Peripheral arterial disease

Peripheral arterial disease is commonly caused by atherosclerosis, and symptoms depend on the location and size of the affected artery, metabolic demands on the tissue, and the presence or absence of a collateral circulation. This article reviews the current evidence for the diagnosis and management of peripheral arterial disease.

Peripheral arterial disease is a general term used to describe arterial occlusive disease in the peripheral extremis. The common cause is atherosclerosis leading to progressive stenosis and/or occlusion of vessels and subsequent ischaemia of the tissues they supply. Symptoms of peripheral arterial disease depend on location and size of the affected artery, presence or absence of a collateral circulation, and the metabolic demands placed upon the ischaemic tissues.

According to the Trans-Atlantic inter-Society Consensus II on peripheral arterial disease (TASC II), the prevalence of symptomatic peripheral arterial disease in the general UK population is 15–20% in those over 70 years of age (Norgren et al, 2007).

Risk factors

Risk factors for development and progression of peripheral arterial disease are divided into modifiable and non-modifiable (*Table 1*). Non-modifiable risk factors include positive family history, increasing age, male gender (male:female = 2:1), chronic renal insufficiency and race (Criqui et al, 2005). There is a two-fold increase in risk in those of African descent. Interestingly, despite South Asians having poorer risk factor profiles than the British population as a whole, studies in both the UK and India imply that the prevalence of peripheral arterial disease is lower in South Asians than caucasians in the general population, diabetic and coronary artery disease cohorts (UK Prospective Diabetes Study Group, 1994; Mohan et al, 1995; Premalatha et al, 2000; Chaturvedi et al, 2007; Bennett et al, 2009).

Modifiable risk factors include smoking, diabetes mellitus, hypertension, dyslipidaemia, sedentary lifestyle and obesity (Hamish et al, 2008). Early identification and minimization of these through simple lifestyle alterations or readily available pharmacological intervention may limit disease progression and its complications.

Table 1. Non-modifiable and modifiable risk factors for development and progression of peripheral arterial disease

Non-modifiable	Increasing age
	Male gender
	Race
	Type 1 diabetes mellitus
	Positive family history
	Genotype
	Chronic renal insufficiency
Modifiable	Smoking
	Dyslipidaemia
	Hyperhomocysteinaemia
	Metabolic syndrome, type 2 diabetes mellitus or impaired glucose tolerance
	Hypertension
	Sedentary lifestyle
	Poor diet

Dr Alexander J Hills *is Foundation Doctor,* **Mr Joseph Shalhoub** *is Clinical Research Fellow and Honorary Clinical Lecturer,* **Miss Amanda C Shepherd** *is Clinical Research Fellow and* **Professor Alun H Davies** *is Professor of Vascular Surgery and Honorary Consultant Surgeon at Imperial Vascular Unit, Imperial College London, Charing Cross Hospital, London W6 8RF*

Correspondence to: Mr J Shalhoub

Clinical assessment: features in the history

Symptoms commonly associated with peripheral arterial disease include intermittent claudication and rest pain. Intermittent claudication is cramping discomfort upon muscular exertion that is relieved by its discontinuation. This is commonly calf pain presenting after walking a given distance, resolving rapidly with stopping, and is a reliably reproducible phenomenon. If arterial insufficiency lies proximally in the lower limb arterial tree, i.e. the aorto-iliac segment, then buttock claudication may result (gluteal musculature is supplied by branches of the internal iliac artery) and may be associated with impotence in men (known as Leriche syndrome). Lower down in the calves, it is secondary to superficial femoral and popliteal artery atherosclerosis.

If pain is present when the patient is not exercising this is called rest pain. This often manifests at night when the legs are elevated in bed and the effect of gravity in facilitating blood flow to the feet and toes is lost. Consequently, sufferers of rest pain often sleep with the affected limb dangling off the bed side, or in a chair such that the legs are dependent. If patients suffer from mixed arterial and venous disease, then the system that is troubling the patient most may be determined by asking whether he/she prefers to keep his/her legs up or down, as patients with venous insufficiency prefer elevation to facilitate venous return and reduce swelling.

Arterial claudication may be distinguished from spinal claudication on the basis of history. Peripheral arterial disease sufferers develop symptoms while cycling and

negotiating gradients. Because the spinal canal is at its widest when the vertebral column is flexed, this may not be the case in spinal claudication.

Importantly, peripheral arterial disease is a reflection of arterial disease ongoing throughout an individual's arterial tree. As well as addressing cardiovascular risk factors as above, the history must account for features of coronary arterial disease (angina, myocardial infarction or cardiac failure), cerebrovascular disease (stroke, transient ischaemic attack and amaurosis fugax), renovascular disease (uncontrolled hypertension, which can be investigated through renal arterial duplex for stenosis), and mesenteric arterial disease (history of bowel ischaemia).

Examination of the peripheral arterial system

Relevant and common peripheral stigmata of potential peripheral arterial disease include tar staining of the fingers and fingernails of smokers, and sites of capillary blood glucose measurement on the pulps of the fingers of individuals with diabetes mellitus. A complete corneal arcus, peri-ocular xanthelasmata and tendon xanthomata may point towards dyslipidaemia.

Lower limb inspection of patients with chronic peripheral arterial disease will reveal trophic changes indicative of longstanding ischaemia. These include thin and shiny skin, hair loss, dystrophic nails (onycholysis), and pallor. The patient should be checked for tissue loss, including ulceration, gangrene (dry or wet) or amputation (auto-amputation or iatrogenic). Ulceration should actively be excluded at pressure areas including the malleoli, heels, metatarsal heads, interphalangeal joints, tips of the digits and inter-digital clefts.

It is important to look for scars. These may be from healed ulceration, access to arteries in the operative treatment of peripheral arterial disease, or acquisition of saphenous vein to act as a bypass conduit for the ipsilateral lower limb, contralateral lower limb or coronary artery bypass (check for median sternotomy scar).

Abdominal palpation should exclude a pulsatile and expansile mass in the epigastrium suggestive of an abdominal aortic aneurysm. Palpate for the temperature of the feet and check capillary refill time bilaterally: this is normally <2 seconds and is likely to be prolonged in peripheral arterial disease. The common femoral, popliteal, dorsalis pedis and posterior pulses should be assessed. Is the pulse absent, reduced, normal or potentially aneurysmal? Auscultate for abdominal bruits, and bruits over common femoral arteries and adductor canals.

Buerger's test requires elevation of the lower limbs to an angle of 45°, where they are held for more than 1 minute. In this time, inspection for pallor and venous guttering is undertaken. The patient is then helped into a sitting position on the side of the examination couch, with his/her legs dangling dependent. Rubor of the digits and/or feet suggests significant peripheral arterial disease. This rubor is reactive hyperaemia occurring with return of blood flow into a dilated arteriolar and capillary bed; dilatation is caused by release of vasoactive anaerobic metabolites by ischaemic tissues during leg elevation.

Ankle–brachial pressure index (ABPI), an objective and reproducible measurement for peripheral arterial disease assessment (*Table 2*), is measured using a hand-held Doppler probe over the dorsalis pedis and posterior tibial arteries. With the probe held still, a cuff (attached to a sphygmomanometer) is inflated around the calf until the signal disappears. Repeated at the brachial artery with the cuff around the upper arm, dorsalis pedis and posterior tibial pressures are each divided by brachial pressure to give two ABPI measurements for each lower limb.

ABPI ≤0.90 has approximately 95% sensitivity in detecting arteriogram-positive peripheral arterial disease, and is almost 100% specific in identifying those without (Norgren et al, 2007). However, ABPI results can occasionally be misleading, and arterial calcification seen in diabetes mellitus may result in arteries being incompressible by the cuff, thus artificially elevating the ABPI. ABPI interpretation in light of the overall clinical picture is necessary. ABPI assesses the macrovasculature, while microvascular disease is problematic in diabetic patients.

Exercise testing may be considered as an adjunctive test. Serial ABPI measurements before and after exercise offer arterial evaluation in those with claudicant pain without clinical evidence of peripheral arterial disease at rest.

Investigations

Blood tests may reveal risk factors for or pathologies that can exacerbate peripheral arterial disease. Fasting blood glucose and lipids should be measured to check for diabetes mellitus and dyslipidaemia respectively, and urea and creatinine should be measured for renal impairment. If clinically suspected, full blood count will exclude causes of hyperviscosity, and a thrombophilia screen will rule out causes of a procoagulant state. A vasculitic screen should be considered in patients with a characteristic vasculitic rash or in those with atypical distribution of arterial disease, for example the upper limbs.

Assessment of peripheral arterial disease anatomy may be undertaken using duplex ultrasound. The accuracy of this is highly operator dependent, so it is commonly performed by specially trained vascular scientists.

Table 2. Peripheral arterial disease assessment using the ankle brachial pressure index

Ankle brachial pressure index	Clinical presentation
>0.9	Normal
0.9–0.5	Peripheral arterial disease, often associated with intermittent claudication
0.5–0.3	Severe peripheral arterial disease, often associated with rest pain
<0.3	Impending tissue loss

From Ricotta (1985)

Magnetic resonance angiography or computed tomography angiography play a role in confirming and locating suspected disease, especially where intervention is being considered. Digital subtraction angiography is the current gold standard and can be intraoperative (Sritharan and Davies, 2006), but it is two-dimensional and requires nephrotoxic iodinated contrast, as does computed tomography angiography. Digital subtraction angiography should be performed with a view to proceeding to endovascular therapy where appropriate, negating the need for repeated contrast administration if subsequent endovascular therapy is considered.

In planning for intervention, these may be used alone or in combination, depending on local availability, expertise and preference, the lesion, and patient comorbidities.

Classification

Peripheral arterial disease can be classified in a variety of ways. The Fontaine staging system, based on clinical signs and symptoms, is popular (Fontaine et al, 1954):

I. Asymptomatic
II. Intermittent claudication
   a. Pain free at rest, claudication on walking >200 m
   b. Pain free at rest, claudication on walking <200 m
III. Rest or nocturnal ischaemic pain
IV. Necrosis or gangrene (tissue loss).

Asymptomatic peripheral arterial disease

Asymptomatic disease is predominantly diagnosed through ABPI measurement in patients with suggestive risk factors. Asymptomatic disease is treated by modification of these risk factors through lifestyle and pharmacological interventions. Current guidelines recommend best medical therapy to include: smoking cessation, glycaemic control, cholesterol management and hypertension control.

Smoking cessation

Cessation of smoking, a known cause of atherosclerotic disease, is recommended by TASC II (Norgren et al, 2007). Cessation can reduce the relative risk of developing intermittent claudication in smokers from 3.7 to 3.0 in less than 5 years (Fowkes et al, 1991). These patients also show improved overall long-term survival rates.

Glycaemic control

Peripheral arterial disease is associated with diabetes mellitus and been linked to impaired glucose tolerance, doubling the risk of developing intermittent claudication (Criqui et al, 1989). Blood glucose level optimization, with regular measurement of glycosylated haemoglobin A_{1C} (HbA_{1C}) levels, is supported by the Scottish Intercollegiate Guidelines Network (SIGN) (2009). The percentage of HbA_{1C} should fall with improved control.

Cholesterol management

SIGN (2009) recommends statin therapy in those with cholesterol levels >3.5 mmol/litre. Others advocate their use regardless of cholesterol level as the cardiovascular protection conferred by statins may be partly independent of lipid-lowering effect, through reducing inflammation seen in atherosclerosis (British Cardiac Society et al, 2005). Statin use in peripheral arterial disease significantly reduces all vascular events (Heart Protection Study Collaborative group, 2002) and TASC II (Norgren et al, 2007) states that statins should be used in patients with symptomatic peripheral arterial disease.

Hypertension control

Tight blood pressure control is important, and maintaining blood pressure in accordance with European guidelines is recommended by TASC II (Norgren et al, 2007). The Heart Outcomes Prevention Evaluation (HOPE) study showed blood pressure modification in patients with ABPI <0.9 was twice as effective in preventing major adverse cardiovascular events than in those with ABPI >0.9 (Yusuf et al, 2000).

Earlier and more aggressive pharmacological intervention may be warranted in patients at high risk of disease progression, such as those with diabetes or renal disease.

Intermittent claudication

Claudication, translating from the Latin claudicare meaning 'to limp', is a term used to describe deep cramping pain occurring at a fixed distance during walking and relieved by rest. As disease progresses, pain occurs at shorter distances and/or shallower gradients.

Optimal medical management of claudicants includes use of best medical therapy used as in asymptomatic patients (described above) alongside long-term antiplatelet therapy, exercise and cilostazol.

Long-term antiplatelet therapy

TASC II advocates long-term antiplatelet therapy in patients with symptomatic disease (Norgren et al, 2007), either aspirin or clopidogrel 75 mg once daily.

Exercise

Regular exercise improves pain-free and maximum walking distances in claudicants (Holm et al, 1973), as well as improving the sense of wellbeing (Clifford et al, 1980). Mechanisms thought to be responsible include improving collateral circulation, muscle coordination, and a reduction in intramuscular pressure in the non-contracted state with an increased blood pressure while exercising (Shalhoub et al, 2009).

Supervised is better than unsupervised exercise (Patterson et al, 1997; Regensteiner et al, 1997), improving symptoms, quality of life and distance walked, with benefits maintained after stopping exercise (Cheetham et al, 2004). Mechanisms underlying the benefit of supervision are unknown, although it has been hypothesized that a combination of factors including motivation, misinterpretation of exertion, reduced efficiency and timing of exercise are involved (Shalhoub et al, 2009).

Exercise is the most cost-effective non-invasive intervention to improve walking (Brevetti et al, 2002). TASC II (Norgren et al, 2007) and SIGN (Scottish Intercollegiate Guidelines Network, 2009) recommend supervised exercise as part of initial treatment for all peripheral arterial disease patients.

Cilostazol

Phosphodiesterase III inhibitors such as cilostazol have a strong evidence base for use in intermittent claudication (Norgren et al, 2007), improving maximum treadmill walking distance and health-related quality of life (Regensteiner et al, 2002). Effects are exerted through platelet inhibition (preventing thrombus formation) and vasodilation (promoting blood flow). Common side effects of cilostazol include headaches, dizziness and diarrhoea. A 3–6-month course is recommended as first-line pharmacotherapy for claudication relief (Norgren et al, 2007), but it should be stopped if there is no improvement at 3 months or non-compliance occurs. Caution must be taken in patients with congestive cardiac failure.

Naftidrofuryl

Use of naftidrofuryl should be considered in patients with poor quality of life caused by intermittent claudication (Heart Protection Study Collaborative group, 2002). Symptomatic relief is achieved through vasodilation.

Prevention is better than cure as patients with intermittent claudication have a threefold higher risk of death compared with age-matched controls (Housley, 1988). Early diagnosis and treatment to prevent disease progression at an early stage is key.

Critical limb ischaemia

Clinical diagnosis of critical limb ischaemia is made when there is rest pain or tissue loss secondary to peripheral arterial disease (Fontaine stages III and IV) (Fontaine et al, 1954). A more objective definition is outlined by the Second European Consensus, using haemodynamic and clinical parameters (Dormandy et al, 1991) (*Table 3*). Critical limb ischaemia is estimated to cost the NHS approximately £200 million per annum (Hart and Guest, 1995).

Patients may present late with rest pain, having adopted a sedentary lifestyle or because comorbidities such as chronic obstructive pulmonary disease limit activity below the claudication threshold.

Critical limb ischaemia is progressive with worsening rest pain, impaired wound healing and tissue viability. Treatment of critical limb ischaemia again demands risk factor modification and antiplatelet therapy. Where possible, revascularization should be considered to prevent limb loss. Without revascularization, 19% of limbs with tissue loss are lost at 6 months, and 23% are lost at 1 year (Marston et al, 2006). Revascularization may be endovascular or surgical.

Endovascular techniques

Endovascular therapy comprises balloon angioplasty and stent deployment. Angioplasty can be transluminal or, where guide-wires cannot cross a stenosis or occlusion, subintimal. In subintimal angioplasty, specialized guidewires puncture the intima, cross the diseased arterial segment in the subintimal plane and re-enter the lumen beyond. Angioplasty may be coupled with stent deployment in an attempt to improve long-term patency. The complication rate of percutaneous transluminal angioplasty is approximately 9% (Chong et al, 2000), with a 15–50% 1–2-year infra-inguinal patency (Atar et al, 2005). In aorto-iliac occlusive disease, stent use improves technical success rates and reduces long-term failure risk by about 39%, maintaining a similar complication rate to percutaneous transluminal angioplasty. Restenosis does not always correlate with the recurrence of symptoms.

Long-term benefit of percutaneous transluminal angioplasty over exercise has yet to be proven. Despite therapeutic angioplasty offering better results at 6 months, there appears to be no significant difference in treadmill walking distance or quality of life scores between exercise and percutaneous transluminal angioplasty groups by 24 months (Chong et al, 2000).

Surgical bypass

Options for bypassing diseased arterial segments are numerous, can be anatomical or extra-anatomical, and use autologous or synthetic material as the conduit. Autologous conduits are often the superficial saphenous veins, commonly from the ipsilateral limb, which may be reversed to negate the action of valves or used in situ. In situ bypass, often used for femoro-popliteal bypass in superficial femoral artery disease, eliminates anastomotic vessel size mismatch, the valves destroyed using a valvulotome device. Autologous vein grafts have superior patency and infection profiles compared with synthetic conduits, being first choice where available and of good quality. Vein may have been harvested for prior peripheral arterial disease or coronary artery bypass procedures,

Table 3. Definitions of critical limb ischaemia

Reference	Definition
Fontaine et al (1954)	Stage III: rest pain caused by arterial disease
	Stage IV: ulceration or gangrene secondary to arterial disease
European Society of Vascular Surgery (1992)	Recurring ischaemic rest pain requiring analgesia for 2 weeks and ankle systolic pressure <50 mmHg, toe systolic pressure <30 mmHg or ulceration or gangrene of foot or toes with ankle systolic pressure <50 mmHg, toe systolic pressure <30 mmHg
European Consensus on Critical Limb Ischaemia (Anonymous, 1989)	Severe rest pain requiring opiate analgesia >2 weeks or ulceration or gangrene with ankle systolic pressure <50 mmHg
Bell et al (1982)	Severe rest pain requiring opiate analgesia >2 weeks and either ankle systolic pressure <40 mmHg or tissue necrosis or digital gangrene

therefore vein from the contralateral lower limb or arms may be considered. Preoperatively, duplex ultrasonography is used to 'map' suitable vein for harvest as required.

Synthetic grafts used include knitted polyester (Dacron) and polytetrafluoroethylene (PTFE), which may be externally reinforced if the bypass crosses a joint or is prone to compression. Dacron is commonly used for aorto-bifemoral bypass grafts, with a 5-year patency rate of over 90%; perioperative mortality is up to 5% (Murie, 2008).

Patency rates for above-knee femoropopliteal bypasses with autologous vein are similar to those for Dacron or PTFE for the first 2 years, at approximately 80% (Beard and Gaines, 2001). By 4 years, the patency of above-knee vein bypass is 61% while for PTFE it is 38% (Veith et al, 1986). In the same study, below-knee femoropopliteal bypasses had 4-year patency rates of 76% and 54% for vein and PTFE respectively (Veith et al, 1986). Use of a vein cuff at the distal anastomosis is beneficial in femoral to below-knee popliteal PTFE bypass, in one study improving cumulative 3-year patency from 19% to 45% (P=0.018) (Griffiths et al, 2004).

Other options for symptom relief in critical limb ischaemia include sympathectomy (lumbar ganglionectomy) (Pearl, 1939), spinal cord stimulation, and prostanoid drugs such as ilioprost.

Acute limb ischaemia

Acute limb ischaemia may be caused by thromboembolism or can occur as a result of in-situ thrombosis at the site of a ruptured atherosclerotic plaque. In the absence of pre-existing significant peripheral arterial disease, hence absence of developed collateral channels, this may present as 'the six Ps' of acute limb ischaemia: pain, perishingly cold (poikilothermia), pallor, pulselessness, paraesthesia and paralysis. At presentation, the limb may be viable, threatened or dead. If the limb is viable, the patient may be started on a heparin infusion while further investigations are undertaken and interventions planned. If the limb is threatened, urgent intervention to revascularize the limb is essential. This may include catheter-guided targeted thrombolysis, thromboembolectomy (using a Fogarty catheter or under direct vision) or, particularly if there is underlying peripheral arterial disease, bypass surgery.

Amputation

In situations where tissue is beyond salvage or there is extensive tissue death then amputation may be required. Necrotic tissue is an ideal environment for pathogens to multiply, offering a nidus for infection. If tissue putrefies, becoming wet gangrene, this can lead to local cellulitis, systemic sepsis or death, so prompt removal of the infective focus is indicated. In the case of dry gangrene, where tissues become mummified, tissue can be left to demarcate and autoamputate.

Non-major amputations performed are digital (with excision of associated metatarsal head), Ray (digit and whole corresponding metatarsal), trans-metatarsal, tarso-metatarsal, and Symes (trans-tarsal).

Less than 2% of peripheral arterial disease patients require major amputation, including below-knee, through-knee (Gritti-Stokes), above-knee or hind-quarter (Kannel et al, 1970; Widmer et al, 1985). Major amputation is considered when non-reconstructable peripheral arterial disease exists with ongoing deterioration, often significant chronic non-resolving infection, or severe intractable pain where amputation can help improve the quality of life.

Peripheral arterial disease as an indicator of cardiovascular morbidity

Implications for peripheral arterial disease patients are not limited to the direct morbidity and mortality of the disease itself, but also through its validity as a surrogate marker of global arterial occlusive disease (including coronary artery, cerebrovascular and renovascular disease) (Davies, 2000).

Peripheral arterial disease serves as a strong prognostic indicator for development and progression of these other arterial conditions with high morbidities and mortalities in their own right. This is emphasized by a doubling in the mortality risk of patients with clinical peripheral arterial disease (17.5%) relative to those with ABPIs within normal range (8.5%) (P<0.0001) (Östergren et al, 2004), and a 1-year morbidity and mortality rate of 17.65–18.37% for cardiovascular death, myocardial infarction, cerebral infarction or hospitalization in clinical peripheral arterial disease sufferers (Cacoub et al, 2009). To these ends, appropriate management of risk factors (common to all arterial occlusive diseases) and regular cardiovascular review in peripheral arterial disease patients would go some way towards minimizing the overall mortality and morbidity in this cohort. Importantly, medical management and appropriate regular follow up of those with diabetes mellitus should address potential macro- and microvascular complications, including chiropody and diabetic foot clinics (Kannel et al, 1970).

Conclusions

Peripheral arterial disease is highly prevalent and responsible for a significant degree of morbidity. As such peripheral arterial disease is a considerable burden for both patient and society, a fact made more poignant by the shifting demographics of the 21st century. The earlier patients and at-risk groups are recognized and treated, the better their prognosis. The use of conservative measures alongside pharmacotherapy, in risk factor modulation, can help avoid the need for endovascular and surgical intervention. Even simple modifications in diet and exercise confer significant reductions in long-term disease progression, if maintained, and should be actively encouraged. **BJHM**

Conflict of interest: none.

Anonymous (1989) European consensus on critical limb ischaemia. *Lancet* **i**: 737–8

Atar E, Siegel Y, Avrahami R, Bartal G, Bachar GN, Belenky A (2005) Balloon angioplasty of popliteal and crural arteries in elderly with critical chronic limb ischemia. *Eur J Radiol* **53**(2): 287–92
Beard JD, Gaines PA (2001) Treatment of chronic lower limb ischaemia. In: Beard JD, Gaines PA, eds. *Vascular and Endovascular Surgery.* 2nd edn. Harcourt Publishers, London: 55–88
Bell PRF, Charlesworth D, De Palma RG et al (1982) The definition of critical ischaemia of a limb. Working party of the International Vascular Symposium (Editorial). *Br J Surg* **69**(Suppl): S2
Bennett PC, Silverman S, Gill PS, Lip GYH (2009) Ethnicity and peripheral artery disease. *QJM* **102**(1): 3–16
Brevetti G, Annecchini R, Bucur R (2002) Intermittent claudication: pharmacoeconomic and quality-of-life aspects of treatment. *Pharmacoeconomics* **20**: 169–81
British Cardiac Society, British Hypertension Society, Diabetes UK, HEART UK, Primary Care Cardiovascular Society, Stroke Association (2005) Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. *Heart* **91**(Suppl 5): v1–52
Cacoub PP, Abola MT, Baumgartner I et al (2009) Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Continued Health (REACH) Registry. *Atherosclerosis* **204**: e86–e92
Chaturvedi N, Coady E, Mayet J et al (2007) Indian Asian men have less peripheral arterial disease than European men for equivalent levels of coronary disease. *Atherosclerosis* **193**: 204–12
Cheetham DR, Burgess L, Ellis M, Williams A, Greenhalgh RM, Davies AH (2004) Does supervised exercise offer adjuvant benefit over exercise advice alone for the treatment of intermittent claudication? A randomised trial. *Eur J Vasc Endovasc Surg* **27**(1): 17–23
Chong PF, Golledge J, Greenhalgh RM et al (2000) Exercise therapy or angioplasty? A summation analysis. *Eur J Vasc Endovasc Surg* **20**: 4–12
Clifford PC, Davies PW, Hayne JA, Baird RN (1980) Intermittent claudication: is a supervised exercise class worthwhile? *BMJ* **280**(6230): 1503–5
Criqui MH, Browner D, Fronek A et al (1989) Peripheral arterial disease in large vessels is epidemiologically distinct from small vessel disease: an analysis of risk factors. *Am J Epidemiol* **129**: 1110–19
Criqui MH, Vargas V, Denenberg JO et al (2005) Ethnicity and peripheral arterial disease: the San Diego Population Study. *Circulation* **112**(17): 2703–7
Davies A (2000) The practical management of claudication. *BMJ* **321**: 911–12
Dormandy J, Verstraete M, Andreani D et al (1991) Second European consensus document on chronic critical leg ischemia. *Circulation* **84**(Suppl 4): 1–26
European Society of Vascular Surgery (1992) Consensus document II. *Eur J Vasc Surg* **6**(Suppl A): 1–32
Fontaine R, Kim M, Kieny R (1954) Die chirugische Behandlung der peripheren Durchblutungsstörungen. (Surgical treatment of peripheral circulation disorders) [in German]. *Helvetica Chirurgica Acta* **21**(5/6): 499–533
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. *Int J Epidemiol* **20**(2): 384–92
Griffiths GD, Nagy J, Black D, Stonebridge PA (2004) Randomized clinical trial of distal anastomotic interposition vein cuff in infrainguinal polytetrafluoroethylene bypass grafting. *Br J Surg* **91**(5): 560–2
Hamish M, Gohel MS, Davies AH (2008) Peripheral arterial disease in patients with diabetes. *Br J Hosp Med* **69**(10): 570–4
Hart WM, Guest JF (1995) Critical limb ischaemia: the burden of illness in the UK. *Br J Med Econ* **8**: 211–21
Heart Protection Study Collaborative group (2002) MRC/BHF heart Protection study of Cholesterol lowering Simvastatin in 20536 high-risk individuals: a randomised, placebo-controlled trial. *Lancet* **360**: 7–22
Holm J, Dahllof AG, Bjorntorp P, Schersten T (1973) Enzyme studies in muscles of patients with intermittent claudication. Effect of training. *Scand J Clin Lab Invest Suppl* **128**: 201–5
Housley E (1988) Treating claudication in five words. *BMJ (Clin Res Ed)* **296**(6635): 1483–4
Kannel WB, Skinner JJ Jr, Schwartz MJ, Shurtleff D (1970) Intermittent claudication. Incidence in the Framingham Study. *Circulation* **41**(5): 875–83
Marston WA, Davies SW, Armstrong B et al (2006) Natural history of limbs with arterial insufficiency and chronic ulceration treated without revascularization. *J Vasc Surg* **44**(1): 108–14
Mohan V, Premalatha G, Sastry NG (1995) Peripheral vascular disease in non insulin dependent diabetes mellitus in south India. *Diabetes Res Clin Pract* **27**: 235–40
Murie JA (2008) Arterial disorders. In: Williams N, Bulstrode C, O'Connell PR, eds. *Bailey and Love's Short Practice of Surgery.* 25th edn. Edward Arnold, London: 899–924
Norgren L, Hiatt Wr, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR (2007) Inter-Society consensus for the management of peripheral arterial disease (TASCII). *Eur J Vasc Endovasc Surg* **3**(1): S1–S75
Östergren J, Sleight P, Dagenais G et al (2004) Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J* **25**(1): 17–24
Patterson RB, Pinto B, Marcus B, Colucci A, Braun T, Roberts M (1997) Value of a supervised exercise program for the therapy of arterial claudication. *J Vasc Surg* **25**: 312–18
Pearl FL (1939) The management of chronic occlusive peripheral vascular disease. *Am J Surg* **43**: 106–8
Premalatha G, Markovitz J, Shanthirani S, Mohan V, Deepa R (2000) Prevalence and risk factors of peripheral vascular disease in a selected South Indian population. *Diabetes Care* **23**: 1295–300
Regensteiner JG, Meyer TJ, Krupski WC et al (1997). Hospital vs home-based exercise rehabilitation for patients with peripheral arterial occlusive disease. *Angiology* **48**: 291–300
Regensteiner JG, Ware JE Jr, McCarthy WJ et al (2002) Effect of cilostazol on treadmill walking, community-based walking ability, and health related quality of life in patients with intermittent claudication due to peripheral arterial disease: meta-analysis of six randomized controlled trials. *J Am Geriatr Soc* **50**(12): 1939–46
Ricotta JJ (1985) Vascular laboratory examinations for arterial disease. In: Dudley H, Cater D, eds. *Rob and Smith's Operative Surgery.* 4th edn. Butterworth, London: 7
Scottish Intercollegiate Guidelines Network (2006) *Diagnosis and management of peripheral arterial disease: a national clinical guideline.* Guideline no 89. Scottish Intercollegiate Guidelines Network, Edinburgh (www.sign.ac.uk/pdf/sign89.pdf accessed 25 May 2009)
Shalhoub J, Qureshi M, Davies A (2009) Supervised exercise in intermittent claudication: a sedentary notion? *Vascular* **17**(2): 66–73
Sritharan K, Davies AH (2006) The ischaemic leg. *Br J Hosp Med* **67**(3): M56–8
UK Prospective Diabetes Study Group (1994) UK Prospective Diabetes Study XII: differences between Asian, Afro-Caribbean and white Caucasian type 2 diabetic patients at diagnosis of diabetes. *Diabet Med* **11**(7): 670–7
Veith FJ, Gupta SK, Ascer E et al (1986) Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. *J Vasc Surg* **3**(1): 104–14
Widmer LK, Biland L, DaSilva A (1985) Risk profile and occlusive periphery artery disease (OPAD) June 1985. In: Proceedings of the 13th International Congress of Angiology. Athens, Greece: 28
Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G (2000) Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study investigators. *N Engl J Med* **342**(3): 145–53

KEY POINTS

- Peripheral arterial disease is common in the western world. Despite South Asians having poorer risk factor profiles than the British population as a whole, their prevalence of peripheral arterial disease is lower.
- Peripheral arterial disease is an indicator of an individual's atherosclerotic burden and cardiovascular prognosis.
- Management of peripheral arterial disease includes risk factor modification, exercise and pharmacotherapy in the first instance. Endovascular intervention and surgical bypass are often used to treat critical limb ischaemia.