

An Evidence-Based Approach to Foot Ulcer Prevention in Patients with Diabetes

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Introduction

Foot ulcers and amputations are among the most common and costly complications of diabetes. Advocacy groups frequently claim that 80% of these amputations are preventable [1], and it is a goal of Healthy People 2000 to reduce amputations by 50% [2]. However, there is no universal consensus on how best to prevent foot ulcer and amputation.

Guidelines on the management of the foot of the diabetic patient exist, and these guidelines address prevention [3,4]. The guidelines recommend frequent foot examinations and annual assessment of patients' risk for ulcer by means of a history and physical examination; the history and physical examination includes documentation of prior foot ulcer, examination for sensory neuropathy, and, in some guidelines, examination of peripheral pulses and assessment of foot deformity. Adherence to these guidelines is mediocre; only about 60% of patients with diabetes receive even an annual foot examination [5].

To determine appropriate interventions for prevention of disease, at least five issues must be addressed [6]: disease burden; identification of a target population for the intervention; effectiveness of the intervention; cost-effectiveness of the intervention; and patient adherence to the intervention. The purpose of this article is to review the scientific literature on foot ulcer prevention within the framework of addressing these issues and to make evidence-based recommendations for preventing diabetic foot ulcers.

How Severe Is the Burden of Diabetic Foot Disease?

It is difficult to overestimate the burden of diabetic foot complications. There are more than 500,000 ulcers annually in the United States, leading to more than 50,000 amputations [7]. The direct costs associated with diabetic foot disease are unknown, but best estimates are more than \$2 billion annually [1]. Quality of life with a chronic ulcer [8] and after a major leg amputation [9] is very poor. Careful investigation into the prevention of diabetic foot disease is clearly warranted given its impact on patient function and well-being and its financial impact on the health care system.

Which Patients Should Be Targeted for Foot Ulcer Prevention?

It could be argued that all patients with diabetes should be targeted for foot ulcer and amputation prevention. Evidence-based guidelines, however, suggest stratifying patients based on risk of imminent foot ulcer, with increased resources going to high-risk patients [3,4]. Much is known about pathways to diabetic foot ulcer, and successful approaches to stratification of patients with diabetes according to foot ulcer risk have been developed.

Many studies have shown that diabetic neuropathy is critical to the overwhelming majority of foot ulcers and amputations [10–16]. All schema for stratifying for foot ulcer risk in the patient with diabetes include the assessment of peripheral sensory neuropathy as the central component. While there is discussion as to the relative importance of sensory neuropathy versus the concomitant autonomic neuropathy and microvascular disease that occur in neuropathic patients, bedside measurement of sensation is easy to perform and is therefore the hallmark of risk stratification in diabetic foot disease.

Predictors of Ulcer Formation

The system for ulcer risk stratification that has the best prospective validation was developed by Rith-Najarian et al in a population of Chippewa receiving care from the Indian Health Service [16]. Patients with diabetes systematically received a structured history and physical examination and were then followed for an average of 3.5 years. The independent predictors of risk for ulcer were prior history of ulcer, sensory neuropathy, and foot deformity. **Table 1** outlines a system for risk stratification based on these factors. It is worth examining these three elements of the risk stratification system in detail.

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Table 1. Classification of Diabetic Patients by Foot Ulcer Risk

| Clinical Characteristics | Annual Risk of Ulcer |
|--|----------------------|
| History of ulcer or amputation | 33% |
| Insensate to 5.07 monofilament, bony deformity, no history of ulcer or amputation | 19% |
| Insensate to 5.07 monofilament, no bony deformity, no history of ulcer or amputation | 11% |
| Normal examination, no history of ulcer or amputation | 0.6% |

Adapted from Edelman D, Sanders LJ, Pogach L. Reproducibility and accuracy among primary care providers of a screening examination for foot ulcer risk among diabetic patients. *Prev Med* 1998;27:274-8 with data from Rith-Najarian SJ, Stolusky T, Gohdes DM. Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting. A prospective evaluation of simple screening criteria. *Diabetes Care* 1992;15:1386-9.

History of ulcer. History of previous foot ulcer has been found in multiple studies to be the strongest predictor of new ulcer formation. The ulcer is not always at the site where the new ulcer will evolve or even on the same foot, but the history of ulcer indicates that all the pathophysiologic precursors of ulcer are in place.

Sensory neuropathy. Diabetic peripheral neuropathy can be assessed in many ways. However, use of the Semmes-Weinstein 5.07 monofilament is recommended. The monofilament is a piece of nylon manufactured to provide 10 g of force when applied to the foot (**Figure 1**). The filament is traditionally applied to 10 places on each foot: the first, third, and fifth toes; the first, third, and fifth metatarsal heads; the lateral and medial arches; the heel; and the dorsum of the foot. A normal examination is sensation in all 20 locations. Rith-Najarian et al used an eight-point examination (three toes, three metatarsal heads, two arches) in prospectively establishing that insensation to the monofilament is a risk for impending ulceration. Cross-sectional data demonstrate that four points on each foot (two toes, two metatarsal heads including the first metatarsal head) are as sensitive as the eight-point monofilament exam [17].

Assessment of peripheral neuropathy using the monofilament is recommended for two reasons. First, it was the measure of neuropathy used in the study prospectively validating neuropathy as a risk for ulcer [16]. Second, the examination is performed reproducibly by a broad spectrum of examiners [18]. Other components of the traditional neurological examination, such as vibration using the tuning fork, are more weakly predictive of presence of ulcer in cross-sectional studies [14]

and have mediocre sensitivity and specificity when compared to monofilament examination as a criterion standard [17].

Foot deformity. Foot deformity refers most commonly to hammer toe, claw toe, and Charcot's foot. However, primary care providers miss about half the deformed feet they see, so it is uncertain whether there is value in asking them to use this criterion in screening for high-risk feet [18]. Almost all ulcers forming on deformed feet do so in the presence of insensation to the 5.07 monofilament.

Peripheral vascular disease. It is also worth examining the predictive value of assessment of peripheral vascular disease (PVD) in stratification for risk of foot ulcer, as the American Diabetes Association guidelines call for annual assessment of pedal pulses [4]. Many studies show that PVD is a risk for foot ulcer, and PVD is the dominant risk factor for non-healing of or amputation resulting from foot ulcer [19,20]. However, in studies that assess the independent risk of ulcer formation related to PVD after accounting for neuropathy, the best studies find no additional contribution from PVD [15]. Also, the addition of the measurement of ankle-brachial index contributed no statistically significant additional predictive value for foot ulcer after accounting for monofilament exam, prior ulcer, and foot deformity [16,21]. Thus, despite the clinical guidelines currently in place, no evidence supports the use of the vascular examination in assessing risk for foot ulcer.

In summary, examination of the foot with the Semmes-Weinstein monofilament, in combination with asking the patient if he or she has ever had a foot ulcer, provides the clinician with a rapid, reproducible method for determining which patients with diabetes are most likely to develop a foot ulcer. The vascular history and physical examination do not contribute additional information. Other risk stratification systems [22] are not validated prospectively. Potential target populations for intervention thus include all patients with diabetes, diabetic patients insensate to the 5.07 monofilament, and diabetic patients with prior foot ulcer.

How Effective Are Measures for Preventing Foot Complications?

Much time, effort, and money has been spent on efforts to design interventions to reduce the rate of ulcer/amputation in patients with diabetes. The most tested interventions can be grouped into four categories: glycemic control, health services/systems interventions, special footwear, and neuropathy-reversing medications.

Glycemic Control

The effect of improving glycemic control on reducing foot complications is nearly established. In addition to data from

the Diabetes Control and Complications Trial (DCCT) showing improvement in complications for patients with type 1 diabetes with tight glycaemic control [23], prospective observational data have shown that development of foot ulcers is associated with prior poor glycaemic control [24,25]. Further, the results of the United Kingdom Prospective Diabetes Study (UKPDS) confirm that tight glycaemic control causes decreased neuropathy in patients with type 2 diabetes; there were not enough ulcers in the study to confirm the effect on foot ulcers and amputation [26]. The only remaining question regarding tight glycaemic control is whether it affords any special benefit, or indeed any benefit at all, to those patients who already have peripheral sensory neuropathy. The existing data support the notion that all patients with diabetes should have improved glycaemic control but do not at this time address the issue of whether intensification of control in neuropathic patients can prevent ulcer or amputation.

Health Services Interventions

A large number of systems approaches have been studied for their ability to decrease rate of foot complications in high-risk patients. Three successful randomized controlled trials have been completed.

The first trial offered patients who had either active or recently healed foot ulcer a 1-hour education session on foot care [27]. In that study, patients exhibited a significant decrease in re-ulceration rates over the median 9 months of follow-up, from 28% in the control group to 10% in the intervention group.

The second trial was a mix of a patient education intervention with physician clinical reminders to examine the feet of diabetic patients [28]. In this trial, the incidence of "serious foot lesions" (ulcers, blisters, and calluses) declined approximately 60%; the rate of true ulcer formation was too low for statistical significance to be attributed to the change.

The most recent trial evaluated a screening and intensive follow-up program for patients with diabetes [29]. Patients were randomized to screening or no screening, and those patients randomized to screening were entered into an intensive foot care education program if they had significant peripheral arterial disease, prior foot ulcer, or foot deformity. The intervention failed to reduce the number of ulcers or minor amputations but did reduce the incidence of major amputations. This suggests that the intervention may have been most effective as it related to treatment of ulcers rather than their prevention.

Another notable health systems approach to foot ulcer is the multidisciplinary clinic, which usually consists of at least a wound care nurse, a diabetologist, a foot and ankle surgeon, and a vascular surgeon. While multidisciplinary clinics have been shown to reduce foot ulcer rates in uncontrolled interventional studies [30], no controlled trials exist.

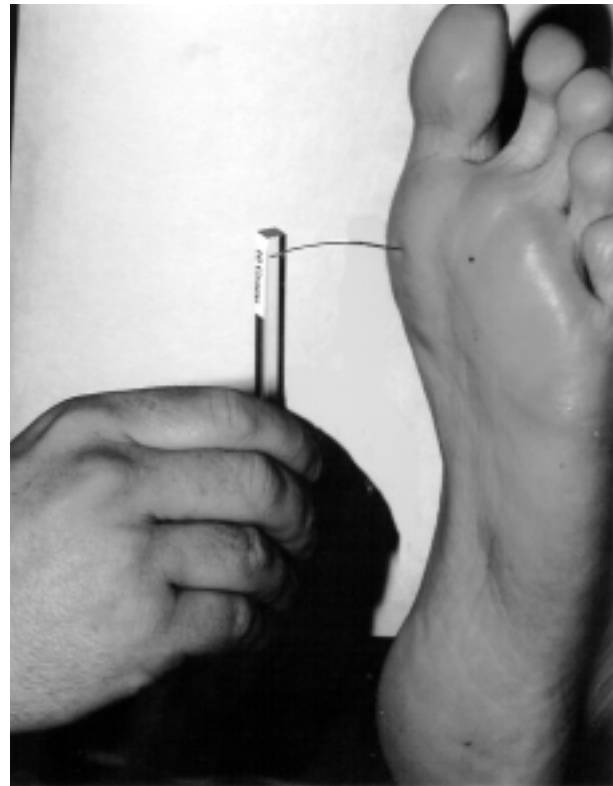


Figure 1. Technique for applying the Semmes-Weinstein 5.07 monofilament. When applied until the filament just bends, 10 g of force are applied.

Similarly, a comprehensive plan to reduce amputations in the Indian Health Service utilizing aggressive reminders for foot examination and early, active treatment of foot ulcer reduced amputations in the context of an uncontrolled public health intervention [31].

Footwear

A number of studies have tested interventions designed to improve the footwear of diabetic patients at high risk for foot complications. The sole completed randomized controlled trial with clinical outcomes among them tested the effectiveness of manufactured extra-depth shoes with custom insoles in patients with prior foot ulcer [32]. After 1 year of follow-up, ulcer rates were approximately 35% lower in the intervention group as compared to the control group; however, the ulcer rate in the control group was quite a bit higher than is generally reported in patients with prior foot ulcer (60%, versus the 30% to 35% reported in most observational studies). A large-scale trial of custom footwear in patients with prior foot ulcer is in progress [33].

Uncontrolled trials of both shoes and socks have demonstrated reduced plantar pressures [34–36]. However, while

Table 2. Recommendations for Care Based on Stage of Diabetic Foot Disease*

| Target Population | Interventions to Perform | Interventions to Consider | Interventions to NOT Perform |
|--|---|--|--|
| All diabetic patients | Screen for history of prior ulcer [27,29] Tight glycemic control [26] | Reminders to practitioners to examine feet [28,30] Screening for neuropathy with Semmes-Weinstein 5.07 monofilament (for prognostic information) [16] | Primary care examination for foot deformity [18] |
| Diabetic patients with neuropathy | Same as for all diabetic patients | Specialized footwear [34-37] Referral to multidisciplinary clinic [30] | Treatment with antineuropathy medication [38,39] |
| Diabetic patients with previous foot ulcer | Referral to formal diabetic foot education [27,29] Specialized footwear (at least extra-depth shoes) [32,34] | Custom-fitted footwear [33,35] Referral to multidisciplinary clinic [30] | Same as for patients with neuropathy |

*Recommendations to perform are based on evidence from randomized controlled trials. Other recommendations are based on evidence of various types and strengths. References to studies supporting the recommendations are in brackets.

plantar pressures are an important intermediate outcome correlated with ulcer formation [37], these pressure changes have not to this point been translated into a decrease in adverse clinical outcomes.

Antineuropathy Medications

While a number of drugs have been reported to improve physiologic measures of sensory neuropathy, none have been demonstrated to improve ulcer incidence or any clinical outcomes intermediate to ulcer incidence [38,39]. While these drugs may have a role in preventing foot ulcer in the future, no such role is defined for them at this time.

Do Patients Adhere to Foot Ulcer Risk Reduction Protocols?

Compliance with foot ulcer risk reduction protocols has been only minimally studied. Patients are very interested in foot care, and quality of foot care contributes significantly to the diabetic patient's overall satisfaction with care [40]. However, there are two types of data supporting the idea that compliance with diabetic foot care is actually poor. The Medicare program providing payment for custom shoes for high-risk patients remains lightly utilized [41,42]. While there is some evidence this may be due to lack of practitioner education about the program, it is also true that even when special footwear is prescribed it is usually worn less than prescribed [43]. Additionally, two studies [29,40] document and quantify the poor adherence to prescribed visits to foot education sessions. Further research is necessary to define the factors underlying nonadherence with foot care and to design mechanisms to improve adherence.

Recommendations

A summary of the evidence on the potential interventions to perform in the management of the foot of the patient with diabetes is presented in **Table 2**. Five clear points of action are supported by the evidence:

1. Every patient with diabetes should be asked about a history of foot ulcer, and those with such a history should be referred to formal foot care education. Additionally, prescription for extra-depth shoes should be considered.
2. Screening for neuropathy (with the Semmes-Weinstein 5.07 monofilament) is an important prognostic tool and should be considered for that reason alone. Patients insensate to the monofilament may benefit from footwear designed to reduce plantar pressures and patient education, but the certainty of this is less than in patients with previous ulcer. Screening for neuropathy cannot be absolutely recommended because of the lack of data to support (or reject) any specialized intervention for these patients in the absence of prior foot ulcer or amputation.
3. Formal programs to remind physicians to examine their diabetic patients' feet at every visit will probably (but not certainly) reduce the rate of foot complications in all patients with diabetes.
4. Intensive glycemic control should be practiced in most patients with diabetes. One of the major benefits of tight control will almost certainly be a reduction in foot complications.

5. All education and footwear interventions should be designed to maximize ease of adherence to the intervention.

From the perspective of a health care system, careful identification and tracking of patients with a history of foot ulcer or amputation in combination with foot care education and footwear consultation for all such patients would likely be the most efficient way to reduce the incidence of foot ulcer or amputation. Other interventions in other lower-risk target populations may be effective but are less certain to succeed.

Further research should focus on better defining the role of intervention in the neuropathic patient without a history of ulcer, clarifying the role of special footwear in patients with prior ulcer, and improving adherence to foot education and footwear use.

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