Diabetic Foot

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Abstract

Diabetic foot problems are eminently preventable and yet represent one of the commonest causes of hospital inpatient admission in Western countries. Realizing the global importance of diabetic foot disease, the International Diabetes Federation focused on the diabetic foot throughout the year 2005, during which there was a worldwide campaign to "put feet first" and highlight the all too common problem of amputation among patients with diabetes throughout the world. To coincide with World Diabetes Day in 2005, *The Lancet* launched an issue almost exclusively dedicated to the diabetic foot: this was the first time that any major nonspecialist journal had focused on this worldwide problem; however, major challenges remain in getting across important messages relating to the diabetic foot. The late sequelae of diabetic peripheral neuropathy include foot ulceration, Charcot neuroarthropathy, and amputation: likewise, peripheral vascular disease is a major etiological factor in diabetic foot lesions. Today, in many countries, it is neuro-ischemic ulcers which are most commonly seen and which present a major challenge in management. The importance of routine diabetic foot care in very high-risk patients is emphasized by a recent observational study from Arizona where the state decided, as a cost-saving measure, to remove routine podiatry from high-risk diabetic patients. This led to an annual saving of $351,000, but the cost of this action measured by increased hospitalization, length of stay, and amputations was $16.7 million per annum.

Keywords

Diabetes · Peripheral vascular disease · Charcot neuroarthropathy · Diabetic peripheral neuropathy

Introduction

Diabetic foot problems are eminently preventable and yet represent one of the commonest causes of hospital inpatient admission in Western countries. Realizing the global importance of diabetic foot disease, the International Diabetes Federation (IDF) focused on the diabetic foot throughout the year 2005, during which there was a worldwide campaign to "put feet first" and highlight the all too common problem of amputation among patients with diabetes throughout the world. To coincide with World Diabetes Day in 2005, *The Lancet* launched an issue almost exclusively dedicated to the diabetic foot: this was the first time that any major nonspecialist journal had focused on this worldwide problem; however, major challenges remain in getting across important messages relating to the diabetic foot (Boulton et al. 2005). The late sequelae of diabetic peripheral neuropathy (DPN) include foot ulceration, Charcot neuroarthropathy (CN), and amputation: likewise, peripheral vascular disease (PVD) is a major etiological factor in diabetic foot lesions. Today, in many countries, it is neuro-ischemic ulcers which are most commonly seen and which present a major challenge in management. The importance of routine diabetic foot care in very high-risk patients is emphasized by a recent observational study from Arizona where the state decided, as a cost-saving measure, to remove routine podiatry from high-risk diabetic patients. This led to an annual saving of $351,000, but the cost of this action measured by increased hospitalization, length of stay, and amputations was $16.7 million per annum (Skrepnek et al. 2014).

The treatment and overall healthcare management of patients with diabetes and foot complications are a prolonged, time-consuming process that requires the involvement of a team of healthcare professionals dedicated to foot health. Singh et al. concluded that 25% of people with diabetes will develop a foot ulcer during the course of their life (Singh et al. 2005). A non-healing foot ulcer complicated by infection is estimated to precede 85% of lower limb amputations (Pecoraro et al. 1990). Foot ulcers can be a lifelong affliction requiring multiple treatment regimens and highly specialized clinicians: indeed, as recurrent foot ulcers are so common, it has recently been suggested that those with a previous foot ulcer history should be described as being in "remission" rather than "healed" in order to help patients appreciate the seriousness of a foot ulcer history (Armstrong et al. 2017).

Economic burdens both nationally and internationally can be extremely high. Recent UK data suggests an annual cost of over $749 million for the diabetic foot (Jeffocate and Young 2016). The financial strain also appears to be influenced by the specific type of ulcer being treated as illustrated in the Eurodiale study (Prompers et al. 2008) which reported an average spend of $13,000 for treating non-infected foot ulcers increasing to $18,000 for infected ulcers with concurrent peripheral arterial disease. A severely infected foot ulcer refractory to treatment can be predicted to incur higher costs still. Calculations, incorporating multiple failed antibiotic regimens, hospital admission for intravenous antibiotics, management of sepsis, attempted limb salvage, and major limb amputation with associated aftercare yielded a total sum of $188,645 (Cavanagh et al. 2012).

Diabetic Peripheral Neuropathy (DPN)

DPN increases the risk of foot ulceration through the loss of protective sensation, in the absence of which patients become vulnerable to trauma (Reiber et al. 1999). Soft tissue trauma is a major causative factor in the development of diabetic foot ulceration in patients with DPN (Boulton 2005). DPN is also associated with an increased risk of falls and alterations in foot architecture. Unlike their healthy counterparts, people with DPN are less likely to notice cuts, grazes, puncture wounds, etc., in the lower extremities due to the loss of protective sensation. The inextricable link between soft tissue trauma and DPN underpins a sevenfold increased risk of first foot ulceration that affects those with DPN compared to diabetic non-neuropathic subjects (Young et al. 1994). (For further detailed discussion of DPN, the reader is referred to ▶ Chap. 8, "Diabetes and the Eye".)

Distal Symmetrical Sensorimotor Peripheral Neuropathy

The symptoms of sensorimotor peripheral neuropathy can be broadly divided into painful and painless forms, although it is possible to experience both simultaneously. Individuals may describe reduced or absent sensation in the lower limb, burning, tingling, stabbing sensation, pain, paresthesia, and a sensation of walking on marbles. In contrast, others may experience numbness, heaviness, or not uncommonly may be asymptomatic (Boulton et al. 2004), until examination reveals a profound sensory loss, thus exposing the high-risk foot. As up to 50% of neuropathic diabetic patients may not complain of any symptomatology whatsoever, the "at risk of ulceration" diabetic foot cannot be identified without a careful examination of both feet with shoes and socks removed.

Peripheral Sympathetic Autonomic Neuropathy

Autonomic dysfunction in the diabetic lower extremity can manifest as anhidrosis predisposing the foot to callus formation beneath weight-bearing areas of the foot (Tentolouris et al. 2009). Autonomic neuropathy also frequently results in a state referred to as "auto-sympathectomy" that leads to the release of sympathetic vasoconstrictor tone resulting in arteriovenous shunting and a warm well-perfused foot. A useful clinical sign of the presence of "auto-sympathectomy" and the absence of peripheral vascular disease is distended dorsal foot veins that remain distended on elevation of the foot. Thus it is the warm, insensate, and often painless foot that is very much the "at-risk foot."

Other Long-Term Risk Factors for Foot Ulceration

Renal disease, even in the preliminary stage of microalbuminuria, is a strong predictor of foot ulceration (Ndip et al. 2010). Those most at risk are patients with end-stage renal disease who are on dialysis (Lavery et al. 2015). Patients who have

undergone renal transplants-combined pancreas–kidney transplants are still at high risk of ulceration post-transplant and should be monitored for long-term foot complications. Although such patients may have normoglycemia and relatively normal renal function, they still have the major risk factors for foot ulceration and other end-stage complications of neuropathy. Such patients often become more active because of their overall better health status, and there have been reports of foot ulcers and even acute Charcot neuroarthropathy in patients some years after simultaneous pancreas–kidney transplantation.

Architectural changes expose the foot to areas of high pressure. Flexion deformities of the digits, hallux valgus, and migration of the plantar fat pad into the sulcus increase the risk of tissue breakdown.

Few studies have examined the role of psychosocial factors in the pathway to foot ulceration, but it appears that patients' behavior is not driven by the abstract designation of being "at risk": it is driven by patients' perception of their risk (Vileikyte 2008). More recently, a prospective study has confirmed that depression predicts first, although not recurrent, diabetic foot ulcers (Gonzalez et al. 2010).

Peripheral Vascular Disease

Peripheral ischemia is frequently one of the component causes that is pivotal in the pathway to ulceration, and in recent years, the percentage of foot ulcers presenting with neuropathy and ischemia has increased in Western countries (Schaper et al. 2012). The specific role of PVD in ulcer pathogenesis is difficult to determine due to the asymptomatic nature of the disease process in the early stages. Patients tend only to seek healthcare advice once they become symptomatic with or without tissue loss. Presenting ulcers, whether infected or not, have increased perfusion demands, but an underlying paucity in supply may decrease the likelihood of healing. Neuroischemic ulcers tend to be deep seated and have a larger area of soft tissue and bone loss than neuropathic ulcers. PVD, especially in the presence of infection, is also associated with increased rates of amputation and mortality. Reducing the risks of developing PVD through structured education programs, i.e., smoking cessation, physical exercise, and healthy diet, has the potential to reduce disease incidence.

Epidemiology of Diabetic Foot Problems

In the UK, the annual incidence and prevalence of foot ulceration in patients with diabetes were calculated at 2.2% and 1.7%, respectively, in 2002 (Abbott et al. 2002). Later, a European multicenter study on Diabetes and the Lower Extremity (Eurodiale) (Prompers et al. 2008) followed 1232 diabetes patients with a foot ulcer for 12 months and found that 5% of these underwent a major amputation (above or below knee) during the follow-up period. Krishnan et al. (2008) reported an amputation rate of 16.5 per 10,000 people with diabetes in the UK. Data extracted from the General Physicians databases in Scotland identified that 2.5% of the diagnosed diabetes population had an active foot ulcer at the beginning of

December 2010 (Leese et al. 2011). Diabetic foot disease is associated with a risk of amputation 23 times that of a person without diabetes (Holman et al. 2012).

There are a few databases that capture diabetic foot ulceration as a distinct entity, but Diabetes UK used data from the Public Health Observatory and National Diabetes In-patient Audit (Health and Social Care Information Centre 2013) to estimate the cost of inpatient care for complicated diabetic foot ulcers (DFUs). For the period 2010–2011, expenditure was £219 million ($285 million) (Diabetes UK 2014). Amputations are expensive due to surgical and inpatient bed use, but financial models of total treatment costs for DFU management versus amputation management have demonstrated that complex DFUs are substantially more expensive than amputations (Kerr et al. 2014).

Prevention of Diabetes-Related Foot Complications

The ideal intervention for diabetic lower limb complications should be prevention. One of the key messages in the UK National Institute for Health and Care Excellence (NICE) guidelines on type 2 diabetes (National Institute for Clinical Excellence 2004) is self-management, whereby patients are educated regarding specific aspects of their condition, thus empowering them to share in the responsibility for their health through self-monitoring. The aim is to achieve an increased awareness, facilitating improved compliance with professional advice, which should ultimately lead to a reduction in complications. Education programs, as recommended in the National Service Framework (NSF) for Diabetes (Department of Health 2010) and NICE (National Institute for Clinical Excellence 2004), have attempted to achieve patient self-management through education sessions from the diabetes multidisciplinary team.

To date, the only intervention proven to halt or reduce the development of diabetes-related complications is strict glycemic control, as reported in the Diabetes Control and Complications Trial (The Diabetes Control and Complications Research Group 1993). No other treatment has demonstrated such a profound impact on clinical diabetic complications, including reduced onset of retinopathy, nephropathy, and neuropathy over 6.5 years, and, as a result, glycemic control remains at the forefront of diabetes management (Inzucchi et al. 2015).

In practice, DPN remains a major cause of diabetic foot ulceration. Treatment of DFUs is based on a sound understanding of the physiological changes that occur in the lower limb as a result of diabetes. However, prevention is always more preferable than attempting to heal an acute or chronic ulcer. Targeting prevention through daily self-inspection of the feet for signs of injury is just one example of risk reduction. Falling in the home or outside and an associated soft tissue injury could be the catalyst for foot ulceration and the development of acute CN. Ulcers can have a devastating impact on a patient's quality of life and psychological profile, not to mention the economic considerations to the healthcare provider (Vileikyte et al. 2004).

Identification of the High-Risk Foot

Patients with diabetic peripheral neuropathy are highly vulnerable to tissue loss having lost their protective sensation "awareness": similarly, regular screening for the presence of PVD is also essential. An annual review by a healthcare professional is vital, but the patient also has a responsibility to actively engage in this process through regular monitoring of their own feet.

Assessment

Up to 50% of older, type 2 diabetic patients have signs of DPN identifiable through proper assessment (Pop-Busui et al. 2017). Guidance can be sought from the American Diabetes Association (ADA) document on the "Comprehensive Diabetic Foot Examination (CDFE)" (Boulton et al. 2008) which provides clarity on the structure and content of a robust assessment. Similarly, PVD may be "silent" in diabetic patients, and assessment of the peripheral circulation is also a pivotal part of the annual review.

A foot examination is the key component of the diabetic foot check and should be placed in the context of a thorough history that identifies specific risk factors for foot ulceration.

History

- Past or present neuropathic symptoms
- Vascular (intermittent claudication/rest pain/past history of bypass surgery or angioplasty)
- History of ulcer or minor/major amputation
- Social factors (living alone, smoking)
- Visual impairment or end-stage renal failure (dialysis or post-transplant)

Clinical Examination

- Skin color, callus, fissures, reduced sweating.
- Bacterial/fungal infection.
- Ulceration?
- Architecture/structural alterations, claw toes, prominent metatarsal heads.
- Anhidrosis.
- Skin temperature: a unilateral, warm, insensate foot should be considered to be acute Charcot neuroarthropathy (CN) until proven otherwise.
- Footwear suitability.

Neurological Assessment

The following tests focus on neuropathy affecting large nerve fibers with an emphasis on ease of administration, portability, ease of decontamination, and speed to carry out in order to meet the demands of annual foot reviews. The 10 g monofilament (Bailey Instruments Ltd., Manchester, UK) is widely used in clinical practice to test pressure perception. It consists of a small length of nylon designed to buckle when a 10 g force is applied: thus the filament is applied to the first, third, and fifth metatarsal heads and the plantar surface of the distal hallux. Patients are asked to respond yes or no regarding whether they have detected the stimulus. A number of studies (Vela et al. 1998; Valk et al. 1997) have demonstrated it is a reliable and highly accurate predictor of foot ulceration.

Other neurological screening tools include the Ipswich Touch Test, which requires the clinician to use their index finger to apply light touch to the tips of the first, third, and fifth toes. Neuropathy is identified when detection of sensation fails at two or more sites (out of the total six). Care should be taken not to provide any additional stimulation to the test area by way of tapping, pushing, or prodding. Although highly simplistic, it has demonstrated strong agreement with other validated tests such as the monofilament (Rayman et al. 2011). The VibraTip™ (McCallan Medical, Nottingham, UK) is a small, battery-operated, disposable vibrating stylus that assesses vibration sensation. It has a battery life of a number of months and is easily cleaned. Levels of agreement with other similar tests are excellent (Bowling et al. 2012).

Vibration perception testing (VPT) uses a handheld device that generates a vibratory stimulus which is applied to the hallux. Objective values for thresholds of vibration perception are obtained and can be used to monitor subsequent deterioration in nerve function. VPT has demonstrated excellent sensitivity and specificity for neuropathy.

A 128 Hz tuning fork is a traditional method of assessing vibration perception when placed over the apices of the hallux bilaterally. It has the advantage of being less expensive than the electrical devices for perception threshold testing but can be cumbersome and prone to misuse. The cold temperature from the metal is also providing additional stimuli in the form of temperature.

A pinprick test is a simple means of testing sensation using a disposable pin over the apex of the halluces. Ankle reflex testing is a standard component of neurological testing whereby the absence of ankle reflexes bilaterally is an abnormal response.

Vascular Assessment

Screening for vascular disease can be difficult in diabetes as many are either asymptomatic or report atypical symptoms. Nevertheless, patients should be questioned about a current or previous history of intermittent claudication or ischemic rest pain. Any history of peripheral vascular procedures including bypass surgery or angioplasty should be recorded.

Palpation for posterior tibial and dorsalis pedis pulses is important, but detection can be influenced by the skill of the clinician and room temperature, so results should be considered within this context. A femoral bruit can also be a strong indicator of peripheral vascular disease.

The use of a Doppler ultrasound probe can be useful to assess flow signal waveforms, although vessel wall calcification can lead to a falsely elevated reading of the ankle-brachial index (ABI).

The High-Risk Patient

Abnormalities identified from the screening tests above or relevant clinical history place an individual at high risk of foot ulceration necessitating the implementation of a number of strategies aimed at risk management. Education of patients is a vital component of ulcer prevention as it promotes self-monitoring and foot hygiene. However, this needs to be supported by regular podiatry and review by the multidisciplinary team.

Wound Classification

The American Diabetes Association guidelines consider size, depth, appearance, and location as important factors to consider in the description of ulcers. Over the past two decades, a number of classification systems have emerged, and these provide the clinician with a reference point for wound monitoring. For describing diabetic foot ulcers, perhaps the most widely used is the Wagner Ulcer Classification System which grades wound depth and tissue necrosis; however, ischemia and infection are not included. The University of Texas classification incorporates all of these parameters resulting in accurate ulcer staging and reliable outcome prediction (Oyibo et al. 2001). See Table 1 for details.

Table 1 Wound classification. The "University of Texas Diabetic Wound Classification" is regularly used for staging diabetic foot ulcers. This classification grades and stages ulcers by their depth and the presence of any infection or ischemia

•	Staging
	A: No infection or ischemia
	B: Infection present
	C: Ischemia present
	D: Infection and ischemia present
•	Grading
	0: Epithelialized wound
	1: Superficial wound
	2: Wound penetrates to the tendon or capsule
	3: Wound penetrates to the bone or joint

Management of Diabetic Foot Ulceration

Neuropathic Ulcers

The treatment of the majority of uncomplicated diabetic foot ulcers consists of debridement of nonviable tissues and an appropriate dressing tailored to the requirements of the individual wound, followed by an optimal off-loading technique (Bakker et al. 2016).

Debridement

The development of hyperkeratotic tissue is a result of shear pressure, and regular removal of this excess callus reduces abnormally high plantar pressures. Wounds with extensive bone and soft tissue involvement require deeper and more aggressive debridement to remove nonviable tissue and provide drainage of purulent discharge. Complete surgical excision can significantly reduce the number of days taken to heal compared with ulcers managed more conservatively.

Off-Loading

This is, perhaps, the key to healing diabetes-related foot ulcers, and outcomes are often positive when off-loading advice is followed. Total contact casts are the gold standard for off-loading, based on evidence of a 90% success rate for ulcer healing, as supported by several randomized controlled trials (Armstrong et al. 2003, 2005; Piaggesi et al. 2007). Other off-loading devices, such as a removable cast walker or adapted footwear, have not demonstrated the same degree of success. The reason for the variation in healing rates was revealed in a study by Armstrong et al. (Armstrong et al. 2003) who covertly recorded the activity levels of patients while they wore a prescribed removable cast walker as treatment for neuropathic foot ulcers. Findings demonstrated that patients only wore the off-loading device for 28% of their total daily activity. Persistence with weight bearing on a diabetic neuropathic foot ulcer will undoubtedly prevent healing and, in most cases, promote further deterioration. A total contact cast, on the other hand, provides the foot with an alternative means of protection in the absence of normal sensation. This was confirmed in two parallel randomized controlled trials carried out in Miami and Tucson. In Miami, patients with non-infected neuropathic plantar ulcers were randomized either to a total contact cast or a removable cast walker rendered irremovable by wrapping with a sheet of cast material. Not surprisingly, there were no differences in healing rates which were generally rapid (Katz et al. 2005). By contrast, in the Tucson study, where patients were randomized either to a total contact cast or a removable cast walker, healing rates were much more rapid in the total contact cast group as the removable walkers were not used for much of the

time in those subjects randomized to this form of off-loading. The use of removable cast walkers made irremovable may therefore be more appropriate in the non-compliant patients.

Total contact casting is contraindicated for use in purely ischemic ulcers and osteomyelitis, due to the risk of additional complications such as ulcer deterioration due to poor arterial inflow and the difficulty in prompt detection with a nonremovable cast.

Wound closure is the ultimate aim in the treatment of DFUs, and key elements for intervention should include removal of pressure, restoration of perfusion, eradication of infection, and local wound care.

Neuro-Ischemic Ulcers

Peripheral ischemia in conjunction with a diabetic foot ulcer is an independent risk factor for amputation. While some patients may only have mild ischemia, others can have profound vascular insufficiency which can significantly impair healing of diabetic foot lesions. More conservative debridement may be necessary using minimal sharp debridement but considering debriding agents such as honey or larval therapy. It is safe to cast neuro-ischemic ulcers as off-loading remains an essential part of management (Nabuurs-Franssen et al. 2005). However, some degree of endovascular or vascular intervention may need consideration in order to increase the potential for healing. Any foot ulcer patient with reduced or absent foot pulses or any other suspicion of ischemia warrants thorough investigation. Initially this should comprise a noninvasive assessment using Doppler ultrasound techniques. Prior to any endovascular interventions or surgical bypass, arteriography is usually indicated. Care should be taken with the use of certain contrast media as many patients with foot ulceration have renal dysfunction. All patients with significant lower extremity PVD should be seen by a vascular surgeon who would normally be a member of the diabetic foot-care team.

Infection

Diabetic foot infections (DFIs) are the most common reason for diabetes-related hospitalization and represent a serious complication which, if not managed appropriately, can result in lower extremity amputation. Diabetic foot ulcers (DFUs) serve as a point of entry for pathogens, and approximately 60% of DFUs are already infected on initial presentation. Gram-positive cocci, especially *Staphylococcus aureus* and to a lesser degree streptococcus species or coagulase-negative staphylococci, have been the main pathogens isolated from DFIs (Lipsky et al. 2012; Citron et al. 2007). The prevalence of Gram-negative bacteria mostly including Pseudomonas and Enterobacteriaceae species is lower but increases in chronic wounds previously treated with antibiotics. Anaerobic infection must also be considered especially in neuro-ischemic ulcers.

Antibiotic-resistant organisms have become an increasing problem in the management of DFIs over recent decades with the rise of methicillin-resistant *Staphylococcus aureus* (MRSA). Multidrug-resistant (MDR) Gram-negative strains such as highly resistant pseudomonas, extended-spectrum β-lactamase (ESBL), and carbapenemase-producing Gram-negative bacilli are also being isolated from diabetic foot wounds (Uckay et al. 2014).

The clinical signs usually associated with a host inflammatory response to pathogens can be reduced or absent in patients with neuropathy and ischemia with approximately 50% remaining asymptomatic for infection. Some patients will demonstrate pain, warmth, erythema, raised temperature, or raised C-reactive protein (CRP), but often wound characteristics such as new onset of tenderness, prolonged healing, and wound malodor may be the only indicators of infection. Wound discharge, poor granulation tissue, and unexpectedly poor glycemic control can be indicative of infection (Lipsky et al. 2012). Tissue samples or deep wound swabs should be taken for culture and sensitivity to inform a specific antibiotic regimen as superficial cultures are too easily contaminated by colonizing bacteria.

Clinically non-infected wounds do not require antibiotics. However, foot ulcers with any suspicion of infection should be treated by appropriate antibiotics that target the likely pathogens in the wound. Whereas superficial wound swabs are often inaccurate and misleading, often only yielding contaminants, deep tissue specimens via a curettage or after aggressive debridement are those that should be sent to the microbiology laboratory. Initial antibiotic therapy should be empirical including activity against *S. aureus* and aerobic *streptococci*. Consider agents against Gram-negative organisms for patients with severe infections. Once culture and sensitivity results are available, a more specific regimen can be initiated that targets just the causative organisms. Data do not favor any particular antibiotic treatment strategy due to local resistance patterns. Limited data support the use of topical antimicrobial treatment. Intravenous vs. oral antibiotics, intravenous antibiotic administration is only indicated in severe infections as most mild to moderate infections will respond to oral antibiotics with a high bioavailability. Appropriate antibiotic treatment is essential for treating infected diabetic foot ulcers alongside sharp debridement, drainage of purulent discharge, and appropriate off-loading. Both the International Working Group on the Diabetic Foot (Peters et al. 2016) and the Infectious Diseases Society of America (Lipsky et al. 2012) have provided useful guidelines to assist in the antibiotic treatment of infected diabetic foot ulcers.

Wound Dressings

Wound healing can be challenging in the diabetic population and is further complicated by neuropathy and/or ischemia. Specialist dressings can provide a favorable wound environment by maintaining a moist protective occlusive layer to the wound bed. A wide range of wound dressings are available despite a meager evidence base. Basic requirements for wound dressings are absorption of exudate, thermal insulation, gas permeability, and impenetrable to microorganisms. An adherent product

should not contact the wound bed itself, thus preventing removal of newly granulated tissue. Selection of the ideal dressing will depend upon the specific characteristics of the ulcer.

As the wound progresses through the stages of healing, it may be necessary to use a variety of different dressings, i.e., sloughy wounds will need a debridement agent; clean moist wounds will need absorbency properties. Products available can be divided into three broad categories, debriding, antiseptic-based, and moisture control, and are listed in Table 2.

Table 2 Wound management products

Dressing	Description	Contraindications	Example
Hydrocolloid	Facilitate rehydration and autolytic debridement Dry, sloughy, necrotic wounds Promote granulation	Infected wounds Twice weekly change	Aquacel: ConvaTec Deeside, Wales, UK Comfeel: Coloplast Peterborough, UK
Hydrogels	Donates liquid to dry wounds and absorbs exudates Dry, sloughy wounds Autolytic debridement	Hydrogel sheets avoided in infected wounds	Intrasite gel: Smith & Nephew Wound Management, Hull, UK Iodosorb: Smith & Nephew Wound Mgt., UK
Silver	Antimicrobial Colonization	Sensitivity to silver	Acticoat: Smith & Nephew Wound Mgt., USA
Vapor-permeable	Provide a moist healing environment Mild exude	Heavily exudating wound	Tegaderm: 3 M, Reading, UK
Foam dressing	Primary or secondary cover Light and heavy exudates	Remove if strike-through occurs	Allevyn: Smith & Nephew Wound Mgt., Europe Lyofoam: Molnlycke, Oldham, UK
Odor absorbent	Absorbs odor Malodorous	Silver (sensitivity)	Actisorb: Johnson & Johnson Medical Skipton, UK
Larval therapy	Debridement, promote granulation Heavily sloughy necrotic wounds	Increase in pain	Maggots: Zoobiotic Bridgend, Wales, UK
Alginate	Hemostat. Heavy exudates	Blockage. Loose fibers	Kaltostate: ConvaTec, UK
Skin substitutes	Living skin. Obstinate wounds	Colonized. Infected wound	Dermagraft: Smith & Nephew Medical, Europe
Iodine	Antibacterial Exudating wounds	Iodine (sensitivity) Renal/thyroid conditions	Iodosorb: Smith & Nephew Medical, Europe
Honey	Antimicrobial Sloughy necrotic wounds Autolytic debridement	Medical grade only	L-Mesitran: Aspen Medical Europe Ltd. Ashby de la Zouch, Europe

Negative-Pressure Wound Therapy

The use of negative-pressure wound therapy (NPWT) is becoming more popular in the outpatient setting as well as in hospitalized patients. Studies have demonstrated that wounds achieve closure in a far shorter period of time than other conventional dressing regimes (Armstrong and Lavery 2005). Increased perfusion and promotion of granulation tissue formation have been reported due to cell deformation thus increasing cell mitosis. A recent systematic review confirmed that there was some evidence to support the use of NPWT in postoperative wounds (Dunville et al. 2013).

Growth Factors and Skin Substitutes

Wound healing involves a complex interplay with a number of growth factors, one of which is platelet-derived growth factor (PDGF). There is a growing interest in the potential application of growth factors to assist in wound healing. Becaplermin is recombinant PDGF ointment, and its use has shown some slight benefit to wounds with delayed healing. Another growth factor is the granulocyte colony-stimulating factor (GCS-F) which has been reported to improve the resolution of infection in one pilot study, while another study claimed it reduced amputation rates, but further substantiation is required (Cruciani et al. 2013). Bioengineered skin (Apligraf) and human dermis (Dermagraft) are types of biologically active implants for ulcers and contain human fibroblasts that deliver growth factors to the wound. However, the evidence base for many of these expensive therapies is weak, and further large-scale randomized controlled trials are needed, which control as best as possible for the many potentially confounding variables, particularly with regard to off-loading. A recent systematic review on interventions that enhance the healing of chronic ulcers concluded that sadly, there is little published evidence to justify the use of any of these newer expensive therapies on a regular basis (Game et al. 2016).

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBO) has been marketed as an effective adjunct in the treatment of diabetic foot ulcers, but early trials have come under close scrutiny due to the small numbers of patients enrolled and methodological and reporting inadequacies. One well-constructed, blinded randomized controlled clinical trial reported that HBO was beneficial in treating chronic neuro-ischemic infected foot ulcers (Löndahl et al. 2010). However, subsequent studies have failed to produce similar results leaving little evidence to support the efficacy of HBO in the diabetic foot, although a large multicenter trial is currently underway in the Netherlands which should provide new data (Stoekenbroek et al. 2015).

Charcot Neuroarthropathy

Charcot neuroarthropathy (CN) is inextricably linked with distal symmetrical somatic and autonomic neuropathy, although the exact pathogenetic mechanisms are unknown. It is characterized by osseous and joint destructive changes ultimately leading to a gross alteration in foot structure and architecture (Fig. 1). Abnormalities may occur in the forefoot, midfoot, peritalar, or ankle regions with avulsion fractures affecting the posterior tuberosity of the calcaneus. Continued mobilization due to a lack of sensory awareness further compounds the osseous structural disorganization. In the latter stages of CN, a complete midfoot collapse can be seen clinically by a rocker bottom foot (Rogers et al. 2011) (Fig. 2). Hindfoot involvement is less common, but a more rapid progression in the bone destruction results in poorer outcomes. Due to the severity and sudden onset of the disease process, there is little doubt that any neuropathic patient who presents with a warm swollen foot with or without pain should be considered to have CN until proven otherwise.

The mainstay of treatment of acute CN is off-loading usually with an irremovable below-knee cast walker. There are no proven medical or pharmacological approaches other than immobilization The timing of surgical intervention for CN is controversial due to a lack of evidence regarding whether this should be performed in the acute or sequence phase of the disease. Exostectomies and tendon transfers can offer a reduction in bony prominences, thereby reducing the risk of ulcerative episodes. There is also little evidence to show that a surgically corrected Charcot deformity functions any better than a nonsurgically corrected deformity (Fig. 3a, b). This is mainly due to the amount of bone fusions needed to acquire adequate correction (Shen and Wukich 2013).

Fig. 1 Chronic Charcot neuroarthropathy involving the midfoot (cuneiform-metatarsal bone area). There was extensive deformity with a large plantar ulcerative lesion under the bony prominence

Fig. 2 Chronic neuropathic foot problems with Charcot deformity and previous amputations of four toes

Fig. 3 (**a**) Radiograph of a chronic Charcot foot demonstrating previous amputation of three digits, vascular calcification, and gross disruption in the cuneiform-metatarsal joints of the midfoot. (**b**) Radiograph showing chronic Charcot neuroarthropathic changes in the midfoot with peri-talar destruction

In addition to CN, a number of other orthopedic problems can occur in the neuropathic foot such as spontaneous fractures with associated tendo-ligamentous damage.

Patient Education

Patient education has long been seen as a means of increasing patient understanding of their condition, thus increasing compliance and subsequently reducing complications. Guidelines by the American Diabetes Association (American Diabetes Association 2015) and International Diabetes Federation (International Diabetes Federation guidelines for type 2 diabetes) provide information for the content and delivery of patient education programs.

Comprehension of the features of peripheral neuropathy and its implications can be difficult for patients to accept, but without such acceptance, daily self-foot examination is unlikely to occur. Successful self-management requires motivation and compliance from the patient to accept a degree of responsibility for their own care; however, foot inspection can be problematic for obese individuals and those with visual impairment. Difficulties understanding the nature and relevance of neuropathy to the individual with diabetes have also been suggested as a barrier to engaging in the education process (Vileikyte 2008).

Some success with patient engagement with diabetes foot care has occurred when an objective self-monitoring tool has been provided to patients such as temperature monitoring (Lavery et al. 2007), the Neuropad plaster to indicate neuropathy (Tentolouris et al. 2008), and a simple foot pressure mat for monitoring pressure changes under the foot (van Schie et al. 1999).

The use of inappropriate footwear, both incorrect size and those without inadequate cushioning, is known to play an important role in the development of ulcers in patients with neuropathy. Tight shoes commonly lead to ulceration at dorsal deformities such as bunions or between the spaces of the toes which have been crushed together. However, loose shoes can also lead to ulceration from the foot slipping inside, creating frictional force. Even simple sports trainers can reduce plantar pressures by 50% compared to leather soles.

Additionally, patients should be advised about other associated risk factors such as controlling high blood pressure, cholesterol, smoking cessation, and obesity. Not only will these measures reduce patients' risk of ulcers, but it will also lower their macrovascular complication risk.

Multidisciplinary Team Input

The delivery of care for patients with diabetes-related foot complications has altered over recent years. Emphasis has transferred from a centralized, diabetes foot-care teams to community-based healthcare groups. Increased awareness among healthcare

professionals and a shift away from hospital-based care have resulted in major changes for the patient and care providers.

Screening for diabetes-related foot ulcers takes place at a community level with opportunities arising in a variety of different environments. The foot-care team now extends to primary care physicians, district nurses, practice-based nurses, and community-based podiatrists.

Successful management of diabetic foot complications depends upon achieving stability in all aspects of diabetes care.

Patients requiring a total package of care from a specialist diabetes foot-care team need a structured management plan in order to contend with the multiple comorbidities and complications associated with diabetes. At the minimum, a specialist diabetes foot-care team should consist of a diabetologist, specialist foot surgeon (podiatric or orthopedic surgeon), specialist diabetes nurse, podiatrists, and a vascular surgeon.

Improved outcomes, including reduced incidence of minor and major amputations, have been demonstrated in a number of studies when care is delivered in this way (Krishnan et al. 2008). One study directly compared outcomes associated with care delivered by an established multidisciplinary diabetes team (MDT) with another hospital lacking a designated diabetes team. Results showed a significant reduction in major amputations performed on patients treated by the MDT (4.7%) versus 21.7% without MDT input ($p < 0.0001$). Mortality during hospitalization was also significantly different between the two groups at 2.5% for the MDT group and 9.4% for the controls (Weck et al. 2013).

Summary

The development of diabetic foot complications involved is dependent on multiple factors primarily arising from prolonged hyperglycemia. The unprecedented global increase in type 2 diabetes is predicted to continue and in turn embed diabetic foot complications further into healthcare provision. Mortality from diabetes-related illness has decreased as a result of a variety of healthcare strategies (Jeffcoate et al. 2016), but morbidity levels also need to be addressed. The tools for reducing diabetes-related foot complications are already available to the multidisciplinary team in the form of consensus and evidence-based guidelines. Clinical effectiveness of diabetes foot care, however, can be limited by lack of patient engagement in their own care and may represent the most significant barrier to future success in the management of the diabetic foot.

Conclusions

Although there has been much progress in our understanding of the etiopathogenesis and management of diabetic foot disorders over the last 30 years, much of what we use in clinical practice today still lack an evidence base. This is particularly true, for

example, for dressings. The International Working Group on the Diabetic Foot recently reported on the details required in the planning and reporting of intervention studies in the prevention and management of diabetic foot lesions (Jeffcoate et al. 2016). Details of the necessary trial design, conduct, and reporting should be taken into account when assessing published studies on interventions in the diabetic foot. Most important of all, however, in the management of patients with diabetic foot disorders is to remember that the patient has frequently lost the "gift of pain" that protects most of us from developing significant foot problems but, when absent, can lead to devastating consequences.

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