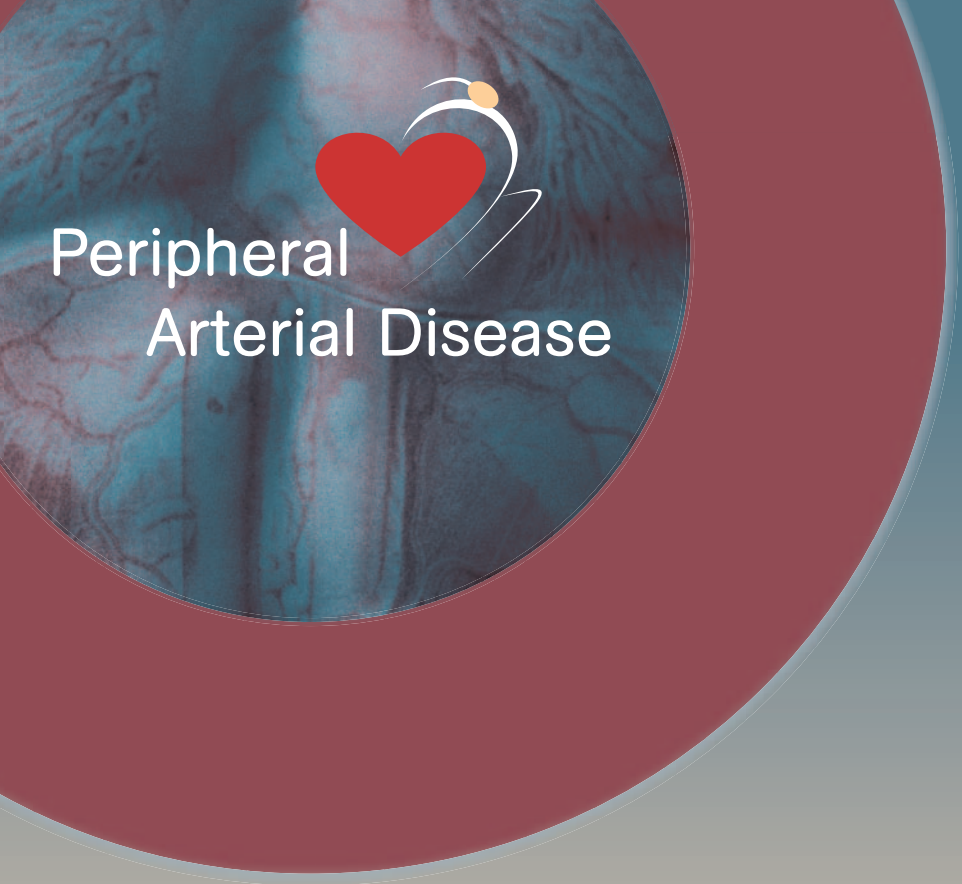

Peripheral Arterial Disease

A Management Guide for General Practice

An opportunity to reduce cardiovascular morbidity and mortality

Home

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Acknowledgments

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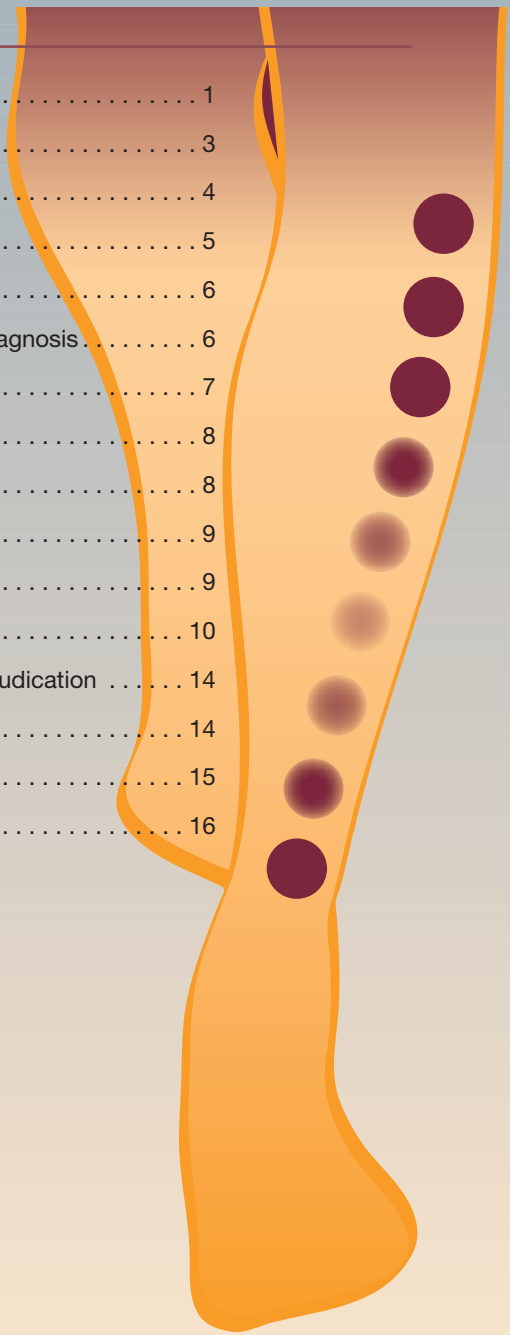


Executive Summary

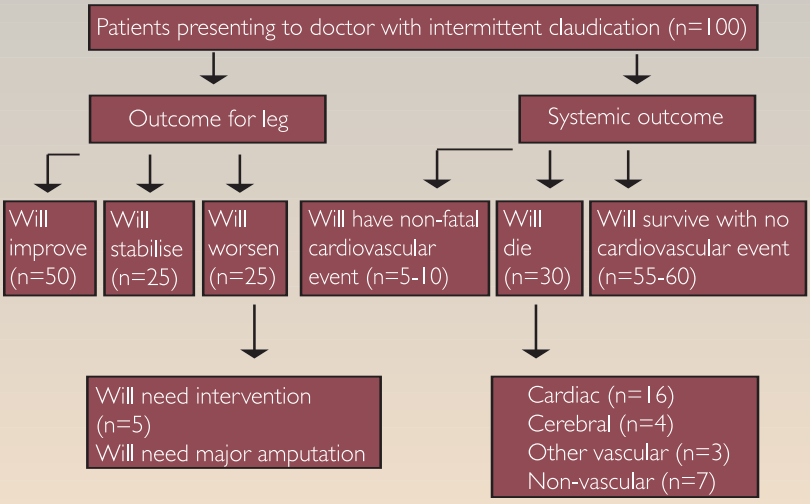
More than one in six people over 55 years of age have Peripheral Arterial Disease (PAD). While only one third of these patients have typical intermittent claudication, many remain asymptomatic, or have atypical symptoms. On diagnosis of PAD, the prime concern of most patients is the possibility of amputation. However, the natural history of PAD is quite different. Only 7 of the 100 patients presenting require intervention.

While few patients require surgical intervention, up to 30% die within 5 years mostly from cardiovascular disease. (Fig 1)

More significantly, the presence of PAD either symptomatic or asymptomatic, is associated with grave prognostic implications for cardiovascular morbidity and mortality. Up to 50% of cases of PAD can be missed on routine history and physical examination.

The identification and appropriate management of this often unidentified, high risk patient group, represents a significant opportunity in general practice to improve survival and reduce the risk of heart attack and stroke.

Fig 1. Five-year natural history of 100 patients presenting to their doctor with intermittent claudication



Ref: Dormandy JA, *Hospital Update* 1991; April:314-318

Click on image to enlarge

What is Peripheral Arterial Disease (PAD)?

Peripheral Arterial Disease is a manifestation of systemic atherosclerosis. In this condition the arterial lumen of all vascular beds becomes progressively narrowed by atherosclerosis. When the resulting obstruction reduces blood flow, symptoms may result, ranging from pain on exertion that is relieved by rest (claudication), the most common manifestation of PAD, to pain at rest, ulceration or gangrene (critical limb ischaemia).

The most important implication of PAD in terms of morbidity and mortality is that PAD serves as a strong marker for the severity of atherosclerotic disease in other vascular territories. Peripheral Arterial Disease therefore is a distinct atherothrombotic syndrome that is associated with an elevated risk of cardiovascular and cerebrovascular events, including death, MI and stroke.

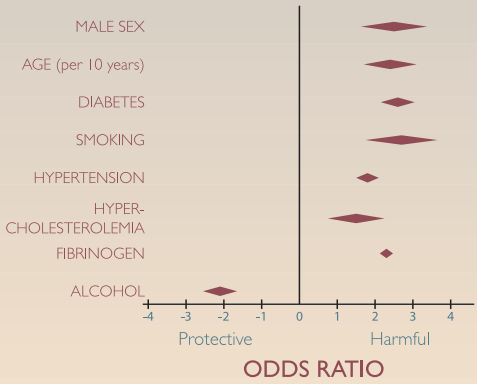
Risk Factors for PAD

- *diabetes**
- *smoking**
- *hypertension*
- *hyperlipidaemia*
- *hyperhomocysteinaemia*
- *elevated plasma fibrinogen*
- *age*
- *male sex*

**which account for over half the attributable risk of PAD.*[2-7]

Fig 2. depicts the range of odds ratios for developing symptomatic PAD. Excluding unmodifiable factors, the most important risk factors for developing intermittent claudication are diabetes and smoking.

Fig. 2 Common PAD risk factors.



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Morbidity and mortality considerations

In patients with PAD, the prevalence of coronary artery disease ranges from 20% to 60% when based on medical history and electrocardiography, and increases up to 90% in patients who have undergone coronary angiography.[8] Cerebrovascular disease has been diagnosed in up to 40% to 50% of patients with PAD.[9]

Cardiovascular disease is the most common cause of death in patients with PAD, accounting for up to 75% of deaths.[10]

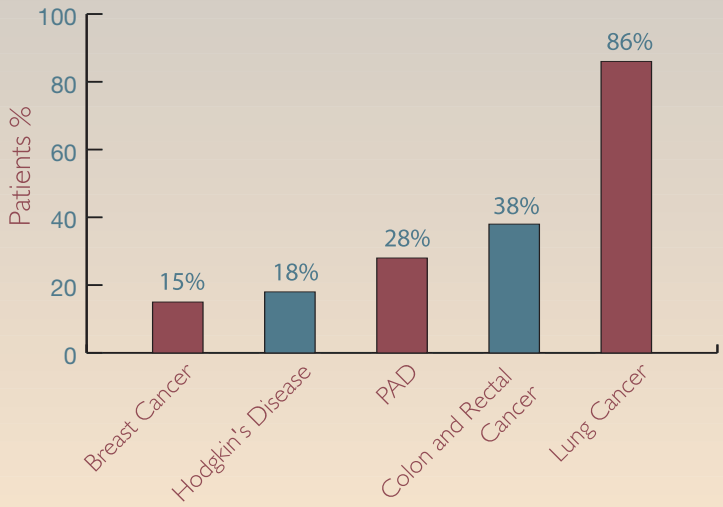
A 10 year mortality study showed that patients with large vessel PAD have an approximate 3-fold greater risk of all-cause mortality and an approximate 7-fold greater risk of death from coronary heart disease, than patients with no PAD.[11]

Only 1 in 4 patients with severe PAD will be alive in 10 years.

The severity of PAD is closely associated with the risk of myocardial infarction, ischaemic stroke and death from vascular disease.

The outcome from time of diagnosis of PAD was found to be worse than the outcome of breast cancer and Hodgkin's disease.

Fig 3. The 5-year mortality rates for common pathological conditions.



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Clinical presentation of PAD

Intermittent claudication is the most typical symptom of peripheral arterial disease.[12,13,14] Claudication is characterised by cramping, or tightness in the calf, thigh or buttock, brought on by exercise and relieved by rest.

As few as 1 in 4 patients with PAD on examination are symptomatic

Calf claudication is by far the commonest symptom but some patients may describe Leriche syndrome, which includes buttock claudication and impotence due to severe aortoiliac disease.

A diagnosis of intermittent claudication can usually be made on the basis of the history alone. The differential diagnosis includes both venous and neurogenic claudication.[16]

Many symptomatic patients do not alert their physicians to the disease, since they attribute it to the non-specific musculoskeletal symptoms of ageing.[15]

Conducting investigations and making a diagnosis

Although the physical examination provides important qualitative information and is critical to overall patient treatment, additional non-invasive testing ensures the diagnosis and aids in risk stratification of patients with suspected PAD.[17]

Physicians who rely on a classic history of claudication alone to detect PAD will miss approximately 85% to 90% of patients who are asymptomatic.[2]

Atherosclerosis is not a focal disease. For this reason, the physical examination should be conducted with attention to its multi-systemic nature. Assessment of the circulatory systems should begin with blood pressure measurement in both arms. The femoral and popiteal and pedal pulses should be assessed. If subclavian or brachiocephalic arterial disease is present, a discrepancy in BP may be detected and the higher of the two values should be used.[19]

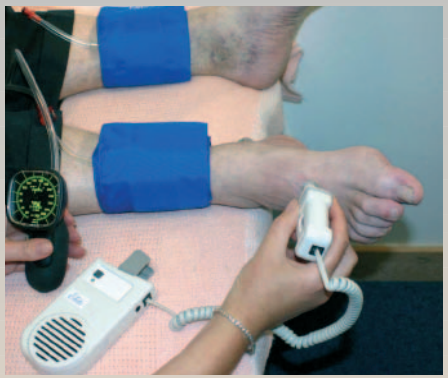
Further examination of the cardiovascular system may disclose signs of subclavian or cervical (both carotid and vertebral) bruits, abdominal aneurysm, cardiac murmurs, arrhythmia, or other conditions that might impact on patient care.[19]

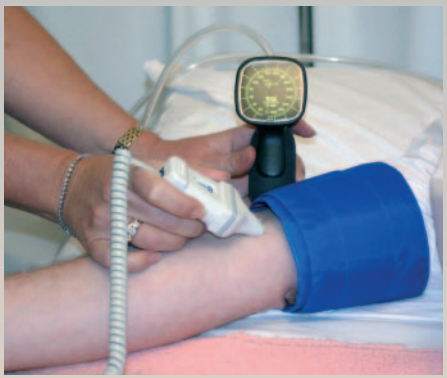
Physicians who rely on the bedside pulse examination alone, valuable as this technique remains, will also miss as many as half of PAD cases in practice.[18]

Ankle Brachial Index (ABI)

The Ankle Brachial Index (ABI) is a non-invasive, simple, highly sensitive and specific, inexpensive measurement to assess the patency of the lower extremity arterial system. The ABI is measured by having the patient lie in the supine position in a warm room, with subsequent performance of the ankle and brachial systolic blood pressure measurements using a 5-8MHz handheld Doppler device.[20] (A maternity Doppler is not suitable for ABI measurement.)

A handheld Doppler device



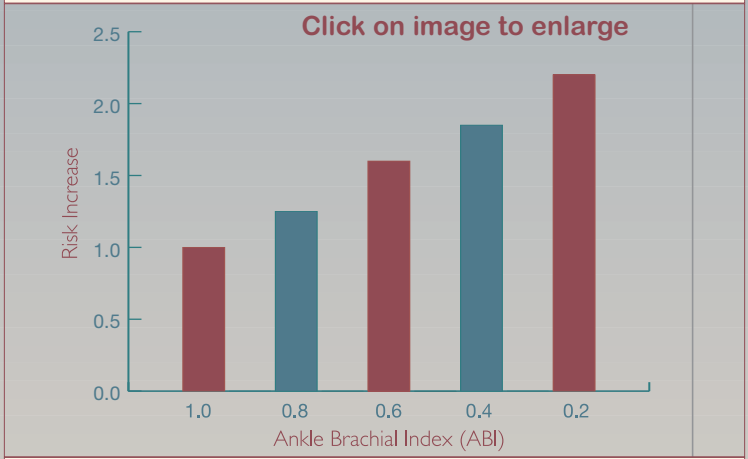


Ideally the posterior tibial and dorsalis pedis artery systolic pressures are both measured and compared with the brachial pressure. The ABI value is calculated by dividing the higher of the ankle systolic pressures by the higher of the two systolic brachial pressures. The ABI takes approximately 10 minutes to perform.[20] Given data from studies in symptomatic and asymptomatic patients with PAD, strong evidence now argues for the more widespread use of the ABI in routine clinical practice. [9, 21, 22, 23, 24, 25]

Some elderly and diabetic patients have calcified arteries which may result in an unusually high ABI reading (>1.30). Patients with high-grade aortoiliac arterial stenosis or occlusions may also occasionally present with a normal ABI at rest due to the presence of collaterals.

Apart from diagnosis, the ABI is useful in assessing the severity and progression of PAD. The ABI is helpful in stratifying the risk of mortality in PAD patients. The lower the ABI, the greater the risk of serious cardiovascular events.

Fig 5. Increase for MI and stroke as a function of ABI measurement.



Ref: Dormandy JA, Creager MA *Cerebrovasc Disc* 1999, 9(supp1):14

Interpretation of an ABI

>1.10	*Normal but consider incompressible (calcified) arteries*
0.90-1.10	*Normal range*
0.70-0.89	*Mild-to-moderate PAD*
<0.7	*Moderate-to-severe PAD*

(Ref: Based on Fowkes FGR, *Int J Epidemiol* 1988;17:201-207)

Who should have an ABI?

The following patients should be considered for an ABI:

- Any patient with absent dorsalis and posterior pulses
- Any patient with symptoms of PAD
- Men greater than 55 years of age with significant risk factors
- Women greater than 65 years of age with significant risk factors

Basic biochemical and haematological investigations

The following routine investigations should be performed:

- full blood count
- urea and creatinine
- fasting blood glucose
- fasting lipid profile

Additional optional parameters include:
HbA1c, serum fibrinogen, serum homocysteine, high sensitivity C reactive protein and an ESR.

Indications for referral to a vascular surgeon

Urgent referral by telephone should be undertaken for patients with critical limb ischaemia (rest pain, gangrene, or ulceration).

consider referral if:

- not confident about the diagnosis
- there is concern that the symptoms may have an unusual cause
- patients present with claudication significantly affecting their quality of life.
- patient preference

Critical limb ischaemia in its most severe form is a threat to the limb and usually signals the need for revascularisation or amputation. Haemodynamic parameters that indicate a diagnosis of critical limb ischaemia include an ABI value less than 0.4, an ankle systolic pressure less than 50mmHg, or a toe systolic pressure less than 30mmHg.

The risk of a person with claudication progressing to critical limb ischaemia and needing amputation is low (<1% per year). However the risk of death mainly from coronary and cerebrovascular events, is high at 5-10% per year.

Surgery is indicated in all patients with critical limb ischaemia and in patients with severe lifestyle limiting claudication. Surgery is only indicated in patients in whom smoking cessation has been successful and in whom the full gamut of secondary prevention is in place.

Secondary prevention for PAD

Smoking cessation

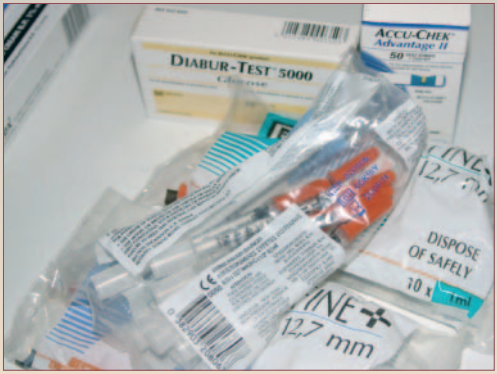
Cigarette smoking is the most preventable cause of cardiovascular mortality and morbidity, and is the primary PAD risk factor. It is important to educate, encourage, and assist the PAD patient in quitting smoking. Treatment strategies include smoking cessation programmes and Nicotine Replacement Therapy (NRT) and these should be considered[27], and offered to all appropriate patients.

Treatment of diabetes mellitus

The risk of lower limb ulceration is exacerbated by microvessel disease and neuropathy, as well as PAD. Amputation rates amongst patients with diabetes (mainly digital amputations) are 40 fold higher than in age-matched non diabetic controls.[28]

Every 10mmHg reduction in systolic BP is associated with a 12% reduction in any diabetes related complication; 15% reduction in death related to diabetes; 11% reduction in MI; and 13% reduction in microvascular complications.[29]

For every 1% increase in HbA1c there is a 28% increased risk of death, independent of age, BP, serum cholesterol and smoking status.[30]



The diagnosis of diabetes can be made on any of 3 grounds:-

- Fasting plasma glucose >7.0 mmol (8 hour fast)
- Symptoms of diabetes and random plasma glucose 11.1mmol/L
- 2 hour post-glucose >11.1 mmol (75g anhydrous glucose dissolved in water)

In the absence of unequivocal hyperglycaemia, these criteria should be confirmed by repeat testing on a different day. The OGTT is not recommended for routine clinical use.

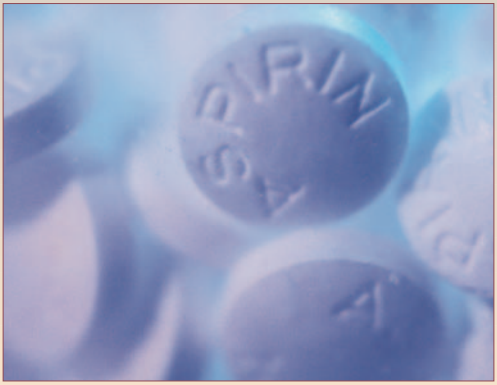
Statin therapy

The Heart Protection Study[31] has shown that lowering total cholesterol and low density lipoprotein cholesterol by 25% with a statin, reduces cardiovascular mortality and morbidity in patients with PAD by up to 25%, irrespective of age, sex, or baseline cholesterol concentration.

The implication is that every patient with PAD should be started on a statin. The lipid profile should be checked after 6 weeks to ensure a 25% reduction is achieved.

Antiplatelet therapy

Aspirin: data suggests that aspirin therapy may modify the natural history of chronic lower extremity insufficiency and reduce the risk of associated cardiovascular events.[32] There is no evidence however of increased efficacy for increasing doses of aspirin between 75mg and 300mg.



Observed side effects are lower with lower doses. Hence the available evidence supports daily doses of aspirin in the range of 75-150mg.

Clopidogrel has been shown to be more effective than aspirin in preventing Myocardial Infarction, Stroke and Vascular Death in patients with PAD as shown by the CAPRIE study and should therefore be considered as an alternative to aspirin.[33]

There have been no randomised, blinded, placebo controlled trials of dipyridamole alone in the prevention of vascular events.[34]

Blood pressure

Individuals at high risk of developing cardiovascular disease with sustained SBP >140mmHg and/or DBP >90mmHg require drug therapy.[35]

Data is not available to clarify whether treatment will alter the progression of the disease or the risk of claudication.

ACE inhibitors

The results of the HOPE trial would suggest that all patients with symptomatic PAD, where possible, should receive an ACE inhibitor in addition to their other cardiovascular therapies regardless of normal resting blood pressure. This may not be possible in patients with abnormally low blood pressure. As the rate of renal artery stenosis is quite high in the PAD population, it is therefore essential to use a low starting dose and to check the serum electrolytes 1 week and 1 month after commencing or increasing ACE inhibitor therapy.[36]

All patients with PAD should be on an ACE inhibitor, a statin and antiplatelet therapy.

Exercise

Multiple previous studies have shown the benefit of exercise training particularly in patients with claudication. There are many studies which show the benefits of supervised exercise training, i.e., training under the guidance of a physiotherapist associated with exercise on a treadmill. In these programmes the patient exercises approximately three times per week. They have shown huge benefits in improving exercise tolerance of up to 50%. However for practical purposes these programmes are not available universally and are not applicable outside the realms of clinical trials.[37, 38, 39]

It is important that patients be advised correctly how to exercise to improve their claudication distance. Most of the research shows that exercise must be 3-4 times per week. The exercise needs to be of sufficient nature to provoke the sufficiently severe claudication to require the patient to stop. The exercise should be repetitive.

Patients should be advised to exercise 'beyond their symptoms'. ie, the patient will walk until they feel they have to stop, not at the first point they feel the pain.

Patients should be advised to walk the same route on a regular basis 3-4 times per week. They should walk sufficiently fast and for a distance to experience their claudication symptoms. Once reaching the maximum limit of their claudication they should stop and allow the pain to recede. The walk should then continue until the pain recurs again and be repeated until the pain recurs at least a third time. After 1-2 weeks exercise they should try and increase their claudication distance by 5-10 paces each time and to carry on like this repetitively week by week.

Patients should be clearly advised of the benefits of exercise for overall cardiovascular health.

Pharmacological agents for intermittent claudication

Vasodilators: (e.g Inositol nicotinate - Hexopal): Several controlled trials have found no evidence of clinical efficacy of drugs of this class. Thus current data do not support the use of vasodilators for claudication.[40]

Pentoxifylline (Trental): Meta-analyses and two systemic reviews of pentoxifylline concluded that the drug may have a small effect on walking ability, but that the data are insufficient to support its widespread use.[41, 42, 43, 44, 45]

Naftidofuryl (Praxiline): A meta-analyses of naftidofuryl concluded that the drug may have a small effect on walking ability, but that the data was insufficient to support its widespread use.[46,47]

Cilostazol (pletal): Has demonstrated both improved pain free and maximal treadmill walking distance (this agent is currently not available in Ireland).

Surgical and endovascular interventions

The planning of surgical intervention requires arterial diagnostic imaging. Currently there are two types of imaging available:

- *Conventional Digital Subtraction Angiography*
- *Magnetic Resonance Angiography.*

The long term outcome from bypass surgery is excellent. Vein graft patency rates of over 80% at 5 years are reported in most studies. When one equates this with the life expectancy of these patients, these are extremely good results.[48]

These are probably of equal benefit although Magnetic Resonance Angiography has the advantage of being an out-patient procedure, which does not require femoral arterial puncture or nephrotoxic contrast. The lesions visible on arteriography will determine the precise intervention required.

Currently the procedures available include angioplasty +/- stenting, bypass surgery, endarterectomy, or a combination of all of these procedures depending on the lesions involved.

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Managing PAD in Primary Care

Male patients >55 years
OR female patients >65 years
with significant risk for PAD
should be considered

Risk for PAD include:
- Smoking
- Diabetes
- Hyperlipidaemia
- Hypertension

Ankle Brachial Index ABI
>1.1 = Noncompressable
0.9-1.1 = Normal
0.7-0.89 = Mild-to-moderate
<0.7 = Moderate-to-severe

Normal

Look for other causes

Risk Factor Modification include:
- smoking
- exercise
- cholesterol
- BP
- diet, etc

Abnormal

Risk factor Modification
- Statin
- ACE inhibitor
- Anti-platelet

Asymptomatic or acceptable symptoms

Regular follow-up

if deteriorates

Unacceptable symptoms

Vascular Surgeon referral

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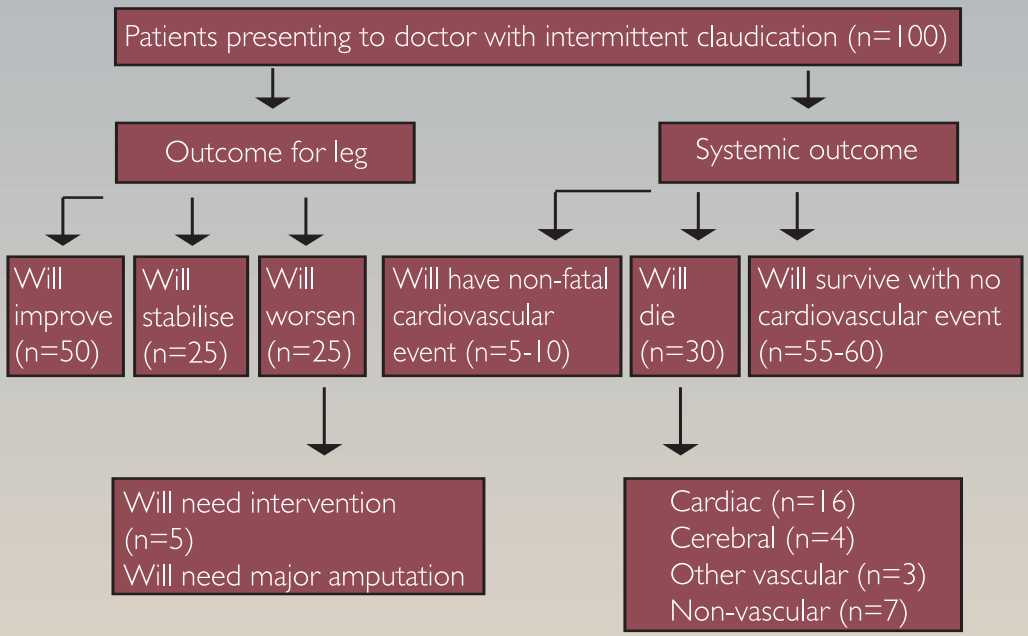
Fig 1. Five-year natural history of 100 patients presenting to their doctor with intermittent claudication



Ref: Dormandy JA, *Hospital Update* 1991; April:314-318

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Fig 2. Common PAD risk factors.

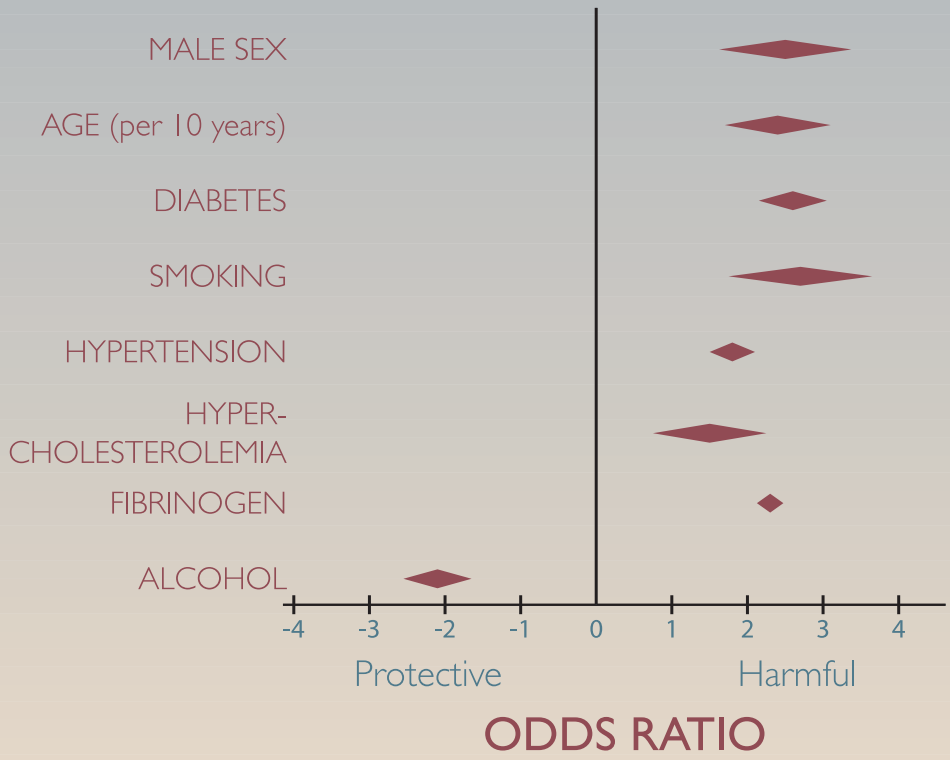

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Fig 3. The 5-year mortality rates for common pathological conditions.

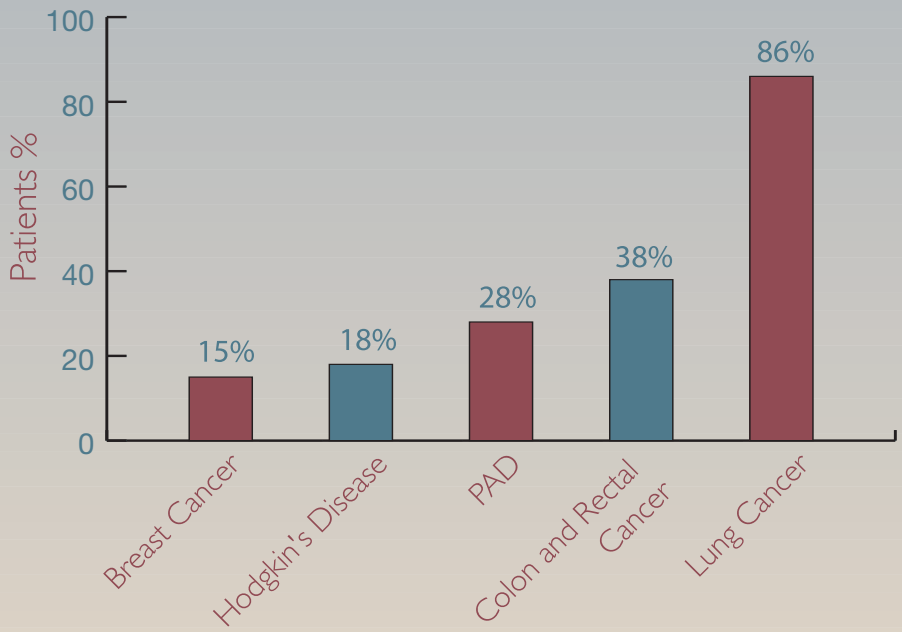

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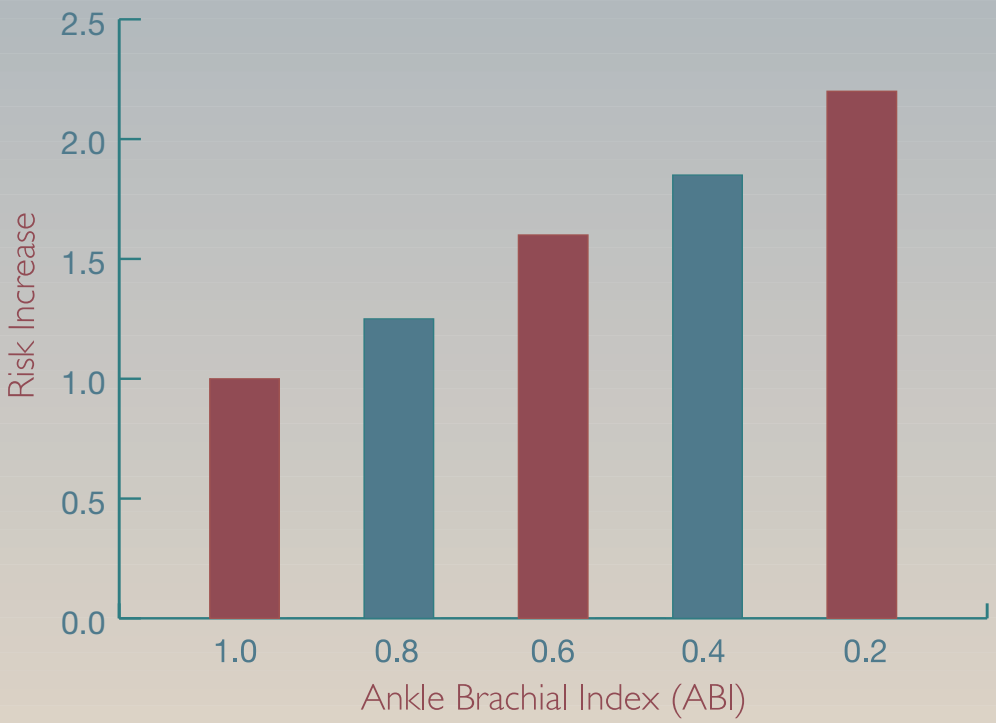
Fig 5. Increase for MI and stroke as a function of ABI measurement.



Ref: Dormandy JA, Creager MA *Cerebrovasc Disc* 1999, 9(supp1):14

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