Lower limb peripheral arterial disease: diagnosis and management

NICE guideline

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If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

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Introduction

Peripheral arterial disease is a marker for increased risk of cardiovascular events even when it is asymptomatic. The most common initial symptom of peripheral arterial disease is leg pain while walking, known as intermittent claudication. Critical limb ischaemia is a severe manifestation of peripheral arterial disease, and is characterised by severely diminished circulation, ischaemic pain, ulceration, tissue loss and/or gangrene.

The incidence of peripheral arterial disease increases with age. Population studies have found that about 20% of people aged over 60 years have some degree of peripheral arterial disease. Incidence is also high in people who smoke, people with diabetes and people with coronary artery disease. In most people with intermittent claudication the symptoms remain stable but approximately 20% will develop increasingly severe symptoms with the development of critical limb ischaemia.

Mild symptoms are generally managed in primary care, with referral to secondary care when symptoms do not resolve or deteriorate. There are several treatment options for people with intermittent claudication. These include advice to exercise, management of cardiovascular risk factors (for example, with aspirin or statins) and vasoactive drug treatment (for example, naftidrofuryl oxalate).

People with severe symptoms that are inadequately controlled are often referred to secondary care for assessment for endovascular treatment (such as angioplasty or stenting), bypass surgery, pain management and/or amputation.

Rapid changes in diagnostic methods, endovascular treatments and vascular services, associated with the emergence of new sub-specialties in surgery and interventional radiology has resulted in considerable uncertainty and variation in practice. This guideline aims to resolve that uncertainty and variation.

Drug recommendations

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Patient-centred care

This guideline offers best practice advice on the care of adults aged 18 years or over with lower limb peripheral arterial disease (known in the document as peripheral arterial disease).

Treatment and care should take into account patients' needs and preferences. People with peripheral arterial disease should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Information requirements for people with peripheral arterial disease

- Offer all people with peripheral arterial disease verbal and written information about their condition and discuss it with them so they can share decision-making, understand the course of the disease and what they can do to help prevent disease progression. Information should include:
  - the causes of their symptoms, such as level of stenosis or occlusion
  - the key modifiable risk factors, such as smoking, managing diabetes, diet, weight and exercise
  - the risks and benefits of all relevant treatment options
  - how they can access support for dealing with depression and anxiety.

  Ensure that information, tailored to the individual needs of the person, is available at diagnosis and subsequently as required, to allow people to make decisions throughout the course of their treatment.

- Offer all people with peripheral arterial disease appropriate information, advice and support in line with NICE guidance (see related NICE guidance section) on:
  - smoking cessation
  - diet, weight management and exercise
  - lipid modification and statin therapy
  - the prevention, diagnosis and management of diabetes
  - the prevention, diagnosis and management of high blood pressure
  - drug therapy with antiplatelet agents.

Diagnosis

- Assess people with suspected peripheral arterial disease by:
  - using structured questioning about the symptoms of intermittent claudication and critical limb ischaemia

  - examining the leg and foot for evidence of critical limb ischaemia, for example ulceration
  - examining the femoral, popliteal and foot pulses
  - measuring the ankle brachial pressure index (see recommendation below).

- Measure ankle brachial pressure index in the following manner:
  - The person should be resting and supine where possible.
  - Systolic blood pressure is recorded with an appropriately sized cuff in both arms and in the posterior tibial, dorsalis pedis and, where possible, the peroneal arteries.
  - Measurements should be taken manually using a Doppler probe of suitable frequency in preference to an automated system.
  - Document the nature of the Doppler ultrasound signals in the foot arteries.
  - The index in each leg is calculated by dividing the highest foot artery pressure by the highest arm pressure.

Imaging for revascularisation

- Offer contrast-enhanced magnetic resonance angiography to people with peripheral arterial disease who need further imaging before considering an intervention.

Management of intermittent claudication

- Offer a supervised exercise programme to all people with intermittent claudication.

Management of critical limb ischaemia

- Ensure that all people with critical limb ischaemia are reviewed by a vascular multidisciplinary team before treatment decisions are made.
- Do not offer major amputation to people with critical limb ischaemia unless all options for revascularisation have been considered by a vascular multidisciplinary team.

1 Guidance

The following guidance is based on the best available evidence. The full guideline [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

1.1 Information requirements

1.1.1 Offer all people with peripheral arterial disease verbal and written information about their condition and discuss it with them so they can share decision-making, understand the course of the disease and what they can do to help prevent disease progression. Information should include:

- the causes of their symptoms, such as level of stenosis or occlusion
- the key modifiable risk factors, such as smoking, managing diabetes, diet, weight and exercise
- the risks and benefits of all relevant treatment options
- how they can access support for dealing with depression and anxiety.

Ensure that information, tailored to the individual needs of the person, is available at diagnosis and subsequently as required, to allow people to make decisions throughout the course of their treatment.

1.1.2 NICE has produced guidance on the components of good patient experience in adult NHS services. Follow the recommendations in 'Patient experience in adult NHS services' (NICE clinical guideline 138).

1.2 Secondary prevention of cardiovascular disease in PAD

1.2.1 Offer all people with peripheral arterial disease appropriate information, advice and support in line with NICE guidance (see related NICE guidance section) on:

- smoking cessation
- diet, weight management and exercise
- lipid modification and statin therapy
- the prevention, diagnosis and management of diabetes
- the prevention, diagnosis and management of high blood pressure
- drug therapy with antiplatelet agents.

1.3 Diagnosis

1.3.1 Assess people with suspected peripheral arterial disease by:

- using structured questioning about the symptoms of intermittent claudication and critical limb ischaemia
- examining the leg and foot for evidence of critical limb ischaemia, for example ulceration
- examining the femoral, popliteal and foot pulses
- measuring the ankle brachial pressure index (see recommendation 1.3.2).

1.3.2 Measure ankle brachial pressure index in the following manner:

- The person should be resting and supine where possible.

- Systolic blood pressure is recorded with an appropriately sized cuff in both arms and in the posterior tibial, dorsalis pedis and, where possible, the peroneal arteries.
- Measurements should be taken manually using a Doppler probe of suitable frequency in preference to an automated system.
- Document the nature of the Doppler ultrasound signals in the foot arteries.
- The index in each leg is calculated by dividing the highest foot artery pressure by the highest arm pressure.

1.4 Imaging for revascularisation

1.4.1 Offer duplex ultrasound as first-line imaging to all people with peripheral arterial disease in whom revascularisation is being considered.

1.4.2 Offer contrast-enhanced magnetic resonance angiography to people with peripheral arterial disease who need further imaging before considering an intervention.

1.4.3 Offer computed tomography angiography in people with peripheral arterial disease where contrast-enhanced magnetic resonance angiography is contraindicated or not tolerated.

1.5 Management of intermittent claudication

Supervised exercise

1.5.1 Offer a supervised exercise programme to all people with intermittent claudication.

Angioplasty and stenting

1.5.2 Offer angioplasty for the treatment of intermittent claudication when:

- advice on the benefits of modifying risk factors has been reinforced (see recommendation 1.2.1)

- supervised exercise has not led to a satisfactory improvement in symptoms, and
- imaging has confirmed the person as appropriate for angioplasty.

1.5.3 Do not offer primary stent placement for the treatment of intermittent claudication caused by aorto-iliac stenosis (as opposed to complete occlusion) or femoro-popliteal disease.

1.5.4 Consider primary stent placement for the treatment of intermittent claudication due to aorto-iliac occlusion (as opposed to stenosis).

1.5.5 Use bare metal stents where stenting is indicated for the treatment of intermittent claudication.

Bypass surgery and graft types

1.5.6 Offer bypass surgery for the treatment of severe lifestyle-limiting intermittent claudication only when:

- angioplasty has been unsuccessful or is unsuitable, and
- imaging has confirmed that the person is suitable for bypass surgery.

1.5.7 Use autologous vein whenever possible for people with intermittent claudication having infra-inguinal bypass surgery.

Naftidrofuryl oxalate

1.5.8 Consider naftidrofuryl oxalate for the treatment of intermittent claudication, starting with the least costly preparation when:

- supervised exercise has not led to satisfactory improvement, and
- the patient prefers not to be referred for consideration of angioplasty or bypass surgery.

Review progress after 3–6 months and discontinue naftidrofuryl oxalate if there has been no symptomatic benefit.

1.6 Management of critical limb ischaemia

1.6.1 Ensure that all people with critical limb ischaemia are reviewed by a vascular multidisciplinary team before treatment decisions are made.

1.6.2 Offer angioplasty or bypass surgery (see also recommendation 1.6.6) for people with critical limb ischaemia requiring revascularisation, taking into consideration:

- comorbidities
- pattern of disease
- availability of vein, and
- patient preference.

1.6.3 Do not offer primary stent placement for the treatment of critical limb ischaemia caused by aorto-iliac stenosis (as opposed to complete occlusion) or femoro-popliteal disease.

1.6.4 Consider primary stent placement using for the treatment of critical limb ischaemia caused by aorto-iliac occlusion (as opposed to stenosis).

1.6.5 Use bare metal stents where stenting is indicated for the treatment of critical limb ischaemia.

1.6.6 Use autologous vein bypass whenever possible in people with critical limb ischaemia having infra-inguinal bypass surgery.

1.7 Management of critical limb ischaemic pain

1.7.1 Offer paracetamol and either weak or strong opioids to people with critical limb ischaemic pain depending on the severity of pain.

1.7.2 Offer drugs such as laxatives and anti-emetics to manage the adverse effects from strong opioids, in line with the patient's needs and preferences, and review on a regular basis.

1.7.3 Refer to a specialist pain management service when critical limb ischaemic pain is not adequately controlled.

1.7.4 Do not offer chemical sympathectomy to people with critical limb ischaemic pain, unless in the context of a clinical trial.

1.8 Amputation for critical limb ischaemia

1.8.1 Do not offer major amputation to people with critical limb ischaemia unless all options for revascularisation have been considered by a vascular multidisciplinary team.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

The guideline covers

- Adults aged 18 and older.
- People who present with symptoms of lower limb peripheral arterial disease, including intermittent claudication, ischaemic rest pain, and/or tissue loss.
- People without symptoms of peripheral arterial disease (for example, those with venous ulceration) who have abnormal ankle brachial pressure index.
- Subgroups based on ethnicity, socioeconomic factors, age or comorbidities (including people with diabetes), for which differences in management and outcome are identified.

The guideline does not cover

- Children and young people aged 17 and younger
- Adults who have acute ischaemia of the lower limb
- Methods of amputation and rehabilitation
- Management of diabetic foot problems
- Use of topical treatments and dressings.

How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations.

There is more information about how NICE clinical guidelines are developed on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is available.

3 Implementation

NICE has developed tools to help organisations implement this guidance.
Note: these details will apply when the guideline is published.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Angioplasty versus bypass surgery for critical limb ischaemia of the infra-geniculate arteries

What is the clinical and cost effectiveness of a bypass surgery first strategy as compared with an angioplasty first strategy for the treatment of people with critical limb ischaemia due to disease of the infra-geniculate (below the knee) arteries?

Why this is important

Many people with critical limb ischaemia, especially those with diabetic vascular disease, also have disease of the infra-geniculate (below the knee) arteries in the calf.

For many years, the standard of care has been bypass surgery. Although such surgery may be associated with significant morbidity the resulting long-term amputation-free survival rates are generally good.

In recent years there has been a trend towards treating infra-geniculate disease with angioplasty on the grounds that it is less morbid than surgery. However, this change in practice is not evidence-based, and there remain serious concerns about the durability of angioplasty in this anatomical area.

A multicentre, randomised controlled trial with a full health economic analysis is required to address this.

The primary endpoint should be amputation-free survival with secondary endpoints including overall survival, health-related quality of life, healing of tissue loss, and relief of ischaemic pain.

4.2 Supervised exercise for intermittent claudication

What is the clinical and cost effectiveness of supervised exercise in comparison with unsupervised exercise for peripheral arterial disease, taking into account the effects on long-term outcomes and continuing levels of exercise?

Why this is important

Research has shown that taking part in exercise and physical activity can lead to improvements in symptoms in the short term for people with peripheral arterial disease. However, the benefits of exercise are quickly lost if not taken on a frequent and regular basis. Supervised exercise programmes have been shown to produce superior results when compared with advice to exercise (unsupervised) in the short term; but they are more expensive, and there is a lack of robust evidence on long-term effectiveness.

A community-based randomised controlled trial is required to compare the long-term clinical and cost effectiveness of a supervised exercise programme and unsupervised exercise. The trial should enrol people with peripheral arterial disease-related claudication, but exclude those with previous endovascular/surgical interventions.

The primary outcome measure should be maximal walking distance. Secondary outcome measures should include quality of life, function and long-term engagement in physical activity.

4.3 Patient attitudes and beliefs

What is the effect of people's attitudes and beliefs regarding their peripheral arterial disease on the management and outcome of their condition?

Why this is important

The evidence reviewed suggested that, among people with peripheral arterial disease, there is a lack of understanding of the causes of the disease, lack of

belief that lifestyle interventions have a positive impact on disease outcomes, and unrealistic expectations of the outcome of surgical interventions. Much of the research has been conducted on the subpopulation of people with peripheral arterial disease who have been referred for surgical intervention, but little evidence is available on the majority of people diagnosed with peripheral arterial disease in a primary care setting. Research is required to further investigate attitudes and beliefs in relation to peripheral arterial disease, interventions that might influence these and how these may have an impact on behavioural changes in relation to risk factors for peripheral arterial disease, attitudes to intervention and clinical outcomes.

4.4 Primary versus secondary stenting of infra-geniculate disease in critical limb ischaemia

What is the clinical and cost effectiveness of selective stent placement in comparison with angioplasty with primary stent placement in the management of critical limb ischaemia due to disease in the infra-geniculate arteries?

Why this is important

Studies comparing angioplasty with selective stent placement with primary stent placement have been limited to the aorto-iliac and femoro-popliteal segment. There remains a significant group of people with critical ischaemia due to disease of the infra-geniculate vessels in which there is a potential for endovascular treatment. Infra-geniculate disease is more complex to treat by endovascular means and the risks and benefits of different treatment options may differ from those in the more proximal vessels.

A multicentre, randomised controlled trial with a full health economic analysis is required to address the optimum policy as regards the choice of method for angioplasty and stent placement of the infra-geniculate arteries.

The primary endpoint should be amputation-free survival with secondary endpoints including overall survival, re-intervention rates, health-related quality of life, healing of tissue loss, and relief of ischaemic pain.

4.5 Chemical sympathectomy for ischaemic pain

What is the clinical and cost effectiveness of chemical sympathectomy in comparison with other methods of pain control for the management of critical limb ischaemic pain?

Why is this important?

Approximately 1 in 5 people with critical limb ischaemia cannot be offered procedures to improve the blood supply to their leg either due to the pattern of their disease or because of other comorbidities. In this group the therapeutic options are pain control or primary amputation. Chemical lumbar sympathectomy, which involves the destruction of the lumbar sympathetic chain (usually the L2 and L3 ganglia), has been suggested to reduce pain, improve wound healing and may avoid amputation in some patients. Initially achieved surgically, it is now most commonly performed using chemical agents such as phenol to destroy the lumbar sympathetic chain.

Despite having been practised for over 60 years the role of chemical lumbar sympathectomy remains unclear. Improvement in skin blood flow and modification of pain perception control have been demonstrated and prompted the use of chemical lumbar sympathectomy in a range in a range of conditions such as regional pain syndrome, vasospastic conditions and critical limb ischaemia.

However, in critical limb ischaemia the use of chemical lumbar sympathectomy varies widely between units in England, the mode of action and indications are unclear and there is currently no evidence demonstrating its clinical value. Therefore, a randomised control trial comparing chemical lumbar sympathectomy with other methods of pain relief is recommended.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, Lower limb peripheral arterial disease: diagnosis and management, contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guideline Centre, and is

available from our website. Note: these details will apply to the published full guideline.

5.2 NICE pathway

The recommendations from this guideline have been incorporated into a NICE pathway. Note: these details will apply when the guideline is published.

5.3 'Understanding NICE guidance'

A summary for patients and carers ('Understanding NICE guidance') is available.

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N[XXXX]). Note: these details will apply when the guideline is published.

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about peripheral arterial disease.

6 Related NICE guidance

Published

- Patient experience in adult NHS services. NICE clinical guideline 138 (2012).
- Cilostazol, naftidrofyryl oxalate, pentoxifylline and inositol nicotinate for the treatment of intermittent claudication in people with peripheral arterial disease. NICE technology appraisal guidance 223 (2011).
- Endovascular stent-grafting for popliteal aneurysms. NICE interventional procedure guidance IPG390 (2011).
- Hypertension. NICE clinical guideline CG127 (2011).
- Diabetic foot problems - inpatient management of people with diabetic foot ulcers and infection. NICE clinical guideline CG119 (2011).
- Preventing type 2 diabetes: population and community-level interventions in high-risk groups and the general population. NICE public health guidance 35 (2011).

- Prevention of cardiovascular disease. NICE public health guidance 25 (2010).
- Clopidogrel and modified release dipyridamole in the prevention of occlusive vascular events. NICE technology appraisal guidance 210 (2010).
- ~~Percutaneous atherectomy of femoro-politeal arterial lesions with plague incision devices.~~Percutaneous atherectomy of femoro-politeal arterial lesions with plaque incision devices. NICE intervention procedure guidance IPG380 (2010).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Lipid modification. NICE clinical guideline 67 (2008).
- Type 2 diabetes. NICE clinical guideline 66 (2008).
- Physical activity and the environment. NICE public health guidance 8 (2008).
- Promoting physical activity in the workplace. NICE public health guidance 13 (2008).
- Smoking cessation services. NICE public health guidance 10 (2008).
- Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. NICE technology appraisal guidance 159 (2008).
- Preventing the uptake of smoking by children and young people. NICE public health guidance 14 (2008).
- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. NICE technology appraisal guidance 132 (2007).
- Varenicline for smoking cessation. NICE technology appraisal guidance 123 (2007)
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006).
- Obesity. NICE clinical guideline 43 (2006).
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health guidance 1 (2006).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).

Field Code Changed

- Type 1 diabetes. NICE clinical guideline 15 (2004)
- Type 2 diabetes – footcare. NICE clinical guideline 10 (2004).
- Guidance on the use of patient-education models for diabetes. NICE technology appraisal guidance 60 (2003).

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations. Please see our website for information about updating the guideline.

Appendix A: The Guideline Development Group, National Collaborating Centre and NICE project team

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