Location of lower-extremity diabetic foot ulcers with concomitant arterial or venous disease

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Diabetes remains a highly prevalent systemic illness associated with significant morbidity, mortality and economic burden. This study investigated whether diabetic foot ulcer (DFU) location affects outcomes. Ninety-three DFU patients categorised as having diabetes only, diabetes plus peripheral arterial disease, or diabetes plus venous insufficiency, were included in this retrospective study. DFUs were identified as forefoot, mid/hindfoot or lower leg ulcers. Data on wound healing, further surgery and amputation were collected. The majority (59%) of the diabetes-only group and half the peripheral arterial disease group had forefoot ulcers. Most (78%) of the venous insufficiency group had lower leg ulcers. Overall, 25.5% of patients achieved wound closure and 18.2% underwent amputation. Forefoot ulcers were most likely to heal and hindfoot ulcers most likely to result in amputation. Healing and amputation rates differed based on DFU location and the presence of concomitant vascular disease.

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The Centers for Disease Control and Prevention (CDC) estimates that over 34 million people in the US are affected by diabetes, which equates to 10.5% of the overall population (CDC, 2020). According to the US Medicare Database, approximately 6% of people with diabetes develop a foot ulcer annually (Rice et al, 2014) and foot ulceration is a major risk factor for future amputation (Pemayun et al, 2015). Overall mortality in patients with diabetic foot ulcers (DFUs) may be as high as 25% at 5 years (Chammas et al, 2016); reaching nearly 50% for patients with prior amputations (Jupiter et al, 2016; Throud et al, 2016). While no study has shown that accelerated DFU closure improves long-term survival, this is a basic premise in many clinical trials.

Development of diabetic foot disease is multifactorial. There is typically prolonged hyperglycaemia and associated protective sensory loss. There is a risk of infection or anatomical deformity associated with excess pressure. Prevention of DFUs remains challenging, as an amalgam of contributing factors lie outside basic wound care and infection control: patient compliance with offloading and glucose control, aggressive lifestyle modification and motivation to achieve success are all significant. Comorbidities, such as peripheral arterial disease (PAD)/chronic ischaemia, are common and contribute to the development of DFUs. PAD in patients with DFU is associated with increasingly severe adverse outcomes, such as longer healing times, higher probability of ulcer recurrence, lower probability of complete healing and higher risk of amputation and mortality (Brownrigg et al, 2013; Aiello et al, 2014). Although the relationship between PAD and DFUs has been widely studied, much less is known about the relationship between diabetes and healing rates in patients with venous leg ulcers.

Lower-extremity DFUs were characterised by location, taking into consideration concomitant PAD or venous disease, to investigate whether wound location is associated with healing rates.

Methods

Current procedural terminology codes were used to identify 174 patients (89% outpatients

Table 1. Proportion and position of ulcers by patient group.					
Patient group	Number of patients	Number of ulcers (%)	Position of ulcer		
			Forefoot	Mid/Hind foot	Leg
Diabetes only	54	59 (54)	35	18	6
Diabetes and peripheral arterial disease	26	32 (29%)	16	11	5
Diabetes and venous insufficiency	13	18 (17%)	3	1	14

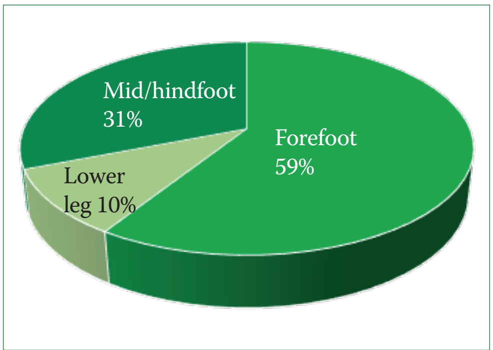

Figure 1. Ulcer location in patients with diabetes only.

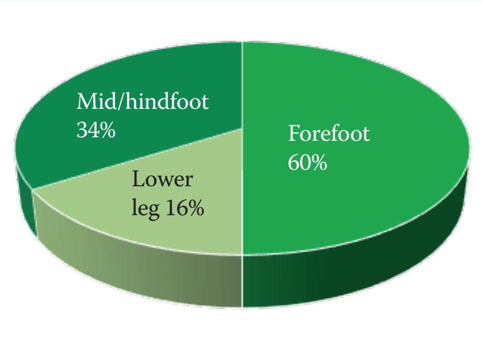

Figure 2. Ulcer location in patients with diabetes and peripheral arterial disease.

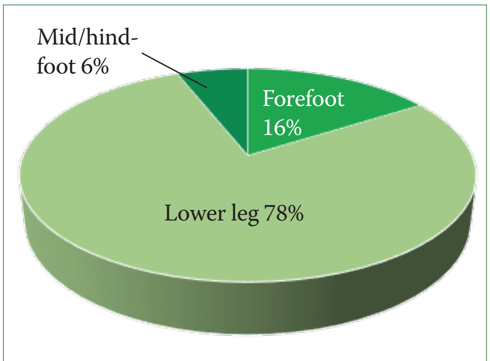

Figure 3. Ulcer location in patients with diabetes and venous disease.

and 11% inpatients) with lower-extremity wounds cared for through a large inner city academic vascular surgery-managed wound care programme between 2016 and 2018. Of these 174 patients, 93 had diabetes. These patients were subcategorised into diabetes only, diabetes with PAD, and diabetes with peripheral venous insufficiency. Patients with wounds on previous amputation sites, hardware-associated wounds, upper-extremity wounds and previously diagnosed rheumatic conditions were excluded. The remaining wounds in each subcategory were then classified into forefoot (proximal metatarsal bones to distal phalanges), mid/hindfoot (calcaneus to proximal metatarsal bones) or leg (malleolar and proximal lower extremity). When patients had multiple ulcers, each ulcer was identified separately and differences in location noted.

Results

A total of 93 patients with 109 individual ulcers were identified. Fifty-four patients had diabetes only, 26 had PAD and 13 had documented venous insufficiency. The location of each ulcer was identified *[Table 1* and *Figures 1–3]*.

Seventeen patients (18.2%) had documented amputation after initial wound debridement. Of these, 64.3% were major amputations (above-knee, below-knee or transmetatarsal amputation) and 35.7% were minor amputations. The average time interval from initial debridement to amputation was 102 days. When categorising which patients required future amputation based on ulcer location, 28.6% had forefoot ulcers, 17.9% had mid-foot ulcers, 39.3% had hind-foot ulcers and 14.2% had leg ulcers. Almost half (47%) of patients who required amputation had PAD.

Wound healing and closure data were extrapolated for patients who had not undergone amputation. A quarter (25.8%) of patients had documented dates of complete wound closure without further surgical intervention (ie amputation). Of this cohort, 45.8% had forefoot ulcers, 37.5% had hind/midfoot ulcers and 16.7% had leg ulcers. There was a lack of wound healing trajectory data in the records and/or documentation of wound closure for the remainder of patients.

In patients with complete wound closure, five (20.8%) had ankle-brachial indexes consistent with PAD and five (20.8%) had venous insufficiency. Eighty per cent of patients with

PAD had forefoot ulcers, while 80% of patients with peripheral insufficiency had leg ulcers.

Discussion

DFUs may be classified as neuropathic, ischaemic or both, and locations of DFUs vary. In this study, the majority of wounds presented at outpatient visits and involved the forefoot, similar to the findings of previous DFU location studies and reflecting known patient risk factors (Prompers et al, 2008). Studies such as EURODIALE have demonstrated that the presence of PAD in patients with DFU, particularly with associated infection, significantly worsens wound healing, amputation and mortality (Prompers et al, 2008). Location also appears to be related to patient comorbidities. The majority of patients with diabetes or diabetes with PAD had forefoot ulcers, with the minority having ulcerations near the malleoli; the opposite was found in patients with diabetes and venous disease. In our very small sample size with limited data collection, complete wound healing was noted to be greatest at the level of the forefoot, while future major amputation was most closely associated with hindfoot wounds. Infection, osteomyelitis and bony resection increase the risk of amputation.

In clinical practice the treatment of DFUs centres around wound care/debridement, infection control and off-loading pressure, as well as workup and evaluation of PAD (Gale et al, 2014). Peripheral revascularisation may lead to better patient outcomes through improved macro- and microcirculation, penetration of antibiotics in light of ongoing infection, and the presence of innate immune cells for wound healing. Studies investigating this are ongoing.

As the majority of ulcerations in patients with diabetes and diabetes with PAD occurred on the forefoot, offloading remains a major concern. Sharp debridement of surrounding callouses, with mechanical or enzymatic debridement of the wound bed, also remain key. Evaluation for signs of infection, and medical or invasive management thereof, is of the utmost importance. Due to the additive negative effect of PAD and infection/risk for infection, patients with DFUs should be evaluated for the presence of impaired arterial circulation. Intervention should be provided where appropriate.

Neuropathic patients and those with calcified arteries may not subjectively experience the discomfort commonly associated with PAD and their ankle-brachial indexes may reflect non-compressible vessels. The presence of forefoot lesions in particular may signal the higher likelihood of comorbid PAD. Unfortunately, no quantitative evaluation of concordance nor motivation to achieve healing is available, let alone adjudicated for these patients.

Patients with suspected or gross concomitant venous disease must be assessed with lower-extremity Doppler ultrasound. Conservative management includes leg elevation, exercise, skin care and compression therapy. Patients with saphenous incompetence may be candidates for venous ablation.

If DFUs do not exhibit timely healing, advanced and/or adjunctive therapies, such as surgical debridement and the application of cellular or tissue-based products, may be utilised to act as dermal regenerative matrices. Consideration should be given to the application of temporary negative pressure wound therapy during the initial postoperative period. Topical oxygen and TLC-NOSF (Technology Lipido-Colloid Nano Oligosaccharide Factor) therapies have demonstrated increased healing rates in chronic wounds including DFUs. The presence of oxygen is necessary for several key steps in the wound healing process, including angiogenesis, the formation of reactive oxygen species, differentiation of fibroblasts and synthesis of collagen (Hayes, 2017). The double-blind TLC-NOSF Explorer trial found that TLC aids the proliferation of fibroblasts and NOSF has promising effects on matrix metalloproteinase inhibition and increases the concentration of growth factors, which accelerate epithelialisation (Shanahan, 2013; Münter et al, 2017).

Due to the large number of DFUs that occur at the forefoot, where proper offloading, glucose control, infection control and PAD contribute greatly to the natural history of the wound, it is clear that the treatment and care of DFUs is a responsibility shared between clinicians and patients. Wound care clinicians and vascular surgeons can manage local and/or advanced wound care, provide offloading footwear, diagnose and treat PAD and provide continuing education. Patient compliance with offloading, strict adherence to the management of systemic metabolic derangements (eg hyperglycaemia) through medication and lifestyle modification is paramount to the prevention and treatment of DFUs and their complications.

Conclusions

Wound healing and amputation rates differed depending on DFU location, which was affected by the presence of PAD or venous disease. Forefoot wounds were most commonly associated with concomitant PAD and had the highest rates of successful wound closure. Wound location and vascular comorbidities should be taken into account when devising management strategies. WINT

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