Lower extremity peripheral artery disease: a basic approach

Keith A Chan[1]

Alex Junia[1]

Author details can be found at the end of this article

Correspondence to:
Keith A Chan; keithachan@gmail.com

Abstract

Peripheral artery disease of the lower limbs is a chronically progressive disorder characterised by the presence of occlusive lesions in the medium and large arteries that result in symptoms secondary to insufficient blood flow to the lower extremities. It is both a manifestation of systemic atherosclerosis and a marker of increased cardiovascular morbidity and mortality. Because of its highly heterogenous clinical picture, a detailed history and physical assessment, a high degree of suspicion for peripheral artery disease and the use of the ankle–brachial pressure index is essential to identify patients with peripheral artery disease. This will allow early administration of basic pharmacotherapy and lifestyle changes to reduce cardiovascular events, minimise claudication symptoms and enable optimal revascularisation to prevent loss of limb function.

Key words: Ankle–brachial pressure index; Lower extremity peripheral artery disease; Peripheral artery disease

Submitted: 26 August 2019; accepted following double blind peer review: 4 November 2019

Introduction

Peripheral artery disease of the lower limbs is a chronically progressive disorder, affecting 3–7% of the general population and 20% of individuals over the age of 75 years (Layden et al, 2012). Peripheral artery disease is characterised by the presence of occlusive lesions in the medium and large arteries that result in signs and symptoms secondary to insufficient blood flow to the limbs. It is both a manifestation of systemic atherosclerosis and a marker of increased cardiovascular morbidity and mortality, potential limb loss and reduced quality of life (Shu and Santulli, 2018). However, peripheral artery disease remains under-recognised in the UK, despite being a measure in the Quality and Outcomes Framework for GPs (Davies et al, 2017). It is thus essential that medical trainees familiarise themselves with the diagnosis and assessment of peripheral artery disease to allow appropriate early risk modification and treatment.

Table 1. Risk factors for peripheral artery disease
Smoking
Diabetes
Hypertension
Dyslipidaemia
Chronic kidney disease
Older age
Male sex
Sedentary habits
Obesity

Aetiologies and risk factors

Peripheral artery disease is most commonly the result of atherosclerosis. However, there are several other aetiologies, including anatomical variations, cystic adventitial disease, endofibrosis and vasculitis, which are generally referred to as non-atherosclerotic peripheral artery diseases (Weinberg and Jaff, 2012). This article focuses exclusively on peripheral artery disease and its atherosclerotic risk factors.

The development of peripheral artery disease is multifactorial with a complex interplay of modifiable and non-modifiable risk factors (Table 1). Cigarette smoking is one of the strongest risk factors, with over half of patients with peripheral artery disease being smokers (Morley et al, 2018). Studies have shown smoking to be a greater contributor to peripheral artery disease than coronary artery disease.

Diabetes is also strongly associated with peripheral artery disease with the strongest associations seen in patients with long-standing and uncontrolled diabetes. Newly diagnosed cases of diabetes and patients with impaired fasting glucose were noted to have peripheral artery disease of only borderline significance (Criqui and Aboyans, 2015).

Large population studies have also found strong associations between hypertension and peripheral artery disease, particularly between systolic blood pressure rather than diastolic blood pressure. This may be because databases have uncovered the presence of

How to cite this article:
Chan KA, Junia A. Lower extremity peripheral artery disease: a basic approach. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2019.0263

peripheral artery disease in patients with difficult to treat isolated systolic hypertension, but no in-depth analysis has been carried out on this (Clement et al, 2004).

Lipid parameters that are associated with peripheral artery disease include total serum cholesterol, high density lipoprotein and triglycerides. Patients who are older, male and those with chronic kidney disease, particularly end stage renal disease, have a higher incidence of peripheral artery disease (Criqui and Aboyans, 2015).

Lower extremity peripheral artery disease has long been considered to be a risk factor for other atherosclerotic diseases – namely coronary artery disease and cerebrovascular disease – and a marker of poor prognosis. Approximately 60% of patients with peripheral artery disease will have coronary artery disease and 30% will have cerebrovascular disease; approximately 10–15% of symptomatic patients with peripheral artery disease will succumb to cardiovascular-related mortalities (Morley et al, 2018).

Pathophysiology of peripheral artery disease

The pathophysiology of peripheral artery disease is a complex cascade of events occurring in long-standing systemic atherosclerosis and involves interactions between the vascular endothelial cells, smooth muscle cells, fibroblasts, platelets and other cells in the arterial wall. This can be summarised into three main pathophysiological processes:

1. Plaque formation and luminal narrowing
2. Endothelial dysfunction
3. Resultant alterations in blood flow haemodynamics and oxygen delivery.

Atherosclerosis induces a persistent inflammatory milieu that contributes to the formation of plaques with associated thrombosis. This gradually narrows the arterial luminal diameter, resulting in reduced blood flow to the muscles. Symptoms may not initially be evident at rest or with low level activity, which may be a result of compensatory mechanisms of the arteries involving endothelial-dependent vasodilation. However, simultaneous progression of arterial narrowing together with atherosclerosis-induced endothelial dysfunction later results in the typical clinical manifestations of peripheral artery disease (Hiatt et al, 2015). Further biological mechanisms may be activated to sustain sufficient blood flow, which results in the formation of collateral vessels across the severely narrowed region.

Clinical presentation

The initial assessment and history taking of a patient with peripheral artery disease is often difficult because of the heterogeneity of possible complaints and symptoms. However, certain points in the history can lead the examiner towards a suspicion of peripheral artery disease. A review of the patient's history will often reveal risk factors such as smoking, diabetes, hypertension or dyslipidaemia.

Lower extremity peripheral artery disease was previously said to typically present with pain upon walking a fixed, predictable distance, localised in muscle groups that are perfused by the involved atherosclerotic vessels – a symptom referred to as 'claudication'. This typical anginal pain of the lower extremities may be aggravated when the extremities are elevated and relieved when they are dependent, relying on gravity to assist perfusion (Wennberg, 2013). However, such symptoms are rarely elicited in a straightforward manner and the discomfort experienced has been described to be more often atypical than typical.

Patients commonly describe non-specific symptoms of discomfort such as fatigue, soreness and weakness, many times with two or more different sensations experienced over a long period of time. This may be confounded by the long list of possible differentials, such as neurological, orthopaedic and rheumatological pathologies (Wennberg, 2013). There may also be instances when patients are asymptomatic because of the coexisting neuropathy from long-standing diabetes, and instead present with poorly healing or highly chronic foot ulcers (Layden et al, 2012). Several screening questionnaires, such as the Edinburgh Claudication Questionnaire and the San Diego Claudication Questionnaire, have been developed in an attempt to address the atypical symptoms in peripheral artery disease and to better identify these patients. However, these questionnaires lack sensitivity

Table 2. Clinical classification systems of peripheral artery disease				
Fontaine classification		**Rutherford classification**		
Grade	**Symptoms**	**Grade**	**Category**	**Clinical descriptions**
Stage I	Asymptomatic	0	0	Asymptomatic
Stage II	Mild claudication in limb		1	Mild claudication
Stage IIA	Claudication at a distance of >200 m	I	2	Moderate claudication
Stage IIB	Claudication at a distance of <200 m		3	Severe claudication
Stage III	Rest pain, mostly in the feet	II	4	Ischaemic rest pain
Stage IV	Necrosis and/or gangrene of the limb	III	5	Minor tissue loss – non-healing ulcer, focal gangrene with diffuse pedal ischaemia
			6	Major tissue loss – extending above transmetatarsal level, functional foot no longer salvageable

From Fontaine et al (1954); Rutherford et al (1997)

and are affected by numerous confounders, such as age, gender, comorbidities and atypical presentations (Schorr and Treat-Jacobson, 2013).

As mentioned earlier, claudication has typically been described as a cramp or sharp pain in a particular muscle group, causing alteration in gait occurring at a fixed, reproducible level of activity. Levels of activity involving specific muscle groups are helpful in localising the level of obstruction, which is noted to be one joint level above the involved group. Other information which is helpful to elicit includes:

- The specific level of activity at which symptoms are experienced, which are the basis of several classification systems (Table 2)
- Exacerbation of pain at night ('night cramps') or with elevation, and prolonged, subconscious changes in daily routines, such as self-limitation of activity or walking at slower speeds
- Avoidance of climbing stairs and other actions involving major exertion of muscle groups (Wennberg, 2013).

Physical examination of the lower extremities

When conducting a physical examination of the patient's lower extremities, standard bedside procedures should be observed: you should first introduce yourself, explain the purpose of the examination and obtain the patient's consent. The patient should then be asked to remove any clothing or jewellery from their lower extremities. Surgical dressings from previous procedures will have to be removed to allow comprehensive examination of the extremities (Gogalniceanu et al, 2018). The examination consists mostly of inspection, palpation, auscultation and several special manoeuvres that can be performed at the bedside (Table 3).

The patient's lower extremities should be surveyed for cyanosis, trauma, soft tissue loss or injury, and the patient asked about the presence of tenderness or pain in specific regions. A detailed and systematic inspection of the lower extremities is then carried out, with an emphasis on finding pathologies that may point to the cause of the patient's symptoms: prior surgical scars, evidence of erythema from ongoing infection, tissue loss from repetitive trauma, unilateral or bilateral oedema or ulcerations. Ulcers are defined as any breaks in skin integrity and are graded based on their depth in relation to deeper tissue structures (Gogalniceanu et al, 2018). Asking a patient to point out pre-existing ulcers will enable one to gauge the patient's awareness of the injury, or lack thereof. Most patients are often unaware of these lesions, and this is usually seen in peripheral artery disease where advanced neuropathies have set in (Wennberg, 2013).

Palpation and manoeuvring of the patient's lower extremities allows further assessment of arterial perfusion and differentiates the vascular discomfort of claudication from

Table 3. Physical examination points for peripheral artery disease	
Inspection	■ Prior scars from trauma or surgical procedures ■ Erythema and signs of inflammation ■ Oedema, unilateral or bilateral ■ Cyanosis ■ Ulcers and soft tissue loss ■ Bone structure and gross deformities
Palpation	■ Pulses – strength, quality, regularity ■ Tenderness in specific regions or muscle groups ■ Skin temperature ■ Tissue loss or atrophy ■ Paraesthesia or sensory deficits ■ Capillary refill time
Special manoeuvres and tests	■ Burger's test for limb ischaemia ■ Pulse oximetry ■ Pulse oximetry ■ Ankle–brachial pressure index

neurological or rheumatological differentials. Light palpation of the extremities to assess skin temperature gives an index of perfusion – most patients with critical peripheral artery disease have markedly colder extremities. Palpation of all pulses in the lower extremity gives information on the presence of obstructive lesions distal to the pulse. Pulses accessible to palpation include:

1. The femoral pulse, located at the mid-inguinal level between the anterior superior iliac spine and the symphysis pubis
2. The popliteal pulse located deep within the popliteal fossa
3. The dorsalis pedis pulse, most prominent when the great toe is dorsiflexed
4. The posterior tibial pulses located close to the medial malleolus (Gogalniceanu et al, 2018).

Pulses should be compared bilaterally and may be graded on a 4-point scale for more objective documentation, but reliably identifying the presence or absence of a strong, bounding pulse is often adequate for initial assessment of peripheral artery disease (Hirsch et al, 2006). Auscultation may be used to detect 'bruits', or audible turbulent blood flow across a blood vessel indicative of narrowing. Capillary refill time (the time needed for nail bed capillary reperfusion after gentle pressure) has traditionally been suggested as an index for arterial perfusion. However, studies have demonstrated wide variability with a number of environmental factors, making it unreliable as a sole index. Instead, comparison of bilateral capillary refill times may provide more significant clinical information by demonstrating differences in perfusion between opposite extremities (Anderson et al, 2008).

Several special manoeuvres may also be done at the bedside to help raise clinical suspicion for peripheral artery disease. Burger's test for limb ischaemia, which is based on changes in skin colour with changes in extremity position, is based on the principle of mandatory gravity-reliant arterial perfusion with more critical peripheral artery disease. This is elicited by noting a period of extremity pallor when elevating the affected extremity with the ankle at 45º when the patient is supine and the presence of rubor or reactive erythema upon placing the extremity in a dependent position (Gogalniceanu et al, 2018). Pulse oximetry is an increasingly popular bedside device that correlates with lower extremity arterial perfusion, with smaller studies suggesting accuracy comparable to an ankle–brachial pressure index (Parameswaran et al, 2005).

The ankle–brachial pressure index: a useful bedside tool

The ankle–brachial pressure index is the ratio of the systolic blood pressure measured at the ankle to that measured at the brachial artery. Since its introduction by Winsor in 1950, it has been validated as a simple, reproducible and reliable test to confirm the diagnosis of peripheral artery disease (Al-Qaisi et al, 2009; Aboyans et al, 2012). It has also been validated to have prognostic significance, being able to identify patients at higher risk of cardiovascular mortality. The procedure itself is simple and can be performed with ease after several supervised training sessions (Table 4). The ankle–brachial pressure index is based on the principle of comparing peripheral to central arterial systolic pressures and current European Society of Cardiology (Aboyans et al, 2018) guidelines strongly recommend performing ankle–brachial pressure index as a test for the diagnosis of peripheral artery disease.

The interpretation of ankle–brachial pressure index is relatively straightforward: test values of <0.9 confirm the presence of lower extremity peripheral artery disease. However, there may be special conditions that may confound test value interpretation. Given that most patients with lower extremity peripheral artery disease are diabetic, there may be instances where their arteries are non-compressible. This may manifest as a patient with two distinct phenotypes: a patient with risk factors and symptoms consistent with peripheral artery disease and a highly elevated ankle–brachial pressure index (>1.4), and a patient with a similar clinical profile, but with a seemingly normal to borderline ankle–brachial pressure index. Both of these scenarios require the patient to be referred for further imaging.

Table 4. Steps in performing an ankle–brachial pressure index

Procedural conditions	■ The patient should be placed in a supine position with the upper and lower extremities exposed; the test should be explained to the patient ■ The room should be set to a comfortable room temperature of approximately 19–22 °C ■ Equipment required to measure the ankle–brachial pressure index includes a standardised blood pressure cuff of appropriate size and a hand-held 8–10 mHz Doppler probe with gel
Step 1	The brachial artery is palpated with the doppler probe applied at a 45–60° angle to the surface of the skin. The Doppler is turned on with the loudest signal isolated
Step 2	The blood pressure cuff is inflated until the last Doppler signal is heard and is inflated another 20 mmHg. From this level, slowly deflate and record the time when the signal returns. This is the Doppler-derived systolic blood pressure
Step 3	Repeat steps 1 and 2 on the dorsalis pedis and posterior tibial pulses of both feet and the contralateral brachial pulse. The recommended sequence is: right brachial, right posterior tibial, right dorsalis pedis, left posterior tibial, left dorsalis pedis, left brachial
Step 4	The right brachial systolic blood pressure is re-taken and compared with the initial reading. If the difference between the initial and the second systolic blood pressure is >10 mmHg, the first reading is discarded and the second reading is considered. If the difference is <10 mmHg, the two values are averaged out and used
Step 5	Once all systolic blood pressures have been recorded, the ankle–brachial pressure indices are calculated as shown in the formulas below: Leg specific ankle–brachial pressure index $\frac{\text{Highest ankle systolic blood pressure in leg}}{\text{Highest brachial systolic blood pressure overall}}$ Overall ankle–brachial pressure index for prognostication $\frac{\text{Lowest ankle systolic blood pressure overall}}{\text{Highest brachial systolic blood pressure overall}}$ Each leg's ankle–brachial pressure index is calculated by taking the highest ankle systolic blood pressure measurement (either the specific leg's posterior tibial or dorsalis pedis) divided by the higher brachial systolic blood pressure of the two arms. For the overall ankle–brachial pressure index, the lowest ankle systolic blood pressure among all pulses are used and divided by the higher brachial systolic blood pressure of the two arms. Peripheral artery disease is diagnosed with an ankle–brachial pressure index <0.9.

Adapted from Aboyans et al (2012)

Vascular imaging modalities

After establishing the presence of peripheral artery disease, imaging may be required to map out the vascular anatomy in order to plan revascularisation procedures (National Institute for Health and Care Excellence, 2018). There are three main vascular imaging modalities: duplex ultrasonography, computed tomography angiography and magnetic resonance angiography.

Duplex ultrasonography is safe, inexpensive and is useful for monitoring patients that have undergone revascularisation. However, it cannot completely visualise the entire arterial system of the lower extremity and is not reliable in instances where there are multiple stenotic segments because it is dependent on colour Doppler techniques.

Computed tomography angiography offers high resolution imaging, and is able to visualise the entire arterial tree and evaluate higher iliac and aortic segments for more proximal stenoses, offering faster scan times than magnetic resonance imaging. However, computed tomography angiography exposes patients to radiation and requires iodinated contrast, which may affect kidney function. The presence of calcifications may limit proper visualisation of arterial segments.

Magnetic resonance angiography offers a reasonable resolution and can image target vessels with and without the use of gadolinium-based contrast. However, it is not readily available in smaller centres and exposes patients to the risk of nephrogenic systemic sclerosis (Pollak et al, 2012).

Further visualisation of the target vessels in peripheral artery disease may also be carried out via peripheral angiography using digital subtraction angiography, but this is rarely done in isolation and is often performed before catheter-based revascularisation (Pollak et al, 2012).

General management principles

The main objectives in the management of lower extremity peripheral artery disease are to reduce the incidence of major adverse cardiovascular events, improve symptoms of claudication, and reduce limb vascular events and loss of viability or function. The National Institute for Health and Care Excellence (2018) guidelines on lower extremity peripheral artery disease advocate a streamlined approach involving a combination of pharmacological, non-pharmacological, interventional and surgical therapies (**Figure 1**).

Therapy to reduce cardiovascular events

This is achieved by a combination of lifestyle modification, particularly smoking cessation, as well medications to reduce cardiovascular risk (Layden et al, 2012) – these include antiplatelet agents (aspirin or P2Y12 inhibitors), statins and blood pressure control using either angiotensin inhibitors or angiotensin-receptor blockers (Aboyans et al, 2018).

Therapy for claudication

Additional therapies that can be prescribed to address claudication include naftidrofuryl oxalate, a peripheral vasodilator that improves walking distances before onset of claudication, as well as enrolment into a supervised exercise programme. Revascularisation may be considered to alleviate claudication that is refractory to best medical therapy and optimised exercise therapy (National Institute for Health and Care Excellence, 2018).

Therapy to prevent limb ischaemic events and limb loss

Chronic limb-threatening ischaemia represents progression of peripheral artery disease to a point where its viability is threatened even at rest, resulting in potential loss of tissue viability and function. Risk factor modification, pain control and immediate treatment of coexisting infection is crucial to optimise limb viability outcomes. Imaging and revascularisation should be done immediately with the goal of maximising limb viability and use. Should any of these measures prove unsuccessful, treatment pathways ultimately culminate in limb amputation.

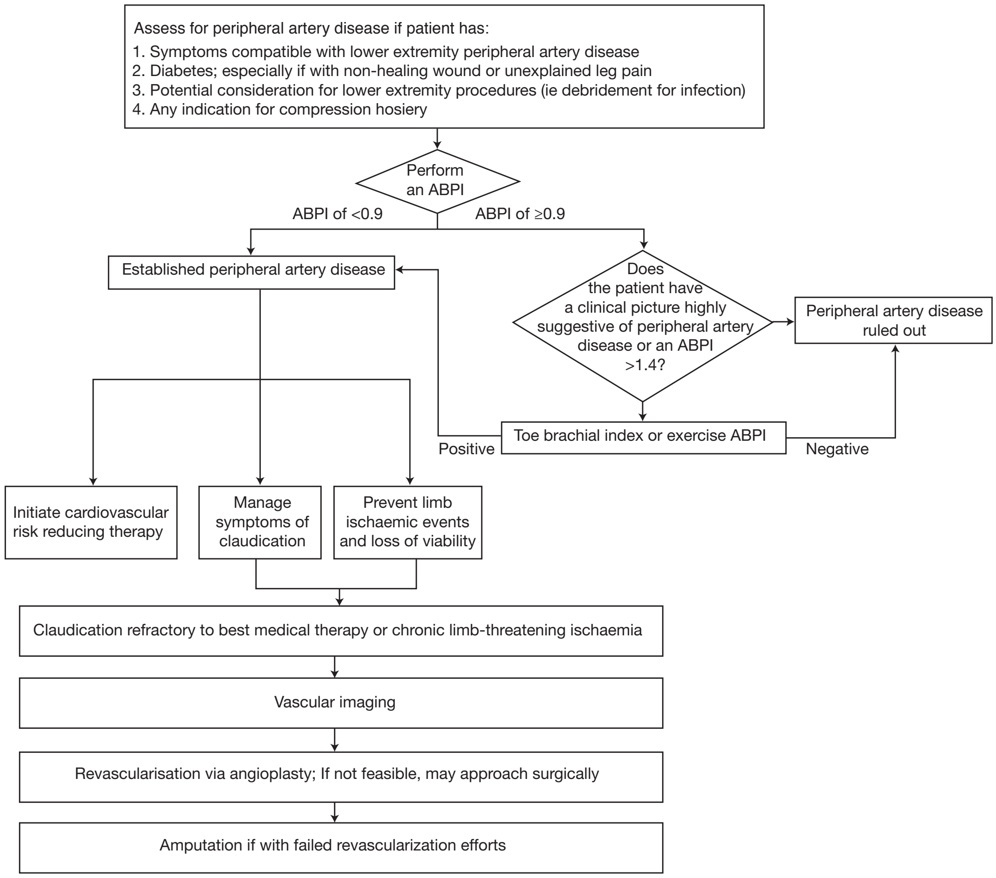

Figure 1. Treatment algorithm for lower extremity peripheral artery disease. Adapted from National Institute for Health and Care Excellence (2018). ABPI = ankle–brachial pressure index.

Prognosis

As with other organs affected by systemic atherosclerosis, peripheral artery disease is highly progressive. A meta-analysis showed that the progression of peripheral artery disease is rapid, with over 21% of patients with intermittent claudication progressing to chronic limb-threatening ischaemia in 5 years. All symptomatic patients with peripheral artery disease had a two-fold greater likelihood of mortality in 5 years (13% *vs* 5%) (Sigvant et al, 2016).

Conclusions

Lower extremity peripheral artery disease is a commonly encountered disease, the diagnosis of which is often confounded by its varying clinical presentations. Claudication is often the most common initial complaint, but may be confused with a long list of alternative differentials. Astute clinical assessment, a high degree of suspicion and the use of ankle–brachial pressure index screening is essential to identify patients with peripheral artery disease. Early administration of basic pharmacotherapy and lifestyle changes may be beneficial in reducing untoward vascular events and may effectively reduce symptoms of peripheral artery disease which may have otherwise been wrongly treated.

Conflicts of interest

The authors declare no conflicts of interest.

Author details

[1]Section of Adult Cardiology, Chong Hua Heart Institute, Cebu City, Philippines

Key points

- Peripheral artery disease of the lower limbs is a commonly encountered, chronic and disabling disorder that manifests as a variety of clinical presentations.
- Establishing risk factors such as smoking, diabetes and hypertension greatly help in raising clinical suspicion and should be part of a thorough clinical history.
- Lower extremity peripheral artery disease may present with claudication (typical pain upon walking), but may also present with a numerous atypical signs and symptoms.
- A thorough, systematic and detailed physical examination of the lower extremities, including an ankle–brachial pressure index should be performed for rapid bedside diagnosis and cardiovascular prognostication.
- Treatment of peripheral artery disease includes a combination of risk-reducing drugs, drugs that improve claudication, rehabilitation and surgical/invasive methods.

Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum

- Managing patients in an outpatient clinic, ambulatory or community setting, including management of long-term conditions
- Managing medical problems in patients in other specialties and special cases
- Managing a multidisciplinary team including effective discharge planning.

Acknowledgements
The authors would like to thank the members of the Chong Hua Heart Institute research faculty and training core and the members of the Philippines Heart Association for their support and commitment to medical research and literature.

References

Aboyans V, Criqui M, Abraham P et al. Measurement and interpretation of the ankle-brachial index. Circulation. 2012;126(24):2890–2909. https://doi.org/10.1161/cir.0b013e318276fbcb

Aboyans V, Ricco J, Bartelink M et al. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European society for vascular surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European stroke organization (ESO)the task force for the diagnosis and treatment of peripheral arteria. Eur Heart J. 2018;39(9):763–816. https://doi.org/10.1093/eurheartj/ehx095

Al-Qaisi M, Nott DM, King DH et al. Ankle brachial pressure index (ABPI): an update for practitioners. Vasc Health Risk Manag. 2009;5:833–841. https://doi.org/10.2147/vhrm.s6759

Anderson B, Kelly A, Kerr D et al. Impact of patient and environmental factors on capillary refill time in adults. Am J Emer Med. 2008;26(1):62–65. https://doi.org/10.1016/j.ajem.2007.06.026

Clement D, De Buyzere M, Duprez D. Hypertension in peripheral arterial disease. Curr Pharm Des. 2004;10(29):3615–3620. https://doi.org/10.2174/1381612043382819

Criqui M, Aboyans V. Epidemiology of peripheral artery disease. Circ Res. 2015;116(9):1509–1526. https://doi.org/10.1161/circresaha.116.303849

Davies J, Richards J, Conway K et al. Primary care screening for peripheral arterial disease: a cross-sectional observational study. Br J Gen Pract. 2017;67(655):e103–e110. https://doi.org/10.3399/bjgp17x689137

Fontaine R, Kim M, Kieny R. Surgical treatment of peripheral circulation disorders [in German]. Helv Chir Acta. 1954;21(5–6):499–533.

Gogalniceanu P, Lancaster R, Patel V. Clinical assessment of peripheral arterial disease of the lower limbs. N Engl J Med. 2018;378(18):e24. https://doi.org/10.1056/nejmvcm1406358

Hiatt W, Armstrong E, Larson C, Brass E. Pathogenesis of the Limb Manifestations and Exercise Limitations in Peripheral Artery Disease. Circ Res. 2015;116(9):1527–1539. https://doi.org/10.1161/circresaha.116.303566

Hirsch AT, Haskal ZJ, Hertzer NR et al. ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary. Circulation. 2006;113:1474–1547. https://doi.org/10.1161/CIRCULATIONAHA.106.174526

Layden J, Michaels J, Bermingham S et al. Diagnosis and management of lower limb peripheral arterial disease: summary of NICE guidance. BMJ. 2012;345(aug08 1):e4947–e4947. https://doi.org/10.1136/bmj.e4947

Morley R, Sharma A, Horsch A, Hinchliffe R. Peripheral artery disease. BMJ. 2018;j5842. https://doi.org/10.1136/bmj.j5842

National Institute for Health and Care Excellence. Guidelines: peripheral arterial disease: diagnosis and management. 2018. nice.org.uk/guidance/cg147 (accessed 13 January 2020)

Parameswaran G, Brand K, Dolan J. Pulse oximetry as a potential screening tool for lower extremity arterial disease in asymptomatic patients with diabetes mellitus. Arch Intern Med. 2005;165(4):442. https://doi.org/10.1001/archinte.165.4.442

Pollak A, Norton P, Kramer C. Multimodality imaging of lower extremity peripheral arterial disease. Circ Cardiovasc Imaging. 2012;5(6):797–807. https://doi.org/10.1161/circimaging.111.970814

Rutherford RB, Baker JD, Ernst C et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg. 1997;26(3):517–538. https://doi.org/10.1016/S0741-5214(97)70045-4

Schorr E, Treat-Jacobson D. Methods of symptom evaluation and their impact on peripheral artery disease (PAD) symptom prevalence: a review. Vasc Med. 2013;18(2):95–111. https://doi.org/10.1177/1358863x13480001

Shu J, Santulli G. Update on peripheral artery disease: epidemiology and evidence-based facts. Atherosclerosis. 2018;275:379–381. https://doi.org/10.1016/j.atherosclerosis.2018.05.033

Sigvant B, Lundin F, Wahlberg E. The risk of disease progression in peripheral arterial disease is higher than expected: a meta-analysis of mortality and disease progression in peripheral arterial disease. Eur J Vasc Endovasc Surg. 2016;51(3):395–403. https://doi.org/10.1016/j.ejvs.2015.10.022

Weinberg I, Jaff M. Nonatherosclerotic arterial disorders of the lower extremities. Circulation. 2012;126(2):213–222. https://doi.org/10.1161/circulationaha.111.060335

Wennberg P. Approach to the patient with peripheral arterial disease. Circulation. 2013;128(20):2241–2250. https://doi.org/10.1161/circulationaha.113.000502