Peripheral arterial disease

Diagnosis and management in general practice

Thuy Bich Au
Jonathan Golledge
Philip J Walker
Kate Haigh
Mark Nelson

Background
Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis. It affects 10–15% of the general population, and is often asymptomatic; leading to under-diagnosis and under-treatment. Atherosclerotic risk factors are often not intensively managed in PAD patients.

Objective
To summarise the information around the diagnosis and management of PAD in the general practice setting.

Discussion
Careful history, clinical examination, and measurement of ankle-brachial index remain the initial means of diagnosing PAD. More detailed anatomic information from duplex imaging, computed tomography angiography and magnetic resonance angiography, is usually unnecessary unless endovascular or surgical intervention is being considered, or if abdominal aortic aneurysm or popliteal aneurysm need to be excluded. Management is focused on lifestyle modification, including smoking cessation and exercise; medical management of atherosclerotic risk factors, including antiplatelet agents, statins, antihypertensive therapy; and agents to improve walking distance, such as cilostazol and ramipril. Endovascular or surgical interventions are usually considered for lifestyle limiting intermittent claudication not responding to conservative therapies, and for critical limb ischaemia.

Keywords
peripheral arterial disease; risk factors; health behaviour; risk reduction behaviour

Peripheral arterial disease (PAD) is a manifestation of systemic atherosclerosis. It affects 10–15% of the general population,[1–4] and approximately 50% of PAD patients are asymptomatic;[2,3] leading to under-diagnosis and under-treatment of the disease.[5]

The most common symptom of PAD is intermittent claudication (IC) affecting the calf muscles, which may be present in as few as 10% of patients.[5] Symptomatic PAD patients have a worse prognosis than patients presenting with coronary artery disease or cerebrovascular disease, but their atherosclerosis risk factors are less intensively treated.[6] Both asymptomatic and symptomatic PAD patients have a high risk of death from cardiovascular disease (CVD),[2,7] therefore early treatment reduces mortality.[8]

Screening for PAD in general practice

Screening for PAD using the ankle-brachial index (ABI) or questionnaire is not currently recommended in Australia, and has not been shown to be of benefit in randomised controlled trials; although it is recommended for screening in other countries.[9,10]

Diagnosis

Careful history and clinical examination remain the initial means of diagnosing PAD. Ankle-brachial index measurement should be the initial diagnostic tool used in general practice, although nurse-determined oscillometric ABI has been shown to lack sensitivity.[11]

For atypical exertional leg pain, post-exercise ABI should be measured. This is usually performed following treadmill exercise (typically performed walking at 3.2 km/h, and a 10–12% grade). If a treadmill is not available, then the walking exercise may be performed by climbing stairs or by walking up and down the hallway.[12] Active pedal plantar flexion compares favourably with treadmill exercise and should be considered an appropriate alternative.[12]

More detailed anatomical information about PAD may be required to exclude abdominal aortic aneurysm (which can occur in up to 10% of patients with PAD[13]), or popliteal aneurysm, which might be suggested by prominent popliteal pulses, and to plan endovascular or open surgical intervention. Detailed anatomic imaging is not necessary if endovascular or open surgical intervention is not planned, and

aneurysmal disease can be confidently excluded on physical examination.

The role of diagnostic imaging

Duplex ultrasound (DUS) is non-invasive, is useful to define sites of stenosis or occlusion, and is often the only imaging required to plan endovascular interventions. It is also the main investigation for follow up of vascular interventions. Duplex ultrasound is, however, operator dependent and therefore reliant on a well-trained sonographer.

Both computed tomography angiography (CTA) and magnetic resonance angiography (MRA) provide good sensitivity and specificity compared to digital subtraction catheter angiography (DSA), although CTA can be more problematic with heavily calcified arteries and MRA does not show calcification,[14] which might be important information when interventions are being planned.

Renal function should be assessed before CTA or MRA are performed, due to issues around contrast nephropathy and nephrogenic systemic fibrosis, which has been associated with exposure to gadolinium based magnetic resonance imaging (MRI) contrast agents.[14]

While catheter DSA remains the gold standard for imaging peripheral arteries, it is rarely used for diagnosis because of its invasive nature and the availability of non-invasive imaging modalities (ie. DUS, CTA, MRA). Duplex ultrasound is used to guide most endovascular interventions, and some surgeons still prefer DSA for planning open revascularisation procedures, particularly for tibial and pedal bypass procedures.[15]

Management

The goals of PAD management are to:

- decrease the occurrence of cardiovascular events and prevent death
- reduce limb symptoms, improve exercise capacity, and thus improve quality of life
- prevent or lessen disability and progression to limb loss.

These goals can be attained through a comprehensive treatment program, which includes lifestyle modifications, exercise and diet, and pharmacotherapy for all PAD patients; and invasive revascularisation for patients with limiting claudication or critical limb ischaemia (CLI).

Lifestyle modifications

Smoking cessation is an important modifiable behaviour. The degree of damage caused by smoking is directly related to the amount of tobacco consumed.[16] Smoking cessation improves walking distance, doubles the 5 year survival rate,[17] and reduces the incidence of post-operative complications.[18]

Exercise and diet

Promotion of physical activity is also an important intervention. Supervised exercise programs have been consistently demonstrated to improve walking time and walking distance.[19,20] Exercise is beneficial, even among asymptomatic PAD patients.[21] It improves overall wellbeing and is cardioprotective.[22] Outcomes of supervised exercise programs are similar and longer lasting than that of endovascular interventions,[23] although unfortunately, such programs are not commonly available in Australia. Without them, patients are usually advised to walk until pain occurs, rest until the pain subsides, and repeat the cycle to a total of 30 minutes, progressing to 60 minutes a day, 3–5 times per week.[11]

A well balanced diet with a low salt, low fat, and moderate amounts of added sugar intake, as per the National Health and Medical Research Council (NHMRC) guidelines,[24] reduces the risk of chronic disease in general, and CVD in particular, and should be followed.

Obesity has been linked with complications of PAD,[1] and diet and exercise should be focused on obtaining a healthy weight.

Pharmacotherapy

Antiplatelet agents reduce all-cause mortality and fatal cardiovascular events in patients with IC.[1] However, bleeding complications need to be weighed against the benefits for each patient. Evidence on the effectiveness of aspirin versus either placebo or an alternative antiplatelet agent is lacking.[25,26] There is no reduction in vascular events in asymptomatic subjects with a low ABI randomised to daily aspirin.[27] The evidence to support aspirin use for patients without clinical CVD is not strong, with the number needed to treat (263) to prevent a major cardiovascular event offset by the number needed to harm (261).[26] Clopidogrel (75 mg/day) is superior to aspirin (325 mg/day) in reducing the combined risk of ischaemic stroke, myocardial infarction, or vascular death, with a relative risk reduction of 24% for PAD patients.[28] Clopidogrel is not Pharmaceutical Benefits Scheme (PBS) listed for the primary prevention of PAD.

Lipid lowering agents improve pain-free walking distance and reduce total cardiovascular events, due primarily to an overall reduction in coronary events.[8] Adding simvastatin (40 mg/day) to existing treatments reduces the rates of myocardial infarction, stroke and revascularisation,[29] chiefly by reducing overall risk of major vascular events rather than blood lipid concentrations alone. Statins are the only type of lipid lowering drug for which consistent, clear evidence of a beneficial effect is available for total cardiovascular events, total coronary events and stroke.[30] Statins are not PBS listed for asymptomatic PAD.

Cilostazol, a phosphodiesterase III inhibitor (newly introduced in Australia), is well tolerated and has been shown to improve walking distance in people with IC.[31] There is no data on whether it reduces cardiovascular events. Cilostazol is not available on the PBS. Another agent to improve walking distance is pentoxifylline, although current data indicate that its benefit is marginal.[32]

The angiotensin converting enzyme inhibitor (ACEI) ramipril (10 mg/day), has recently been shown to increase pain-free walking distance, maximum walking time and Walking Improvement Questionnaire scores in a small randomised placebo controlled study.[33] This has been replicated in a larger study where ramipril 10 mg/day increased mean pain-free walking time by 92% (87 seconds) and maximum walking time by 139% (193 seconds).[34]

There is currently no evidence that beta-blockers adversely affect walking distance in people with IC.[35] The underlying principle is that if a beta-blocker is required for cardio-protection, then it should be used.

Calcium channel blockers are protective against all-cause, cardiovascular and cerebrovascular disease mortality.[36] Evidence on various antihypertensive drugs in people with PAD is poor, and the lack of specific data examining outcomes in PAD patients should

not detract from the compelling evidence of the benefit of lowering blood pressure.[37]

Patients with diabetes are at increased risk of cardiovascular events, therefore good glycaemic and CVD risk factor control is desirable.[38]

The role of complementary therapies

There is little evidence to support the role of complementary therapies, including vitamin E,[39] garlic,[40] and ginkgo biloba[41] in the management of PAD.

Surgical intervention

Patients should be referred to a vascular surgeon when:

- the diagnosis is uncertain
- CLI is evident by rest pain, ischaemic ulceration, or gangrene
- claudication symptoms limit work or lifestyle, and there has been no improvement with an exercise program, risk factor modification and medical management after a 4–6 month period
- consideration of interventional management is felt appropriate by the patient and the general practitioner.

Patients with CLI (rest pain, tissue loss, or gangrene) usually require revascularisation to prevent limb loss. Patients with lifestyle limiting symptoms that do not improve with medical management should also be considered for intervention. The main options include endovascular angioplasty or stenting, or open surgical reconstruction by peripheral bypass or endarterectomy. The choice of procedure will depend on the anatomic location of the stenotic/occlusive disease, its extent, and the patient's comorbidities.

Key points

- Screening for PAD is currently not recommended in Australia.
- Careful history, clinical examination, and ABI remain the initial means to diagnose PAD.
- Lifestyle modifications are an important component of PAD management.
- Drug interventions include antiplatelet agents, statins, antihypertensive therapy and cilostazol.
- There is little evidence to support the use of complementary therapies in PAD management.
- Patients should be referred to a vascular surgeon if the diagnosis is uncertain, if medical treatments fail, or if CLI is present.

Authors

Thuy Bich Au MD, MSc, PhD, is Honorary Associate, Menzies Research Institute Tasmania, University of Tasmania and resident medical officer, Royal Hobart Hospital, Hobart, Tasmania. bich.au@utas.edu.au

Jonathan Golledge BA, MA, MChir, FRCS, FRACS, is Professor of Vascular Surgery, Queensland Research Centre for Peripheral Vascular Disease, James Cook University, Townsville, Queensland

Philip J Walker MBBS, FRACS(Vasc), is Professor of Clinical Surgery and Head, Discipline of Surgery, University of Queensland, School of Medicine and Centre for Clinical Research and Department of Vascular Surgery, Royal Brisbane and Women's Hospital, Herston, Queensland

Kate Haigh MBBS(Hons), is an intern, Toowoomba Hospital, Toowoomba, Queensland. kate.haigh@uqconnect.edu.au

Mark Nelson MBBS(Hons), MFM, FRACGP, FAFPHM, PhD, is Professor and Chair, Discipline of General Practice and senior member, Menzies Research Institute Tasmiania, University of Tasmania, Hobart, Tasmania.

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correspondence **afp@racgp.org.au**