] PAD is caused by the occlusion or narrowing of large peripheral arteries, usually from atherosclerosis, and, as such, it shares all the major risk factors that can lead to myocardial infarction (MI) or stroke. Most patients with PAD will also have disease (either symptomatic or asymptomatic) in their coronary and cerebral circulation, and MI and stroke are common causes of death in patients with PAD. Vigilance for the condition will provide opportunities to reduce cardiovascular risk in a group who are high risk. Accurate diagnosis and assessment will reveal those who would most benefit from specialist intervention.

1. Are the patient's symptoms consistent with PAD?

The most common presentation of PAD is pain in the leg on walking – vascular claudication. Oxygen delivery to the muscles is sufficient at rest but not on exercise. As a result the patient experiences pain in their muscles, most often the calf muscles, during exercise due to the build up of anaerobic metabolites such as lactic acid.

The following features are typical and make the diagnosis of vascular claudication more likely:

- Pain that occurs in the calf muscles on walking, rather than diffuse leg pain
- Symptoms that come on more quickly when hurrying or walking up hill
- Pain, which resolves quickly with rest, usually less than five minutes
- The pain is not present at rest
- Absence of numbness/weakness of the legs.

Heaviness or weakness in the legs, rather than pain in specific muscle groups, may suggest a spinal or nerve root cause for the pain. Spinal canal claudication, for example, usually produces symptoms not localised to a muscle group, and symptoms are often of weakness or heaviness on walking. Degenerative back disorders causing radiation into the legs are usually associated with pain in the back, some pain or discomfort at rest, exacerbation in certain positions or postures, and are often associated with bilateral symptoms. Musculoskeletal causes for pain in the leg are usually apparent on clinical assessment.

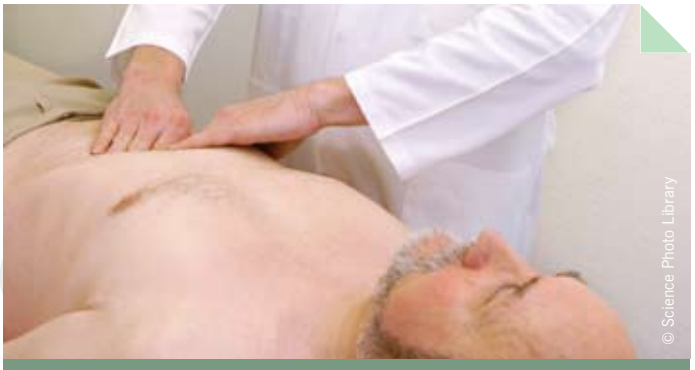
There are no other conditions that give the typical symptoms of claudication. A clear-cut history is highly sensitive and specific for vascular claudication. This history may not be volunteered by patients who accept the symptoms as part of growing older or believe the symptoms are due to arthritis. Other patients may not give this typical history because of other reasons for poor mobility or associated conditions such as joint or spinal problems. Chronic obstructive pulmonary disease (COPD), which shares with PAD an origin in smoking, may so limit activity that vascular claudication is not seen as something significant enough to warrant a medical opinion. In cases of diagnostic uncertainty referral for vascular imaging may be appropriate.

2. Assess and optimise cardiovascular risk factors and other cardiovascular disorders

Enquire about other cardiovascular disease and risk factors. The risk factors for PAD are:

- History of MI/angina
- Smoking history
- History of stroke/transient ischaemic attack (TIA)
- Obesity
- Atherogenic diet
- Hypertension
- Family history
- Dyslipidaemia
- Diabetes
- Impaired glucose tolerance
- Male gender.

Modifiable risk factors should be identified and advice/treatment given.



3. Examine the patient

Examination of patients with PAD is essential. It is important to take the blood pressure and feel for pulses, and if they are clearly absent (or present) this can be helpful. It is usually possible to be confident about the femoral pulses, but popliteal and ankle pulses are notoriously difficult to assess. Likewise, temperature, capillary return and 'soft' signs such as the absence of hair on the foot or leg are unreliable. However, ischaemic lesions such as ulceration or gangrene can be identified, and it is important to inspect between the toes and underneath the foot. It may also be appropriate to examine the abdomen to palpate for aortic aneurysm.

History and examination will usually identify those with critical ischaemia. Vascular rest pain plus or minus gangrene or ulceration will identify those who need urgent referral by letter or phone to the on-call vascular team for advice, or emergency admission.

4. Confirmation of PAD with ankle:brachial pressure index (ABPI)

ABPI measurement offers a simple and objective confirmation and assessment of PAD.[3] To measure the ABPI you need a hand-held Doppler with an 8 MHz probe, a sphygmomanometer and a cuff. Left and right brachial, posterior tibial and dorsalis pedis systolic pressures are measured, and the ratio of the highest ankle pressure/highest brachial pressure is calculated. An ABPI <0.9 is diagnostic of PAD. In some cases the ABPI may be artefactually elevated where the vessels are sclerotic/calcified in diseases such as diabetes and renal failure. Make sure the patient is lying flat, ideally for 10 minutes before starting, as the test is invalid if the patient's legs are not at the same level as the heart. Secure the cuff around the arm as if taking a blood pressure reading in the normal manner. Apply gel over the brachial pulse. Hold the Doppler probe over the brachial pulse, at an angle of 60º to the skin and inflate the cuff until the signal disappears, then gradually deflate until the signal returns. Note the pressure reading on the sphygmomanometer – this is the brachial systolic pressure. Repeat on the other arm and use the highest of the two readings. The dorsalis pedis and posterior tibial arteries are then found on the foot using the Doppler, and the systolic pressures in them are similarly measured with the cuff placed on the lower calf.

5. Stop smoking, keep walking

Smoking is the single biggest risk factor for PAD; people who smoke are 10 to 16 times more likely to develop PAD than someone who does not smoke. Studies have shown that quitting smoking can slow the progression of PAD, reducing the risk of fatal and nonfatal MI and stroke. After MI or stroke, the risk of recurrence is reduced by 50% in patients who stop smoking (even among long-term heavy smokers). Furthermore, smoking cessation has a favourable effect on the progression of intermittent claudication, increasing walking distance by two- to three-fold in 85% of patients, and improves graft patency in patients requiring surgical bypass. All patients with PAD should be encouraged to stop smoking and, if motivated, referred for counselling, nicotine replacement therapy (NRT) and support. Since the associated morbidity and mortality in PAD is so high, the case for prescription of pharmacological support (varenecline or bupropion) is stronger than for routine patients trying to quit and should be considered.

6. Start the patient on an antiplatelet agent

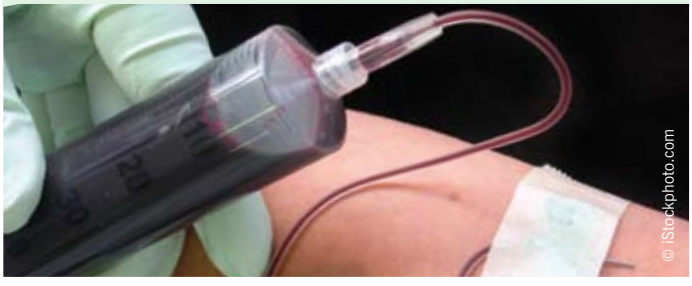
Aspirin is the most widely studied antiplatelet drug and its benefit to PAD patients in reducing the frequency of thrombotic events in the peripheral arteries and overall cardiovascular mortality has been shown in the large meta-analysis carried out by the Antithrombotic Trialists' Collaboration.[4] There has been some debate over the dosage, but studies have shown that long-term therapy using 75 to 150 mg daily is at least as effective as higher daily doses; large doses have no apparent additional benefit but increase the risk of adverse effects.

Data from the Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events (CAPRIE) study[5] showed that clopidogrel (75 mg daily) reduced serious vascular events by 8.7% compared with aspirin (325 mg daily) in patients with recent MI, recent stroke, or established PAD. A subgroup analysis of patients with PAD indicated a 23.8% relative risk reduction in favour of clopidogrel. However, the current costs of clopidogrel have resulted in it not being used as the first-line therapy for PAD in the UK. The role of dipyridamole in the management of PAD remains controversial and it is not recommended. Unless a patient has concomitant problems needing anticoagulation, such as atrial fibrillation, there are no indications for warfarin therapy in non-critical PAD; the risk of bleeding and the management problems far outweigh any theoretical benefit.

7. Perform blood tests

Unless recently checked, some basic blood tests are indicated:

- Full blood count (FBC), to exclude anaemia, polycythaemia, thrombocythaemia
- Urea and electrolytes (U&E), to exclude chronic kidney disease (CKD). Patients with PAD are at higher risk of reno-vascular disease
- Glucose; can be a random sample, but those with a raised level will require a fasting sample taken to exclude diabetes or impaired fasting glycaemia
- Lipid screen
- Liver function tests (LFTs) as baseline
- Thyroid function tests (TFTs) as baseline



8. Start the patient on a statin

Reducing cholesterol with a statin has been shown to reduce the risk of cardiovascular events in patients with PAD.[6,7] Therefore, due to their high risk of MI and stroke, all PAD patients who have high serum cholesterol should be treated. The lipid profile should be measured before and after starting treatment, to ensure that a 25% reduction in cholesterol is being achieved.

Direct evidence supporting the use of statins to lower low-density lipoprotein (LDL)-cholesterol levels in PAD comes from the Heart Protection Study (HPS)[8]. In this study 20,536 high-risk individuals with a total cholesterol level of at least 3.5 mmol/L were randomised to receive either simvastatin 40 mg daily or placebo. A lowering of cholesterol by 25% with the statin reduced cardiovascular mortality and morbidity in patients with PAD but no prior coronary disease producing a highly significant reduction of 22% in the first occurrence of a major vascular event. Similar benefits have also been shown with the use of angiotensin-converting enzyme (ACE) inhibitors in PAD.[7]

9. Refer those who can be managed conservatively to an exercise programme

Conservative management of risk factors and exercise should be recommended for patients with PAD that is not significantly impairing their quality of life. Many patients will improve over a period of three to six months as collaterals open up. They should be advised to exercise 'through the pain'. Exercise other than walking may also be useful, e.g. cycling and swimming.

A Cochrane review has shown that supervised exercise treatment can produce a significant increase in walking distance (150%) in most PAD patients with claudication.[9] Although it has been suggested that repeated ischaemia-reperfusion injury provoked by walking might have deleterious systemic effects, regular exercise actually reduces concentrations of serum inflammatory markers.

Exercise improves the blood flow to the legs by helping to open new collateral arteries, which carry some of the blood the narrowed arteries are unable to deliver and helps the leg muscles cope with anaerobic metabolism more efficiently. In order for exercise to be effective, a three- to six-month supervised exercise programme is required. There is little evidence that simple advice to exercise is effective for most patients. Unfortunately, supervised exercise programmes for claudicants are not universally available.

10. Who should be referred to a vascular surgeon?

Those with critical limb ischaemia (rest pain, gangrene or ulceration) should be referred urgently to a vascular surgeon. Most patients with claudication should initially be managed conservatively. If after three to six months their symptoms are still seriously interfering with their quality of life or employment then they should be referred for consideration of surgical intervention. Other cases which require referral are those where the diagnosis is in doubt. Other cases can be managed appropriately in primary care.

If a patient needs intervention, the two main options are percutaneous transluminal balloon angioplasty (with or without a stent) and peripheral arterial bypass grafting. Angioplasty involves stretching a narrowed or blocked section of the artery with a balloon, usually inserted by a needle in the femoral artery. It is used for short sections of narrowing or blockage. Bypass grafting surgery involves replacing a section of blocked artery, usually with one of the patient's own veins or a synthetic tube. It is usually reserved for long blockages causing severe symptoms and is associated with significant potential complications. Amputation is very rarely required, but is sometimes necessary in severe cases of critical limb ischaemia when there is no chance of saving the leg in any other way. Diabetic patients with PAD are five times more likely to have an amputation than non-diabetics because the disease is more likely to affect smaller more distal vessels, making surgical reconstruction much more difficult or even impossible.

Conflict of interest

MS: none declared. GS has received research funding and fees for speaking and chairing meetings from a number of pharmaceutical companies.

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