

Foot complications in patients with diabetes

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Abstract

Foot complications are a common cause of hospital admission of people with diabetes and a frequent cause of amputation. Neuropathy and arterial disease make the foot particularly vulnerable, but infection is often the pathology precipitating presentation. Recognition of the patient at risk may prevent the development of foot complications, but if they do occur urgent treatment is required to prevent limb loss. The infected foot in a patient with diabetes is a surgical emergency. In addition to antibiotics, debridement and surgical drainage of infection should be considered within the first 24 hours. Once the foot is made safe, revascularization should be undertaken in those with significant arterial disease. Adoption of a multidisciplinary team approach to managing diabetic foot complications has resulted in reduction in major amputations in some European countries.

Keywords Diabetic foot disease; diabetic vascular disease; foot complications of diabetes

Epidemiology

Diabetes is a common chronic disease, rapidly increasing in prevalence. It is estimated to affect approximately 4.6 million people in the UK and it is forecast that by 2025, more than 5 million people in the UK will have a diagnosis of diabetes. Complications of diabetes pose a significant national financial burden, accounting for 9% of total NHS hospital costs, with management of foot problems costing around £650 million a year and accounting for more admissions than any other diabetic complication.

The lifetime risk of foot ulceration in those with diabetes is around 15% (although some recent evidence suggests it may be up to 25%), and the presence of ulceration is a major indicator of poor prognosis. More than 80% of lower limb amputations in UK diabetic patients were preceded by foot ulceration. Having a first amputation carries a high risk of subsequent further amputations. In addition, 5-year mortality following a diabetic foot ulcer is around 50%.

The 2015 International Working Group on the Diabetic Foot (IWGDF) guidance identified prevention as the most important aspect of management of the condition. Identification of the “at risk” foot with regular inspection and examination, education of patient and healthcare professionals, routine wearing of

appropriate footwear, and treatment of pre-ulcerative conditions will significantly reduce ulceration and amputation rates.

Aetiology and pathology

Key risk factors for developing foot complications in diabetes are the presence of peripheral neuropathy and/or peripheral artery disease (PAD), foot deformity and previous history of ulcers or amputation of the toes or part of the foot. It has been estimated that of patients with foot complications, approximately 25–44% are due to neuropathy, 10% are due to ischaemia and 45–60% are neuro-ischaemic, a combination of both. Infection is often the final complication leading to presentation.

Neuropathy

Diabetic polyneuropathy is one of the most common complications of diabetes, affecting the feet of at least 28% of people with diabetes. The exact aetiology of the neuropathy is unclear but it is closely linked to the duration of diabetes and adequacy of glycaemic control. It is strongly associated with the presence of retinopathy and nephropathy. Neuropathy affects sensory, motor and autonomic nerves, each of which has deleterious consequences for the foot.

Sensory neuropathy: results in loss of protective sensation, allowing injury to go unnoticed. Chronic repetitive injury, often from inappropriate footwear, may not become apparent until tissue breakdown occurs. Impaired proprioception has negative effects on gait, and loss of the protective changes in biomechanical load distribution can result in sustained stress and tissue damage. In some patients, sensory nerve damage results in pain or allodynia (perception of pain on light touch).

Motor neuropathy: diabetic neuropathy predominantly affects the small peripheral nerves. The intrinsic muscles of the foot, predominantly flexors, are affected more than the extensor groups in the calf. This imbalance results in clawing of the toes and prominence of the metatarsal heads, with loss of the protective plantar fat pads. This makes the foot prone to injury from both friction by foot wear and abnormal weight distribution (Figure 1). The first clinical sign to look out for is callus formation; its rigidity causes even greater pressure on the tissue beneath, and may cause cracks and fissures, providing portals of entry for infection.

Autonomic neuropathy: loss of sweating may occur, resulting in dry skin that is prone to cracking and infection. Autonomic regulation of skin blood flow may be lost, increasing shunting through arterial venous fistulae, producing skin that feels warm and looks pink, but in fact has reduced nutritional blood supply.

Ischaemia

Peripheral artery disease (PAD): PAD due to atherosclerosis is four times more common in patients with diabetes and around half of patients with a diabetic foot ulcer have co-existing PAD. Atherosclerotic plaque in patients with diabetes contains more calcium and has increased expression of inflammatory markers, perhaps explaining the more aggressive progression of the disease. Macroscopically, the disease affects more distal vessels, particularly in the calf and foot (Figure 2). Patients with diabetes are less likely to form collaterals after vessel occlusion.

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Figure 1 Foot of patient with diabetes. Dry, flaky skin due to the autonomic neuropathy can be seen. The clawing of the toes secondary to the motor neuropathy has resulted in rubbing of the toes and dorsum of the foot on the patient's shoe, of which he was unaware due to reduced sensation.

Identifying PAD, even if asymptomatic, in patients with foot ulceration is important because its presence is associated with worse outcomes, such as slow or non-healing of wounds, higher risk of amputation and of associated cardiovascular events such as heart attack or stroke.

Microcirculation: the microcirculation is not directly affected by atherosclerosis, but diabetes does affect the microcirculation in a number of ways. Vasomotor abnormalities (see above) occur that may reduce capillary flow in the skin. There is thickening of vascular endothelial cells, with associated increased permeability and platelet aggregation. These observations help to explain how wounds, which are healthy and bleeding at the time of surgery, can deteriorate and die back as the vessels in the microcirculation thrombose. It is important to appreciate how the effects of PAD are compounded by microcirculatory abnormalities. What

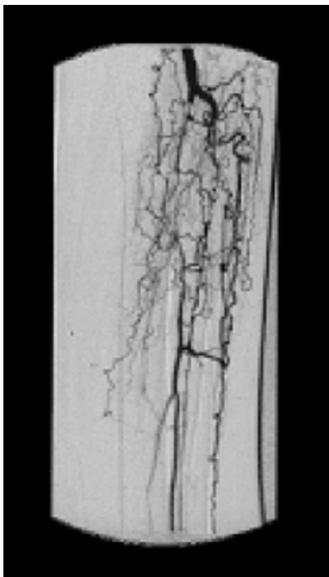


Figure 2 Angiogram of patient with extensive peripheral artery disease affecting the calf arteries.

might seem a relatively minor lesion in a large artery may, when combined with microcirculatory impairment, reduce tissue perfusion below a critical threshold.

Infection

The immune response of patients with diabetes may be abnormal. Neutrophil phagocytosis is impaired, not only increasing the risk of infection but also potentially masking the clinical response. Only about one third of patients with a foot infection will be pyrexial and the white cell count may not be elevated despite extensive sepsis. Infection is often the final common pathway to presentation.

Wound healing

It is a common misconception that diabetes in itself causes delayed wound healing. There are numerous experimental studies that suggest this is not the case, however the co-existence of PAD and infection may complicate or impair wound healing.

Charcot's arthropathy

This is an uncommon complication of diabetic neuropathy. It often follows minor trauma such as a sprain and the foot becomes red, hot and swollen (Figure 3). It is a non-infectious, acute inflammatory state with rapid destruction of bones in the foot. It can be difficult to distinguish from infection and may be misdiagnosed, but the absence of a wound, marked swelling and deformity should prompt the diagnosis and referral to a specialist team. Weight bearing radiographs ± MR scans may show bone destruction and in the absence of an open wound this should raise the suspicion of Charcot's arthropathy.

Treatment involves offloading the foot mechanically to prevent further stress and injury, preferable with a non-removable offloading casting device. Bisphosphonates should only be offered as part of a clinical trial.

Assessment

Everyone with diabetes should undergo a foot assessment at least once a year, which should consist of a vascular, neurological (including biomechanical) and wound (if present) assessment.



Figure 3 Charcot's neuroarthropathy. A swollen red hot foot. A total contact cast has recently been removed.

Vascular assessment

A history of cardiovascular disease increases the likelihood of underlying arterial disease. Ulcers which are painful are more likely to be ischaemic, but sensory neuropathy may mask this. Despite the presence of arterial disease, the foot may appear well perfused and warm due to autonomic neuropathy.

Clinical examination, including palpation of pulses, should be performed, and the absence of pulses should prompt further investigation. As a diagnostic test for PAD, however, both the positive and negative predictive values of pulse palpation are poor, and it should be appreciated in particular that the presence of pedal pulses does not necessarily exclude PAD. It does however help to identify those at risk of subsequent ulceration or amputation.

Ankle-brachial pressure index (ABPI) is a widely used non-invasive test which can be used for screening; peripheral artery disease is suggested if the ABPI is <0.9 ; however, this may be artefactually raised in people with diabetes who may have calcified incompressible lower limb vessels. Toe pressures or toe-brachial index (TBI) are likely to be more meaningful due to relative sparing of the pedal arteries. While ABPI and toe pressures give useful information regarding large vessel disease, transcutaneous oxygen pressure measurement (TcPO₂), if available, gives additional information regarding the microcirculation. Other non-invasive screening tests that can be used include ankle pressure, and distal tibial waveform on ultrasound. In a recent study comparing all these tests to a gold standard (significant disease on duplex ultrasound), the positive and negative likelihood ratios were all unsatisfactory. However, distal tibial waveforms and TBI may be useful in identifying patients who need further diagnostic tests.

For further morphological evaluation of arterial disease, an arterial duplex ultrasound scan would be the most appropriate next investigation. This is readily available, inexpensive and non-invasive. In selected patients, more detailed imaging may be required, especially in supra-inguinal vessels. CT angiography can give clear pictures of the vessels and is relatively non-invasive (Figure 4), although the interpretation of both duplex and CT are limited by calcification, especially of the crural vessels, a common feature of PAD in patients with diabetes. MR angiography can be used but has several disadvantages; it is usually less easily accessible than other imaging modalities, patients may find the scanner claustrophobic, and the contrast agent gadolinium can cause systemic interstitial fibrosis in patients with impaired renal function. Also, interpretation of vascular MR images can be difficult and requires a radiologist with specialist interest.

Neurological assessment

This should constitute assessment of sensory, motor and autonomic neuropathy. On biomechanical inspection, callus formation on weight-bearing areas and changes in foot shape can be indicators of neuropathy. Dry cracked skin suggests autonomic involvement. Screening for sensory neuropathy is important as this may have gone unnoticed by the patient. The Ipswich toe touch test is a useful screen: with the patient's eyes closed, the tester very lightly touches six random toes individually and records the reporting of sensation by the patient. An alternative widely used test is the 10g monofilament test to light touch on ten sites in the foot and/or a 128 Hz tuning fork on the great toe to assess vibration sensation.

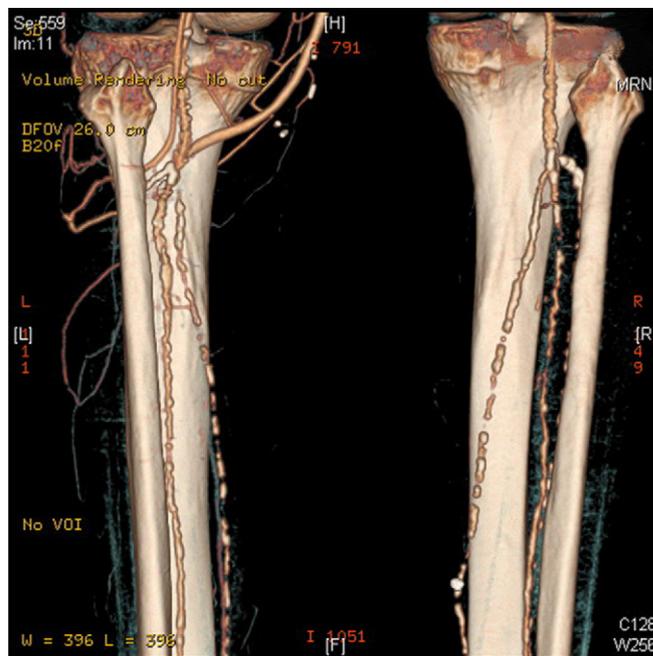


Figure 4 CT angiogram of patient with peripheral artery disease.

Although nociception is commonly impaired in patients with diabetic foot problems, foot pain in someone with diabetes and a foot ulcer should be taken very seriously, as it may be a sign of severe, foot threatening complication.

Wound assessment

Careful wound assessment must be undertaken to determine the depth and involvement of deep structures such as bone, tendon and joints. This can be done by clinical examination and probing the wound for bone in the wound base. Palpation may elicit discharge of pus, which has tracked up tendon sheaths. Plain radiographs should reveal signs of long-standing osteomyelitis, but may not detect early changes. They may also demonstrate gas in the tissues (Figure 5). MR imaging can be used as an adjunct to help plan the extent of resection required, but is often unhelpful in the acute situation. Foot ulcers may be classified using the SINBAD (site, ischaemia, neuropathy, bacterial infection, area and depth) classification. A score of 0 or 1 is given for each component, up to a maximum score of 6.

The Wifl classification is another very useful system, which has been widely adopted. It comprises three components; wound, ischaemia and foot infection, and is graded from 0 to 3 (Table 1). This differs from (and is arguably more valuable than) previous classification systems firstly in that it distinguishes gangrene from ulcers, and more importantly in that it aims to define the disease burden in a meaningful way. This gives useful information on the potential benefit from revascularization and helps to categorize the risk of amputation if left untreated.

Management

The management of people with diabetes at risk of foot complications requires seamless working across both primary and secondary care. The multidisciplinary team should include podiatrists, specialist nurses, diabetic physicians, general



Figure 5 Plain radiograph of infected foot showing extensive gas in the tissues around the fifth toe.

practitioners, vascular and orthopaedic surgeons, orthotists and microbiologists. There should be a clear pathway of care agreed by all those involved and the roles of each member of the team defined.

NICE divides guidance on management of the foot in diabetes into care for those with and those without (but at risk of) a foot lesion.

Management of the at-risk patient with diabetes

All people with diabetes should have at least an annual foot examination as described above, which allows the risk of future ulceration to be stratified. All patients should be told of their risk level and given oral and written advice about foot care and diabetes control. Those identified as low risk should continue having annual reviews. Referral to the foot protection service

should be made for those whose risk is moderate (within 6–8 weeks) or high (within 2–4 weeks). Those at moderate risk should continue to be reviewed every 3–6 months, and those at high risk every 1 week to 2 months.

Careful monitoring by a clinician with the relevant expertise will identify early problems and allow intervention and correction (e.g. better footwear) before significant tissue damage occurs. Good diabetic control and cardiovascular risk assessment is also important at this stage.

Management of the diabetic patient with a foot ulcer

The broad principles of management of the diabetic foot ulcer are control of infection, metabolic control and treatment of comorbidity, restoration of skin perfusion (treatment of PAD), local wound care, relief of pressure and protection of the ulcer (off-loading), education and prevention of recurrence. Figure 6 summarizes the management of an acute diabetic foot problem.

If a diabetic foot problem is detected in the community, patients should be referred to a multidisciplinary foot care service within 1 working day, unless the condition is life or limb threatening (e.g. ulceration with sepsis or critical ischaemia), in which case they should be admitted to hospital acutely. Following admission, the patient should be referred to an inpatient multidisciplinary foot team within 24 hours. Delays in referral from primary care are, unfortunately, common; it is of paramount importance that all members of the clinical team appreciate that delays in treatment of acute diabetic foot problems costs limbs, and larger wounds at presentation are more difficult to heal.

Control of infection: infection is the most common cause of acute presentation. Sepsis severity may be masked in diabetic patients by the lack of ability to feel pain and a lack of systemic response. Inflammatory markers may be normal in patients with diabetes and deranged glycaemic control may be the only indicator of infection. As such, any foot infection in a diabetic patient should be treated aggressively, with a low threshold for admission and intravenous antibiotics.

Early wound debridement is beneficial and, if possible, a soft tissue or bone sample or a deep wound swab should be obtained for culture and sensitivity to guide antibiotic treatment. Osteomyelitis should always be considered and excluded in these patients; however, MRI is rarely helpful in patients presenting with new-onset severe diabetic foot infection. Deep-seated spreading infection or extensive necrotic tissue with sepsis is a surgical

Summary of the Wifl classification

	Wound	Ischaemia (primary determinant is toe pressures)	Foot infection
0	0 = no ulcer, no gangrene	0 = TP >59 mmHg	0 = no infection
1	1 = small, shallow ulcer & no gangrene	1 = TP 40–59 mmHg	1 = mild, superficial (<2cm cellulitis)
2	2 = deeper, larger ulcer & gangrene limited to toes	2 = TP 30–39 mmHg	2 = moderate, deeper (>2cm cellulitis)
3	3 = extensive ulcer and extensive gangrene	3 = TP <30 mmHg	3 = severe and SIRS

Table 1

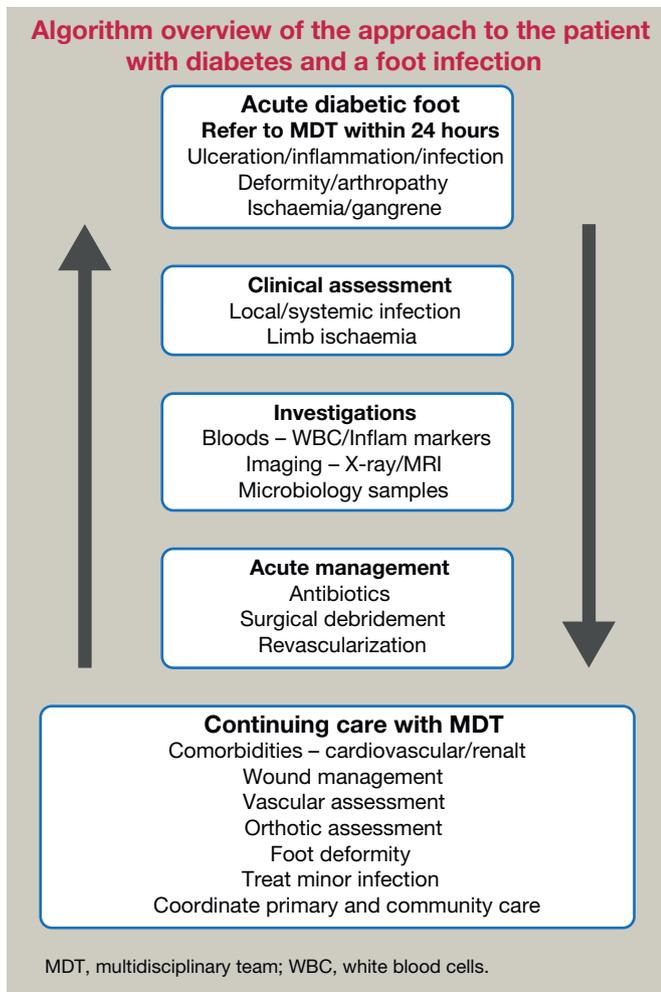


Figure 6

emergency, and debridement should be performed as soon as possible to make the condition safe. Following debridement, offloading of the ulcer is very important, and is discussed further below. In cases of severe uncontrollable sepsis, amputation may be the only life-saving option. In these situations, a guillotine amputation is preferred to remove all infected material, with the amputation revised later when the patient is optimized.

Metabolic control and treatment of comorbidities: blood glucose control may be acutely deranged in the context of infection, and should be monitored and, if necessary, controlled with an insulin sliding scale. Chronic poor blood glucose control is associated with an increased risk of peripheral artery disease and long-term diabetic foot problems. Advice should be sought from the diabetes team if this is suspected.

Diabetic patients with an ischaemic foot ulcer have a high cardiovascular risk, and as such they should be risk assessed, prescribed a statin and antiplatelet agent, treated for existing hypertension and receive smoking cessation support.

Revascularization and restoration of skin perfusion: up to 50% of diabetic patients with a foot ulcer have peripheral artery disease, therefore all should undergo vascular assessment. PAD

in diabetic patients is associated with worse outcomes, including non-healing ulcers, amputation, cardiovascular events and death. Diagnosis can be challenging because diabetic patients may not display the typical symptoms of PAD, and bedside tests can be unreliable. Urgent vascular imaging and revascularization should be considered in those with toe pressures of <30 mmHg or transcutaneous oxygen tension (TcPO₂) less than 25 mmHg, or <50 mmHg with a non-healing ulcer, or a high clinical suspicion. Where PAD is present, early revascularization increases the chance of wound healing. In suitable patients, endovascular and open surgery should be considered and discussed in a vascular MDT setting. There is no strong evidence for one technique over another, and the merits of each should be considered on a case by case basis depending on patient co-morbidities, anatomical distribution of the vascular lesions(s) and local skill set.

It is important to appreciate that, contrary to previous belief, there is no evidence of difference in patency rates of revascularization in patients with diabetes compared to those without. These patients should therefore be considered for intervention with a more optimistic outlook than previously thought.

Wound care: the basic principles of wound care are to remove any dead or infected tissue from the wound environment and to keep the wound surface and surrounding skin as clean and dry as possible to avoid maceration. Following debridement, offloading the wound is of critical importance to remove pressure during the healing period, and can be achieved with bed rest, casting or offloading removable adapted footwear. Wide surgical excision of the chronic wound, with or without underlying bone, may have a role in reducing time to healing, although the current evidence base is not strong. It is generally accepted that surgical foot wounds should be left to heal by secondary intention. Suturing the wound may prevent adequate drainage of infection and puts extra pressure on the wound edge, risking necrosis.

A variety of dressing types have been advocated, many with limited or no evidence to support their use, or to recommend one over another. Further high-quality evidence is needed to guide dressing choices. More complex dressings and treatments should only be utilized when the simple, evidence-based interventions have failed.

The use of negative pressure wound therapy has a prominent role in management of post surgery acute foot wounds. There is promising evidence that it increases the rate of wound healing and portable devices permit an early return to the home environment; however, it is currently only recommended for post-operative wounds as opposed to chronic wounds. Further high-quality studies are needed to evaluate its use in chronic foot wounds. Dermal and skin substitutes can be considered as an adjunct when healing has not progressed with standard care. For extensive tissue loss in patients with good blood supply more complex reconstructions can be considered, including free tissue transfer.

Offloading: after initial wound treatment offloading the foot is crucial. In the early stages, bed rest and foot elevation will reduce oedema and its inhibitory effects on healing. During this time, DVT prophylaxis should be prescribed if indicated, and prevention of new pressure related ulcers is of paramount importance. Early mobilization can be achieved using non-removable casting or adapted footwear.

Education and prevention of recurrence: when a patient leaves hospital it is essential to ensure that they are aware of the risks of further foot problems and take precautions to avoid them. Appropriate foot wear, access to regular follow up and a point of contact if there is deterioration are all important. If the patient has undergone an amputation then advice and care are needed to prevent problems with the stump and with the remaining foot.

Encouragingly there is increasing evidence that implementation of clear policies to identify patients at risk and to intervene early in those who develop complications can have a major impact on hospital admission and major amputation rates and confer a significant cost saving for the NHS. ◆

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