Diabetic foot ulcers: "Just chop it off"?

INTRODUCTION

Diabetes is increasingly common, and is associated with significant patient morbidity, mortality and high socioeconomic costs (Table I). Due to the increasing prevalence of diabetes, almost all clinicians will treat patients who suffer from it, or will treat a direct complication of diabetes. One of the most serious complications affecting orthopaedic surgeons is the diabetic foot ulcer (DFU). The aim of this review is to update clinicians on the optimal management of the DFU.

AETIOLOGY OF DFU

Diabetes is a metabolic disease characterised by hyperglycaemia as a result of defects in insulin secretion or action. In the long-term this leads to damage and dysfunction of organs, specifically the eyes, kidneys, heart, nerves and blood vessels.[4] A break in the skin on the foot in the presence of diabetes is known as a diabetic foot ulcer (DFU), and is the leading cause of hospitalisation in patients with diabetes (Fig. 1).[5,6]

There are multiple risk factors for the development of a DFU (Table II).[5] The most common reasons are related to neuropathy, vasculopathy or a combination of both.[7-9] The vast majority of DFU seen in clinics or presenting as emergencies have combined pathology, and only 10% of DFU are due to isolated vasculopathy or peripheral vascular disease (PVD).[10]

NEUROPATHY

Diabetes is thought to cause damage to the vasa nervorum resulting in an ischaemic insult and a progressive irreversible sensory, motor and autonomic neuropathy. Most presentations of sensory neuropathy are insidious until the onset of complications. The sensory deficit usually occurs below the knee, is denser distally and is bilateral. Sensory deficit results in numbness of the feet with burning, pain or paraesthesia being less common.[9] Autonomic neuropathy leads to stiff, dry and scaly skin, which may crack due to loss of normal skin flexibility, predisposing to softtissue infection. Motor neuropathy is rarer, but in the feet usually affects the intrinsic and extrinsic muscle balance giving claw or hammer toes. These lesser toe deformities can cause pressure points and subsequent ulceration. Motor neuropathy can also present as isolated mononeuritis. This usually affects the peroneal nerve and results in foot drop. Sensory and autonomic neuropathy leads to high foot pressures, foot deformities, and gait instability which leads to increased plantar pressures and the subsequent risk of developing ulcers.[11-13]

VASCULOPATHY

Arteriosclerosis is more common, more aggressive and more diffuse than in non-diabetics. The vasculopathy in diabetic patients affects the large and small arteries as well as the microcirculation, with more diffuse circumferential lesions that are harder to treat in isolation. This is significant in the foot with regards to the DFU, but also explains why diabetic patients have higher risks of cardiovascular complications such as ischaemic heart disease.

In summary, the primary aetiology of a DFU is excessive pressures on softtissues in a neuropathic foot, which is exacerbated by poor vascularity and deformity.

MANAGEMENT OF DFU

There are clear guidelines, recently updated by NICE[14] for the optimal management of the DFU, but for those presenting as an emergency, standards of practice can vary. The infected emergency DFU can be life-threatening; the term 'foot attack' has been coined and appropriately highlights that management needs to be more aggressive.[1]

There is a wealth of evidence and international consensus which demonstrates how a multidisciplinary approach reduces amputation rates, lowers costs and leads to a better quality of life for patients with DFU.[9,14-20] The key NICE recommendation is that every patient with a DFU is referred promptly to the multidisciplinary team (MDT; Table III) and the patient should have a named clinician in charge of their care, which can either be the diabetologist or the surgeon. The benefits of the MDT approach are clear in that diabetes is a multi-system disease and all comorbidities that will affect wound-healing need to be addressed. The MDT approach is preventative, reducing the risk by up to 85% of further DFU and amputation occurrances.[19] In the presence of an emergency or foot attack, the best practice recommendation from NICE is that immediate stabilisation and drainage of pus should be performed by the admitting team, before referral within 24 hours to the foot MDT service.[14]

ASSESSMENT OF THE DFU

A thorough history focussed on the duration of diabetes and its associated complications, time since the development of the ulcer and presence

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Table I. Diabetes-related statistics in the UK

Diabetes: key facts[1]
In 2014, there were 3.3 million people with diabetes in the UK
By 2025, this will increase to 5 million
25% of patients with diabetes will suffer from a diabetic foot ulcer[2]
70% of lower limb amputations are secondary to diabetic foot ulcer[1]
70% mortality rate following amputation at 5 years; only lung and pancreatic cancer have worse mortality[3]
Total cost of diabetes care in the UK in 2014 was £23.7 billion[1]

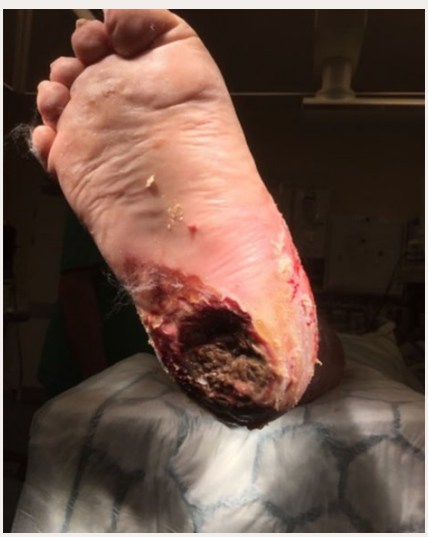

Fig. 1 Necrotic diabetic foot ulcer of calcaneum.

of sensation will help guide treatment and should be taken into account along with the HbA1C level, which is the best indicator of blood sugar control over a 90-day span. High HbA1C correlates to high blood sugar levels, which result in decreased neutrophil function, suppression of the inflammatory response and greater susceptibility to acute infection.[5,21]

Examination should focus in on those problems particularly seen in diabetic feet, pressure areas, callosities and Achilles tendon tightness, which leads to equinus deformity and increased forefoot pressure, predisposing to ulceration. The SINBAD (site, ischaemia, neuropathy, bacterial, infection, area and depth)[14] pneumonic is a simple but effective way to evaluate ulcers; and these should be classified according to the Brodsky classification, which aids in directing treatment (Table IV). The most accurate assessment for neuropathy (or rather protective sensibility) remains the use of the 10 g Semmes-Weinstein monofilament or the use of 128 Hz tuning fork.[22,23] There are commercial variants such as the Vibratip, which have been shown to be equally effective.[24] Thorough vascular assessment is also necessary, and palpable pulses only has a 70% sensitivity in predicting peripheral arterial disease.[25] Simple bedside tests such as the ankle brachial pressure index (ABI), which suggests peripheral arterial disease (PAD) if the ABI is less than 0.8 can be helpful; however calcification of the arteries in diabetics can give a falsely reassuring ABI result. Transcutaneous oxygen tension greater than 30 mm Hg and toe pressures greater than 45 mm Hg are more sensitive and predictive of arterial disease and DFU healing,[26] however these tests are time-consuming and expensive so have not been widely accepted into modern clinical practice.

If there is a suspicion of PVD then early referral is made to a vascular surgeon, with assessment via either digital subtraction angiography or, more commonly, Duplex ultrasound. In select cases a popliteal-to-distal-artery bypass has been shown to be effective in lower limb revascularisation, with an 82% limb salvage rate at three years, and many patients wil benefit from angioplasty where suitable lesions exist.[27]

IMAGING

All patients with a DFU should have weight-bearing foot and ankle radiographs taken to evaluate any gross fractures or deformities as a result of Charcot arthropathy. However with a sensitivity of between 60% and 75% for osteomyelitis, sometimes more detailed assessment is required.[28,29] If the ulcer overlies a bony prominence with radiological changes then osteomyelitis can be assumed, and pencilling of the metatarsal and phalanges occurs in diabetes and is more likely to be as a result of hyperaemia than an infective process.[29] More expensive and specialist imaging such as triple phase bone scans and MRI can be used to compliment clinical examination. However they all suffer from poor specificity and sensitivity and struggle in differentiating between infection and Charcot arthropathy.[9]

Charcot neuroarthropathy is a disease process that results in increased osteoclastic activity, leading to bone resorption, fragmentation and deformity. In the acute phase it is difficult to distinguish between an infection and Charcot arthropathy. Diagnosis is based on clinical findings more heavily than imaging as MRI cannot distinguish between infective oedema and oedema secondary to destructive Charcot.[30]

MICROBIOLOGICAL ASSESSMENT

DFU infections are generally polymicrobial, and due to previous antibiotic use may harbour resistant organisms. Superficial swabs of the ulcers are often carried carried out; however we feel they are of limited value due to colonisation by commensal micro-organism. In our experience they often do not reflect micro-organisms isolated from deep infection. Ultimately, accurate microbiology can only be obtained by either a bone biopsy of suspected osteomyelitic lesions, or from deep-tissue samples during surgical debridement. Initial antibiotic treatment regimes should be broad until accurate cultures are obtained and we would advise deep-tissue sampling or bone biopsy in established cases of osteomyelitis, allowing targeted antibiotic regimes.[31] This is supported in part by NICE, which advocates early referral to the DFU MDT if antibiotics have not worked over a period of 14 days, to allow for earlier diagnosis and assessment.[14]

TREATMENT

Medical management of uncontrolled diabetes and sepsis in the first instance is key to a successful outcome. If there is spreading infection or an

Table II. Risk factors for the development of diabetic foot ulcers[5]

General/systemic	Local
Uncontrolled hyperglycaemia	Peripheral neuropathy
Duration of diabetes	Structural foot deformity
Peripheral vascular disease	Trauma
Blindness/ visual impairment	Callus
Chronic renal disease	Limited joint mobility
Old age	Improperly fitted shoes

Table III. Members of the multidisciplinary team (MDT)

MDT membership	
Diabetologist	Vascular surgeon
Podiatrist	Microbiologist
Diabetes nurse specialist	Orthopaedic surgeon
Plaster tech with skill in casting	Orthotist
General practitioner	

Table IV. Treatment guide for DFU based on the depth-ischaemia classification[9]

Classification	Definition	Treatment
Grade		
0	At-risk foot	Education, accommodative footwear, regular clinical assessment
1	Superficial ulceration	Off-loading with total contact cast
2	Deep ulceration	Surgical debridement, off-loading, targeted antibiotics
3	Extensive +/- pus	Surgical debridement, +/- amputation, off-loading, targeted antibiotics
Ischaemia		
A	Not ischaemic	Nil
B	Ischaemia without gangrene	Vascular assessment and consider vascular reconstruction before debridement
C	Gangrene	Vascular reconstruction +/- amputation

accompanying abscess (a foot attack) then the DFU should be treated as an emergency and urgent decompression of the ulcer performed before transfer of care, ideally within 24 hours, to a team with a specialist interest in this treatment. In our experience, delaying urgent surgical decompression while admitting teams discuss management is associated with increased morbidity and mortality in these diabetic patients.

Wagner first classified and rationalised DFU treatments; his system was subsequently modified by Brodsky, which gives a numerical assessment for depth of ulcer (0-3) and an alphabetic grade for the vascular assessment (A-C; see Table IV).

Grade 0 and Grade A: Loss of protective sensation. There is a loss of protective sensation so the foot is at risk, but there is no ulceration and no ischemia. Treatment consists of patient education, regular examination and accommodative footwear such as a total contact insole, which is contoured to the shape of the foot. The simple measure of foot education in patients has been shown to be the best precautionary measure, preventing up to 50% of DFU occurrences.[32,33]

Grade 1: Loss of protective sensation, and subsequent ulceration. The ulcer is superficial with no signs of infection and no exposed bone or tendon. Treatment consists of offloading with a total contact cast (TCC), removable cast walkers (RCW) or specialist foot wear. TCC is the most effective offloading technique for DFU, with good evidence demonstrating a faster and better healing of tissues time when compared to standard treatments.[34] TCC is a minimally padded cast closely moulded to the shape of the foot, enclosing the toes. This minimises direct pressure on the ulcer by distributing the pressure over the entire surface of the foot, and prevents toes rubbing against the cast.[34] The cast is changed weekly to allow for reduction in oedema and assess the skin for any risk of pressure sores developing. Up to 90% of ulcers will heal within six weeks following this regime.[34-36] Ideally patients would minimise weight-bearing on the DFU to optimise healing; however in the elderly or severely neuropathic this is likely to be optimistic, with patients unable to comply or to judge if they are weight-bearing due to their neuropathy.

Grade 2: Deep ulceration with exposed bone, tendon or joint. These ulcers are at risk of deep infection and are unlikely to improve with offloading devices. They often require surgical debridement of devitalised or exposed tissue with appropriate dressings and offloading.

Grade 3: Extensive ulceration with abscess; presence of infection that can be localised or systemic. These are surgical emergencies ('foot attack') and require urgent surgical debridement or partial amputation. Intravenous antibiotics alone will not work, as they cannot drain pus and are ineffective against the microorganisms' protective biofilm, especially with the poor concentration of antibiotics delivered due to the compromised microvasculature.

Alongside grading based on the depth of the ulcer, consideration is also given to ischaemia. DFU that are ischaemic or vasculopathic but not infected (Grade B) may benefit from vascular reconstruction with angioplasty or bypass, before formal surgical debridement.

DEBRIDEMENT

Debridement decreases bacterial counts, stimulates production of local growth factors and reduces pressure on the wound bed that facilitates healing. Debridement can be surgical, enzymatic, autolytic, mechanical and biological. Surgical debridement is the most effective in reducing complications from DFU, and shortens ulcer healing time.[37,38]

Surgical debridement consists of the complete excision of all dead, devitalised and infected tissue in theatre; in our institution it is often undertaken with regional anaesthesia. Copious lavage and repeat microbiological sampling to determine the level of infection in

the residual wound is essential. Careful antibiotic treatment driven by laboratory results optimises outcomes and closure of the ulcer, as this has been shown to speed up ulcer healing time. In our institution we pack any defects with antibiotic-loaded calcium sulphate, which we have shown shortens the length of hospital stay and speeds up ulcer healing.[31] Non-adherent dressings are applied and wounds are initially checked at weekly intervals. A low threshold for repeat surgical debridement has also been shown to reduce duration and speed ulcer healing.[38]

In our experience, DFU located in the forefoot responds well to prompt, aggressive surgical debridement of the infected tissue, including even ray or toe amputation as required. Reliable limb salvage (and even retention of foot length) can be achieved. Difficulties arise when the ulcers are located in the mid- or hind-foot. The aims still remain the same – salvage the foot and eliminate infection. If the ulcer has resulted in midfoot osteomyelitis and the infection cannot be controlled then a Symes or below-knee amputation can be considered as a two-stage procedure, providing there is appropriate soft-tissue coverage.

Debridement in the midfoot and Charcot collapse results in altered biomechanics, a higher rate of recurrence of ulceration and proximal migration of amputation level. Hindfoot ulcers affecting the calcaneum can be the hardest to manage due to the lack of soft-tissue coverage. Sometimes a partial calcanectomy (with negative pressure wound therapy to minimise the dead space and plastics coverage) can be successful in salvaging the foot. With these partial foot amputations, there are ankle-foot orthoses that can be applied to aid in weight-bearing.

The aim of surgical debridement, and the MDT approach in managing the DFU is to salvage the foot and limb whilst minimising the rate of amputation. Primary amputation should be the last resort after all other salvage techniques have been explored; however in certain patients a below-knee amputation may offer a better functional outcome than repeated attempts at limb salvage and reconstruction, although there are no clear consensus guidelines for this. This decision is individualised and multifactorial to match the patient's lifestyle, medical, physical and psychological comorbidities.

There is increasingly a role for elective prophylactic surgery in the management of DFU, with the aim of correcting deformities that increase plantar pressures and predispose to repeat ulceration. Although this does carry a higher risk of infection and complications when compared with standard foot and ankle elective surgery, the benefits can be considerable. Corrective procedures can range from simple exostectomy; the removal of prominent pressure-causing bone lumps; to full deformity reconstruction via triple arthrodesis or tendon lengthening and tendon transfer. Surgery can be performed using minimally invasive techniques to minimise complications, and recent results are encouraging.[39]

ADJUNCT THERAPIES

Biodegradable fillers

Stimulan is a synthetic, purified form of calcium sulphate, which allows a wide range of antibiotics to be added into the mixture. It is then placed into soft-tissue or bone defects after ulcer debridement (as shown in Figs 2 and 3). It is biodegradable and has a more consistent elution of antibiotics delivered at high concentrations to the local soft-tissues. In our series,[31] it has performed better as filler than gentamicin beads and we have not seen any problems with hypercalceamia, likely due to the smaller amounts being used when compared with revision joint arthroplasty, and the lack of wound leakage problems.

Negative pressure wound therapy (NPWT)

This is not a substitute for the surgical debridement of DFU. It can be used to help heal chronic wounds by removing oedema, chronic exudate, reducing bacterial colonisation, enhancing the formation of new blood vessels, and increasing cellular proliferation and wound oxygenation as a result of applied mechanical force.[40-42] Meta-analysis has shown that NPWT reduces healing times, and increases the number of wounds healed.[43,44] In our experience it works best post- surgical debridement of calcaneal ulcers to asssit in closing up the dead space, before either definitive plastics coverage or wound healing by secondary intention. The main disadvantage of NPWT is the material cost compared with conventional wound dressings.

FUTURE THERAPIES

Hyperbaric oxygen therapy (HBOT) involves intermittent administration of 100% oxygen in daily sessions in a hyperbaric chamber. It is thought that this improves wound tissue hypoxia, enhances perfusion, reduces oedema and promotes ulcer healing.[45] It has also been shown to stimulate vasculogenic stem cells from the bone marrow, 'recruiting' them to the skin wound.[45] However, HBOT is expensive and there is no evidence that it is superior to current treatments. It is not mainstream treatment.

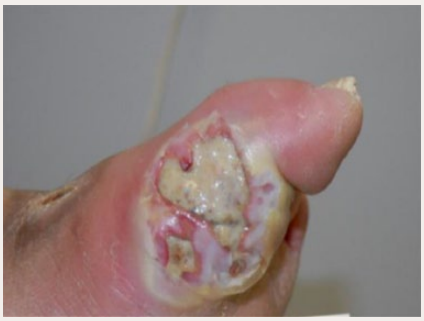

Fig. 2 A forefoot ulcer.

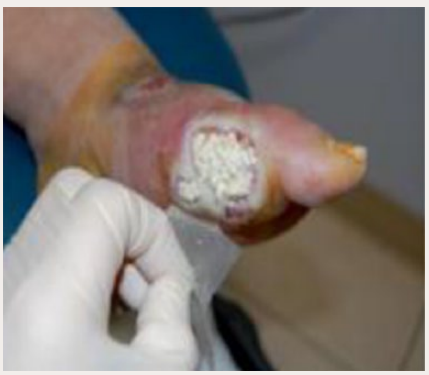

Fig. 3 Ulcer post-debridement and application of Stimulan.

Bioengineered skin (BES)

These are synthetically-produced biological dressings that act as a delivery system for growth factors and extracellular matrix components that promote wound healing and are meant to speed up ulcer healing. They have been used for uninfected, full-thickness ulcers without bone or tendon exposure. Current BES products available include Apligraf (Organnogenesis Inc., Cantom MA), Derma graft (Advanced Bio Healing Inc., La Jolla, CA) and Oasis (Cook Biotech, West Lafayette, IN). These biological dressings have been shown to accelerate DFU healing by the active secretion of growth factors, and providing the cellular substrate and molecular components necessary for healing and angiogenesis.[46] The main disadvantages of BES are the cost; and that they cannot be

used in ischaemic DFU in the presence of infection or without surgery. However they may be a promising avenue for future treatment.

CONCLUSION

DFU is a complicated diagnosis, expensive to treat and increasingly common. It presents a host of challenges and problems to the treating clinician. The primary goal of treatment is to limit the risk of amputation, and further complications. This is best achieved with a multidisciplinary approach. The main components of management include patient education, good blood sugar control, prompt surgical debridement, appropriate antibiotics, offloading with a total contact cast, and (where appropriate) elective prophylactic surgery to minimise future recurrence.

It is important to recognise that the acute presentation of an infected DFU requires prompt surgical drainage of pus, and the term 'foot attack' should be used to promote an understanding of the urgency. Once initial debridement has been carried out, local pathways should exist for the prompt transfer (within 24 hours) to the specialist MDT. On-going management should focus on prevention, *then* dealing with complications, otherwise the financial costs of managing ongoing complications could potentially overwhelm local healthcare budgets.

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 DOI: 10.1302/2048-0105.53.360435