

The diabetic foot

From ulcer to infection

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Diabetic foot disease is a serious and common complication of diabetes mellitus that is associated with infection, delayed wound healing and increased risk of limb amputation. GP assessment, based on examination and history, will determine patient treatment and management. Classification tools, such as the Wound, Ischemia and foot Infection classification system, are useful in guiding GPs through assessment and when referral to a podiatrist or specialist is warranted.

KEY POINTS

- Diabetic foot complications are the most common cause of 'nontraumatic' lower limb amputation.
- The combination of foot deformity, loss of protective sensation, dry skin, inadequate offloading and repetitive minor trauma can lead to tissue damage and ulceration.
- Once an ulcer has formed, healing may be delayed or not occur, particularly if significant ischaemia is present.
- Peripheral artery disease is common in patients with diabetes and associated with delayed wound healing.
- Conventional methods of assessing tissue perfusion in the peripheral circulation are frequently unreliable in patients with diabetes.
- Wound, Ischemia and foot Infection classification should be used for assessing limb staging in the diabetic foot.
- The principles of management of diabetic patients with foot ulcers include offloading, wound management, management of infection, assessment of perfusion and revascularisation if required.



Diabetic foot disease is a serious and common complication of diabetes mellitus. It is a source of major suffering for the patient and a financial burden for the patient and healthcare system. It is estimated that people with diabetes have a 34% lifetime risk of developing a foot ulcer, with more than 50% of these ulcers becoming infected.^{1,2} Of all amputations in people with diabetes, 85% are preceded by foot ulceration. Diabetic foot disease is Australia's leading cause of amputations and is among the top 20 causes of all hospitalisations.^{3,4} More than three-quarters of people with diabetic foot ulcers can achieve primary healing within one year.^{2,5,6} Unfortunately, after a wound heals, 40% of people with diabetes will have reulceration within one year, and nearly 60% within three years.² Thus, it is important to consider that patients who have achieved wound closure are in remission rather than cured.² As a consequence, the Australian government has recently provided new funding for a 'FootForward' program – a new diabetes-related amputation prevention initiative that aims at preventing ulcer formation in the first place.

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Pathophysiology

The pathogenesis of foot ulceration is complex and requires an awareness of the role of several contributory factors, including peripheral neuropathy, peripheral artery disease (PAD), biomechanical abnormalities of the foot and susceptibility to infection.

Diabetic peripheral neuropathy has sensory, motor and autonomic components that result in loss of protective sensation, foot deformity and sudomotor dysfunction, respectively.⁷ Foot deformity and limited joint mobility cause abnormal foot pressure points and subsequent callus formation. The callus then leads to a further increase in the loading of the foot, often with subcutaneous haemorrhage, and eventually skin ulceration. In people with neuropathy, even minor trauma (e.g. from ill-fitting shoes) can precipitate ulceration of the foot. Without 'the gift of pain', patients are often not aware of the severity of foot disease and delay presenting to health care (Figure).

PAD is also common in individuals with diabetes, and around 50% of patients with a diabetic foot ulcer have coexisting PAD.^{6,8,9} The presence of PAD is significantly associated with delayed wound healing and increased risk of major amputation.^{6,8}

The presence of concurrent infection has significant therapeutic and prognostic implications for patients with diabetic foot ulcers. It is the most common precipitating event leading to hospitalisation and lower extremity amputation.^{10,11} Diabetic foot infection nearly always occurs in open wounds and is clinically identified by the presence of manifestations of an inflammatory process in any tissue below the malleoli in a person with diabetes mellitus.

Classification of diabetic foot ulcers

In 2019, the Global Vascular Guidelines (GVG) on the Management of Chronic Limb Threatening Ischemia (CLTI) was released. The new term CLTI represents

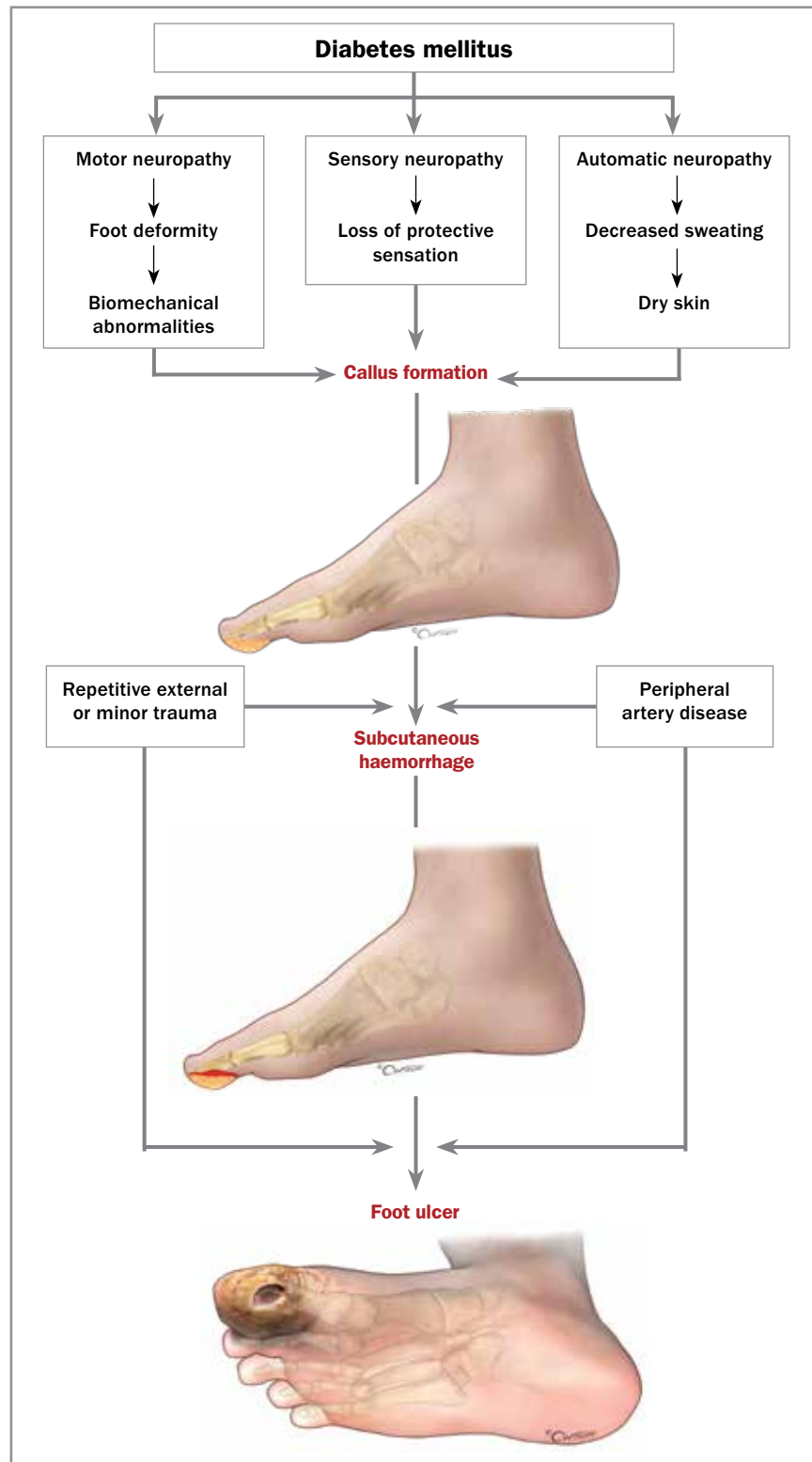


Figure. Pathophysiology of diabetic foot ulceration.

TABLE 1. WOUND, ISCHEMIA AND FOOT INFECTION (WIFI) ASSESSMENT OF DIABETIC FOOT ULCERS TO PREDICT THE 1-YEAR RISK OF AMPUTATION AND BENEFIT OF REVASCULARISATION¹³

Grade	Component		
	Wound	Ischaemia (toe pressure)	Foot infection
0	No ulcer and no gangrene	60 mmHg or greater	Uninfected
1	Small ulcer and no gangrene	Between 40 and 59 mmHg	Mild (cellulitis of 2 cm or less)
2	Deep ulcer or gangrene limited to the toes	Between 30 and 39 mmHg	Moderate (cellulitis/purulence of more than 2 cm)
3	Extensive ulcer or extensive gangrene	Less than 30 mmHg	Severe (systemic response/sepsis)

Adapted from Boulton AJM, et al. Diagnosis and management of diabetic foot complications. American Diabetes Association (2018).¹³

the spectrum of PADs that affect patients with and without diabetes and is of sufficient severity to delay wound healing and increase amputation risk.¹² The Wound, Ischemia and foot Infection (WIFI) classification is recommended for assessment of limb status in patients with CLTI, including patients with diabetic foot ulcers. The WIFI system assesses three key components of a threatened limb (wound, ischemia and foot infection), each with four grades of severity (none, mild, moderate and severe) to predict the 1-year risk of amputation and benefit of revascularisation (Table 1¹³). Wounds are stratified or graded from 0 to 3 based on size, depth, severity and anticipated difficulty achieving wound healing. Ischaemia is classified based on ankle brachial index (ABI), toe pressure (TP) or transcutaneous oxygen saturation (TcPO₂). TP or TcPO₂ measurements are preferred in patients with diabetes mellitus or the elderly when ABI measurements may be falsely elevated because of medial arterial calcinosis. Infection is classified according to severity.¹⁴

An important concept of the WIFI classification system is that the amount of perfusion required to heal a foot wound depends on wound complexity and presence of infection.¹⁵ As an example, a patient with a superficial, uninfected toe ulcer is likely to need less perfusion to heal the foot compared with a patient with forefoot gangrene.

Peripheral artery disease in diabetes

PAD is common in patients with diabetes and is associated with an increased risk of nonhealing ulcers, infection, major limb amputation and death.¹⁶ PAD may remain undiagnosed in patients with diabetes until they present with gangrene or nonhealing ulcers. It is common for patients with diabetes to lack typical symptoms of arterial insufficiency such as claudication or rest pain.¹⁷ Furthermore, diagnostic tests such as ABI may be less reliable due to the presence of medial arterial calcification.

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People with diabetes are more prone to severe below-knee atherosclerosis, often associated with extensive calcification and long-segment occlusions.^{18,19} The propensity for multiple tibial vessel involvement, combined with extensive calf arterial calcification, increases the technical challenges associated with revascularisation using either open bypass or endovascular techniques.¹⁷ Furthermore, in patients with diabetes, a similar degree of anatomical arterial disease can result in a more severe

perfusion deficit because of a paucity of collateral vessels, as well as the influence of physiological factors associated with diabetes, such as arteriolar shunting.¹⁸ The presence of PAD among patients with foot ulceration is associated with adverse outcomes such as poor wound healing and higher rates of lower extremity amputation.¹⁸ This becomes a more important issue when associated with underlying diabetes.¹⁸

Advances in endovascular therapy have widened the options for treating PAD percutaneously and revascularisation is increasingly attempted, initially by endovascular means. However, decisions regarding revascularisation indication and technique are complex and involve assessing patient risk and comorbidities, limb status (using WIFI assessment), anatomy of the limb arterial disease and availability of autogenous venous conduit (for bypass).^{12,16} Treatment of PAD is technically challenging and is often associated with a higher risk of early technical failure and lower patency rate following revascularisation in patients with diabetes.¹²

Prevention of diabetic foot ulcers and identification of the at-risk foot

Careful inspection and examination of the foot is an integral part of the medical review of all patients with diabetes. GPs should ask about a history of foot

TABLE 2. THE INTERNATIONAL WORKING GROUP OF THE DIABETIC FOOT RISK STRATIFICATION SYSTEM AND CORRESPONDING FOOT SCREENING AND EXAMINATION FREQUENCY¹¹

Category	Ulcer risk	Foot characteristics	Frequency of follow up
0	Very Low	No LOPS and no PAD	Once a year
1	Low	LOPS or PAD	Once every six to 12 months
2	Moderate	LOPS and PAD or LOPS and foot deformity or PAD and foot deformity	Once every three to six months
3	High	LOPS or PAD, and one or more of the following: <ul style="list-style-type: none"> • history of foot ulcer • a lower-extremity amputation (minor or major) • end-stage renal disease 	Once every one to three months

Abbreviations: LOPS = loss of protective sensation; PAD = peripheral artery disease.

Adapted from Lipsky BA, et al. Guidelines on the diagnosis and treatment of foot ulcers in persons with diabetes (IWGDF 2019 update). *Diab Metab Res Rev* 2020.¹¹

ulceration or amputation (minor and major) and should examine for:

- previous amputations
- presence of foot deformity
- signs of peripheral neuropathy
- limited joint mobility
- abundant calluses, which can create shearing forces leading to foot ulceration
- ingrown or thickened toe nails
- fungal infections
- any preulcerative signs on the foot,

1. CLINICAL ASSESSMENT OF A PATIENT WITH A DIABETIC FOOT

Vascular assessment

- Manual palpation of pulses
- Capillary fill time
- Skin quality
- Lower extremity venous skin changes

Neurological assessment

- Protective sensation – monofilament testing
- Vibration sensation

Musculoskeletal examination

- Presence of deformities
- Foot type with weight bearing (i.e. high arch)
- Previous amputations
- Shoe evaluation

including the presence of blisters, fissures or haemorrhage, which are strong predictors of ulceration.¹¹

Aboriginal and Torres Strait Islander people with diabetes are considered to be at high risk of developing foot complications and will therefore require foot checks at every clinical encounter and active follow up.²⁰ Table 2 outlines the International Working Group on Diabetic Foot (IWGDF) screening and examination frequency recommendations.¹¹

Educating patients with diabetes and their family on the importance of foot care is essential. As a basic principle, the feet need to be protected against trauma. Patients must be advised not to walk barefoot, in socks without shoes or in thin-soled slippers. All footwear needs to be checked by a specialist or allied health professional and patients with diabetes need to wear footwear that fits, protects and accommodates the shape of their feet.

Podiatry review is a central component of a foot protection program. In general, all patients with diabetes and evidence of neuropathic changes should see a podiatrist regularly. For people with a foot deformity or preulcerative lesion, prescription medical grade shoes, such as custom-made shoes or insoles, should be considered through an orthotist.

Management of patients with diabetic foot ulcers

Treatment of diabetic foot ulcers is complex and should involve a multidisciplinary team. The goals of therapy are to achieve wound healing and consequently avoid (particularly major) amputations and improve quality of life. Once a wound is healed, every effort should be made to prevent recurrence and maintain the patient in foot remission.

At clinical assessment of a patient with a diabetic foot (Box 1), the GP should refer the patient to a high-risk foot clinic at any sign of infection of a diabetic foot ulcer, and administer appropriate antibiotic therapy and wound dressing in cases of mild infection. The GP faces the difficult decision of either referring a patient for outpatient management, or admitting them to hospital for intravenous antibiotics, surgical debridement and/or revascularisation, based on the severity of the infection. It is important to note that high-risk foot clinics are only integrated into some hospital services and there is significant variation in the high-risk foot services provided across Australian states and territories. Most multidisciplinary high-risk foot services comprise a variation of specialties including podiatry, orthotics, vascular surgery, orthopaedic surgery, endocrinology and infectious disease

2. PRINCIPLES OF MANAGEMENT OF PATIENTS WITH DIABETIC FOOT ULCERS

GPs should always refer a patient with diabetes to a high-risk foot clinic, or appropriate specialist/allied health professional when a high-risk foot clinic is unavailable, at the first sign of diabetic foot infection. Further management according to the International Working Group on the Diabetic Foot guidelines are summarised below.

Offloading

- First-line therapy includes nonremovable knee-high device such as a total contact cast or removable cast walker
- Adherence to offloading devices is critical to wound healing

Wound management

- Hospital admission for patients with severe infection and those needing urgent surgical intervention is critical
- Consider a diagnosis of osteomyelitis (OM) using probe-to-bone test, inflammatory test and imaging
- Patients with diabetic foot ulceration should be evaluated for peripheral artery disease (PAD)

Infection management

- Severe infection requires parenteral antibiotic therapy
- Wound tissue is clinically more useful than swabs in identifying pathogens for antibiotic therapy
- Patients with OM typically undergo surgical resection of infected bone; alternatively, conservative therapy with six weeks of antibiotics may be considered for some patients

Revascularisation if required

- Assessment is recommended for patients with foot ulceration and evidence of PAD
- Secondary vascular imaging and appropriate revascularisation is required for patient with ulcers that do not improve within six weeks.
- Shoe evaluation

specialists. When high-risk foot services are not available, patients should be referred to a vascular surgeon or a podiatrist who specialises in diabetic foot ulcers. The recently developed 'FootForward' integrated diabetes foot care pathway provides useful guidance for assessment and management of patients with a diabetic foot, and includes the contact details of

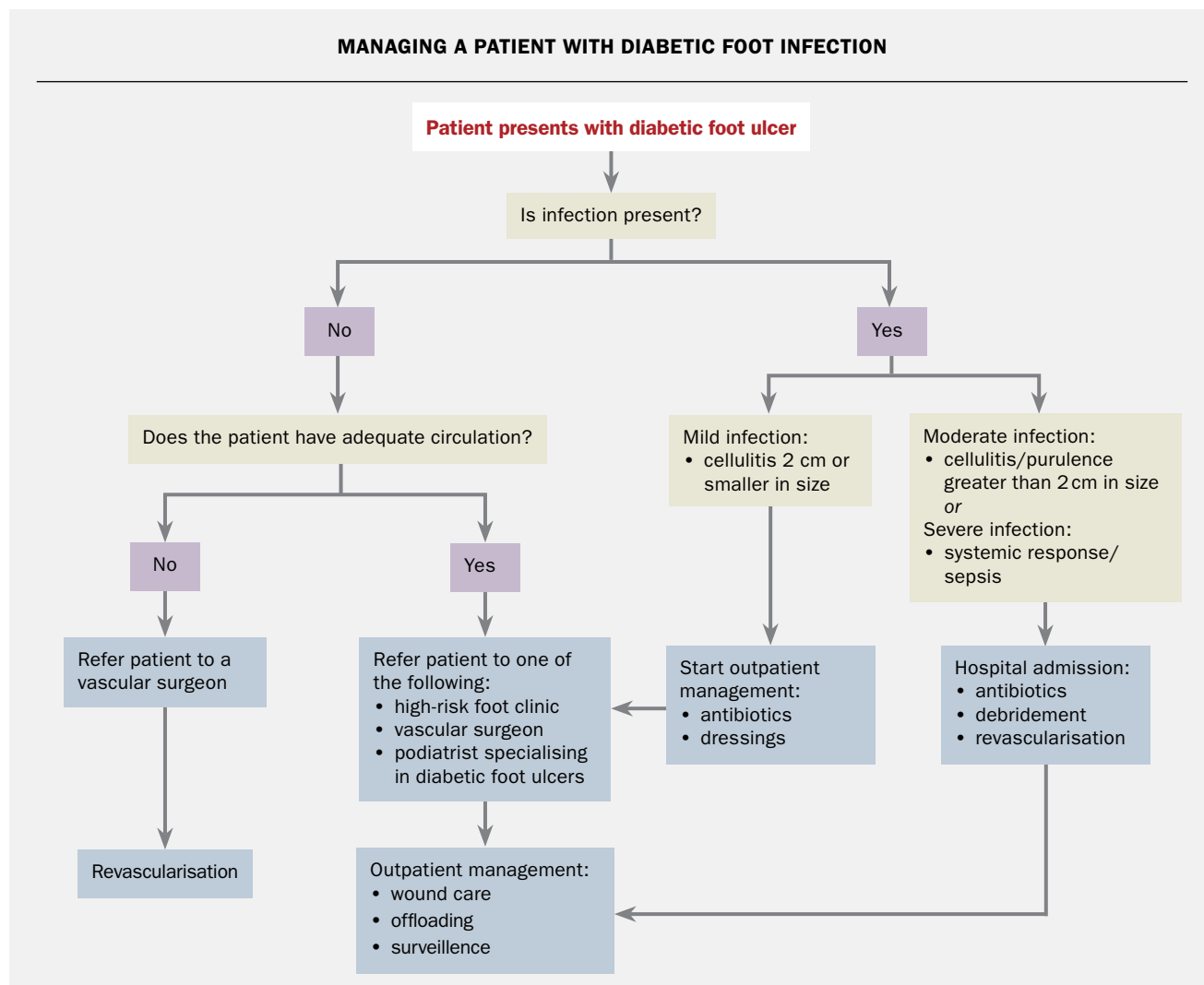
specialist podiatry services. Further details of this pathway can be accessed by signing on to the national diabetes services scheme (<https://nadc.net.au/footforward/>).

The principles of managing patients with diabetic foot ulcers include offloading (reducing pressure on the affected area of the foot and redistributing pressure on the weight-bearing areas of the foot),

wound management, management of infection and revascularisation if required (Box 2). The International Working Group on the Diabetic Foot has specific guidelines for each of these elements.^{11,16,21,22}

Offloading

Offloading is of paramount importance in the management of a patient with a diabetic



foot ulcer. For people with plantar ulcers, the use of nonremovable knee-high devices, such as a total contact cast or removable cast walker made irremovable, is the first line of offloading therapy. If a nonremovable knee-high offloading device is contraindicated or not tolerated, a removable device, preferably knee high, can be considered.^{23,24} It is important for GPs to encourage offloading treatment adherence as these devices are only effective when worn consistently.

Wound management and infection

Infection plays an important role in the initial decision for antibiotic therapy and a simple algorithm for managing a patient

with a diabetic foot ulcer is outlined in the Flowchart. In general, patients with no or mild infection can be initially managed in an outpatient setting, with timely referral to a high-risk foot clinic or specialist/allied health professional (as discussed above). Patients with severe infection (Box 3) should be admitted to hospital for parenteral antibiotic therapy, fluid resuscitation and prompt access to surgical consultation. Patients requiring urgent surgical intervention (such as the presence of a deep abscess) with significant comorbidities (e.g. severe PAD, end-stage renal failure, immunosuppression) or social vulnerability may also require admission.¹¹ The presence of osteomyelitis (OM) infection does not

necessarily require urgent hospitalisation unless associated with systemic symptoms or considerable soft tissue infection.

Diagnosis of OM is challenging. A combination probe-to-bone test, inflammatory test (c-reactive protein) and plain x-rays are reasonable initial assessments. If diagnosis of OM remains in question, advanced imaging (e.g. CT scan, MRI, bone scan) is recommended. Surgical resection of infected bone has long been the standard treatment of OM; however, conservative therapy with six weeks of antibiotics has been shown to be effective in selected patients.²⁵

Microbiology studies of infected ulcers provide useful information on the

causative pathogens and their antibiotic susceptibility, allowing appropriate selection of antibiotic therapy. Specimens of wound tissue (obtained by curettage or biopsy after cleansing the ulcer) are clinically more useful than specimens obtained by superficial swabs.^{26,27}

All patients with diabetic foot ulceration should be evaluated for the presence of PAD. Taking relevant vascular history and palpating peripheral pulses is mandatory in all patients with diabetes with foot ulceration. However, clinical examination does not reliably exclude PAD and objective basic noninvasive testing (most frequently, ABI and TP) should be performed.¹⁶

PAD evaluation and revascularisation

Patients with foot ulceration and evidence of PAD should be referred to a vascular surgeon for assessment of the benefit of revascularisation. The aim of revascularisation is to treat the perfusion deficit and improve wound healing by restoring direct flow to at least one of the foot arteries, preferably the artery that supplies the anatomical region affected.¹² Unfortunately, in patients with a diabetic foot ulcer and PAD, no specific symptoms or signs of

PAD reliably predict healing of the ulcer. Simple bedside tests such as a skin perfusion pressure of 40 mmHg or more, a TP of 30 mmHg or more, or a TcPO₂ of 25 mmHg or more increase the probability of healing without revascularisation. Ulcers that do not improve within six weeks despite optimal management require secondary vascular imaging and appropriate revascularisation.¹⁶

Taking relevant vascular history and palpating peripheral pulses is mandatory in all patients with diabetes with foot ulceration

Vascular imaging includes duplex ultrasonography, CT angiography, MR angiography and digital subtraction angiography. Each modality has its own advantages and disadvantages. As highlighted earlier, it is important to visualise the entire lower extremity arterial circulation, especially the below-the-knee and pedal arteries because PAD secondary to diabetes commonly spares the femoropopliteal segments and affects the tibial and pedal vessels. In cases of widespread ischaemia and infection, inline flow to the direct arterial bed is required for wound healing and salvage from major limb amputations. Where this is only minor ischemia and infection, despite underlying PAD, the collateral circulation is enough to heal the wound.

3. SIGNS OF SEVERE INFECTION OF A DIABETIC FOOT ULCER

- Increased surface temperature around the ulcer (i.e. warm to the touch)
- Increased systemic temperature (i.e. fever)
- Redness of the surrounding skin
- Necrosis
- Localised oedema
- Odour from infected ulcer

Conclusion

Diabetic foot complications are a major public health challenge in Australia and one of the 10 major causes of disability worldwide. The prevention of diabetic foot ulcers is essential to reduce the risks to the patient and the resultant economic burden to society. Once an ulcer has developed, management is complex, and requires a multidisciplinary team approach to optimise outcomes. Treatment should be evidence-based and includes offloading, wound management, management of infection and revascularisation. **MT**

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

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The diabetic foot

Managing diabetic foot complications

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