

DETECTION OF DIABETIC PERIPHERAL NEUROPATHY: STRATEGIES FOR SCREENING AND DIAGNOSIS*

David G. Armstrong, DPM, MSc, PhD†

ABSTRACT

Diabetes is a devastating disease that affects every part of the body, with complications both microvascular and macrovascular in nature. Examining microvascular disease (the foot in particular), statistics reveal that infected foot wounds commonly progress, with at least half of all infections of the lower extremity resulting in ulceration and a disturbing 1 in 5 of these events leading to lower-extremity amputation. Half of all patients who undergo amputation die within 3 years. This is tantamount in terms of morbidity and mortality to a high-grade carcinoma, yet even when patients are admitted to the hospital for a diabetic foot complication, they are frequently evaluated in a manner that is less than adequate. It is vital that clinicians identify and stratify risk among their patients with diabetes. Specifically, to determine ulcer risk, healthcare practitioners should determine whether there is loss of protective sensation, whether the patient has a deformity that results in high pressure to certain areas of the foot, and whether there is a prior history of ulcers and amputations. The diagnosis of diabetic peripheral neuropathy and the subsequent assessment of ulcer risk can only be made via careful and (at least) annual clinical examination.

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It is widely recognized that diabetes affects every part of the body (Figure 1), with complications of both a microvascular and macrovascular nature. The most significant microvascular complications include retinopathy, nephropathy, and diabetic neuropathy. It also is well established that diabetes can result in macrovascular disease; specifically, individuals with diabetes experience a 2- to 4-fold increase in cardiovascular mortality and stroke. Examining microvascular disease (of the foot in particular) in comparison to all of the other complications of diabetes, statistics reveal that infected foot wounds commonly progress, with an infection-to-ulcer ratio equal to 0.56¹; in other words, at least half of all infections of the lower extremity will result in ulceration. Furthermore, a disturbing 1 in 5 of these events leads to lower-extremity amputation (Figure 2).¹⁻⁴ Diabetic foot wounds comprise at least 25% of all diabetes-related hospital admissions in the United States and up to half in some parts of Europe, notably some National Health Service districts in the United Kingdom.⁵

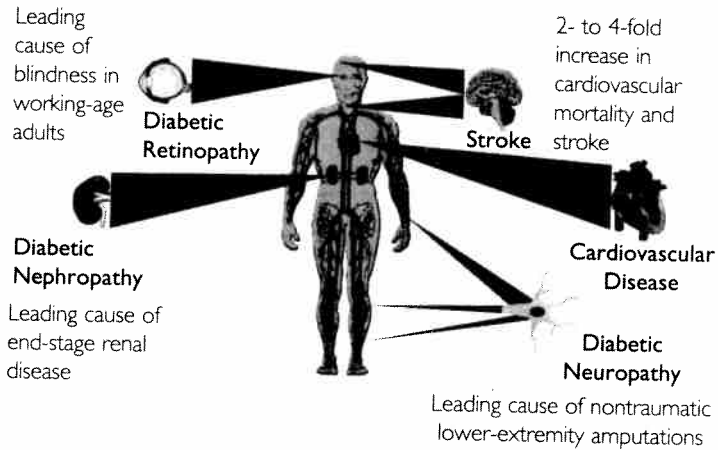
Even when patients are admitted for a diabetic foot complication, they frequently are evaluated in a less than adequate manner—perhaps because, as a result of the perception among clinicians that there are so many risk factors to assess and deal with in these patients, a feeling of nihilism sets in. This results in poor treatment and tragic outcomes for many patients. In fact, the top-line data concerning morbidity following amputations for patients with diabetes have not changed in 40 to 50 years. Specifically, after an initial amputation, 7 out of 10 patients require contralateral amputation within 5 years, and 50% will die within 3 years. This is tantamount in terms of morbidity and mortality to a high-grade carcinoma. These patients tend to die of cardiovascular complications, because greater cardiovascular reserve is required to accommo-

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†Professor of Surgery, Chair of Research, and Assistant Dean, Dr William M Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science; Director, Center for Lower Extremity Ambulatory Research (CLEAR) at Rosalind Franklin University of Medicine and Science, North Chicago, Ill.

Address correspondence to: David G. Armstrong, DPM, PhD, Dr William M. Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science, 3333 Green Bay Rd, North Chicago, IL 60064. E-mail: Armstrong@faiv.com.

Figure 1. Diabetic Complications Affect Every Part of the Body*



Diabetic microvascular complications are most commonly manifested in the eyes, kidneys, and nerves.

*Data from National Diabetes Information Clearinghouse. Diabetes Statistics-Complications of Diabetes. Available at: www.niddk.nih.gov/health/diabetes/pubs/dmstats/dmstats.htm#comp. Accessed May 1, 2001.

date and adjust to the stresses of walking with a missing limb. Of those who survive, 25% are institutionalized postoperatively, whereas only 2% had been in long-term care prior to the need for amputation.⁵ These patients—frequently of a pre-Medicare age group—are transformed from being active and productive members of society to being minimally functional, with all of the socioeconomic consequences that brings.

In 1996, our group published a retrospective review of a 4-year consecutive sample population of 255 patients who were admitted to a hospital for care of an infected diabetic foot ulceration. The 4 major variable categories included: (1) whether the patient underwent a lower-extremity amputation; (2) whether the patient was admitted once or multiple times; (3) whether the patient underwent intraoperative debridement; and (4) whether the patient was admitted to medical or surgical services. The authors determined that all patients had undergone a less-than-adequate foot examination, independent of their category. Specifically, of the admitted patients, 31.4% did not have their pedal pulses documented, and 59.7% were not evaluated for the presence or absence of protective sensation. Nearly 90% of the patients' wounds were not evaluated for involvement of underlying structures, and x-rays of the affected limb were not performed

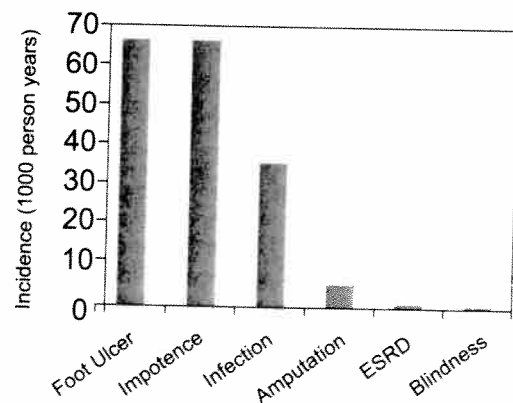
in 32.9% of the patients. Other inadequacies in the workup of these patients included the preference for ordering blood cultures rather than the more appropriate wound cultures—the former being ordered 62% of the time vs 51.4% for the latter. The authors concluded from their results that there is a need for a “systematic, detailed lower-extremity examination of every patient with diabetes who is admitted to a hospital.”⁶ Yet, this study revealed that only <14% of patients had been evaluated with even minimal competency.

Preliminary data from the Glycemic Optimization with Algorithms and Labs At Point of Care (GOAL A_{1c}) study revealed that of the first 7378 patients to be evaluated (out of 14 000), 37% had diabetic peripheral neuropathy (DPN) that was missed by 63% of generalists and specialists.⁷ If neuropathy (resulting in the loss of protective sensation) is the key to preventing ulceration, knowing the risk factors and comprehensively evaluating and diagnosing DPN is vital to the preservation of life and limb.

EVALUATING PERIPHERAL NEUROPATHY AND DETERMINING RISK

Lavery et al conducted a study to determine the

Figure 2. How Do Microvascular Complications Stack Up?*



Infected wounds: most common reason for hospital admission (infection : ulcer ratio = 0.56). 1 in 5 leads to lower-extremity amputation.
*Data from: Lavery LA et al¹; Trautner C et al²; Fedele D et al³; Bruno G et al.⁴

clinical risk factors for developing foot ulcerations with the goal of aiding clinicians to categorize patients by their risk status and schedule intervention resources accordingly to prevent amputation. The investigators studied 225 age-matched controls of both sexes (76 case patients and 149 controls; 47% were male). Case patients were defined as individuals who had existing foot ulceration or a recent history of foot ulceration, whereas controls had no such history. The authors determined that all of the following were significant risk factors ($P < .001$) for foot ulceration:

- An elevated plantar pressure ($>65 \text{ N/cm}^2$)
- History of amputation, lengthy duration of diabetes (>10 years)
- Foot deformities (eg, hallux rigidus or hammer toes)
- Limited joint mobility
- Male sex
- Poor diabetes control (glycosylated hemoglobin $>9\%$)
- 1 or more subjective symptoms of neuropathy
- An elevated vibration perception threshold ($>25 \text{ V}$)

In addition, 59 patients (78%) with ulceration had a rigid deformity directly associated with the site of ulceration. On the other hand, there were no significant associations between the presence of vascular disease, level of formal education, nephropathy, retinopathy, impaired vision, alcohol and tobacco use, or obesity.⁸ It should be noted, however, that though vascular disease and renal disease were not risk factors for acquiring an ulcer, they almost certainly are contributors to delayed healing and, therefore, amputation.

Besides identifying risk factors, it also is important to stratify risk; that is, to ask whether various identifiable risk factors for ulceration are cumulative. For example, a patient with neuropathy is at approximately twice the risk of developing a lesion on his foot as is someone without DPN. If both neuropathy and foot deformity are present, the patient is at approximately a 12-times greater risk. Furthermore, if a patient has a history of ulcer or amputation, he or she is at about a 36-fold greater risk of ulceration than someone without any risk factors resulting from alterations in foot dynamics (that then cause the abnormal distribution of plantar pressure, again resulting in an increased risk of skin breakdown) (Table).⁸⁻¹⁰ This type of assessment helps to determine in order of priority which patients

need specialized shoes, more education, and more frequent follow-up visits.

Three basic questions are important to address during the history and physical examination to determine ulcer risk: The first is, "Is there loss of protective sensation?" To further evaluate this, 2 tools are commonly used. Some years ago, our group conducted a prospective cross-sectional study to measure the degree of peripheral sensory neuropathy in patients with diabetes with and without foot ulcers, comparing these 2 instruments and using a brief questionnaire. The authors enrolled 115 age-matched patients with diabetes (40% male; 30 cases and 85 controls). Cases were defined as individuals who had existing foot ulceration or a history of a recently (<4 weeks) healed foot ulceration. Controls were defined as subjects with no history of foot ulceration. The sensitivity and specificity of 2 commonly used nephropathy assessment tools (vibration perception threshold testing using 25 V and the Semmes-Weinstein 10-g monofilament) and a 4-question verbal neuropathy score were evaluated to determine which was the more effective and practical screening tool for identifying patients at risk for diabetic foot ulceration. The study suggested that poor vibration perception and lack of perception at e4 sites using the Semmes-Weinstein 10-g monofilament had a significantly higher specificity than the neuropathy score, although the neuropathy score was most sensitive when e1 response(s) were affirmative. Furthermore, the authors determined that when

Table. Cumulative Risk for Ulceration by Foot Risk Category*

Risk Category for Ulceration	Odds Ratio (95% CI)
Foot Risk Category 0	N/A
Foot Risk Category 1	1.7 (0.7-4.3)
Foot Risk Category 2	12.1† (5.2-28.3)
Foot Risk Category 3	36.4† (16.1-82.3)

Risk Category 0: Protective Sensation Intact, No Deformity

Risk Category 1: Loss of Protective Sensation (Lops)

Risk Category 2: Lops + Deformity

Risk Category 3: History of Previous Ulcer or Amputation

CI = confidence interval.

*Data from Armstrong, et al. *Arch Intern Med.* 1998;158:289-292.*

† $P < .05$

modalities were combined, particularly the monofilament wire system plus vibration perception threshold testing and the neuropathy score plus the monofilament, there was "a substantial increase in specificity with little or no diminution in sensitivity."⁹

A 10-g (5.07 Semmes-Weinstein) nylon monofilament that has been standardized to deliver a 10-g force when applied may be used to test a patient's sensation by introducing it to 10 random sites on the plantar surface of the foot while the patient has his or her eyes closed. The monofilament should be applied in a smooth, perpendicular motion, taking care not to drag it across the skin, and introduced repeatedly to the same site, or applied to the damaged skin (ie, the site of the ulcer, callus, scar, or necrotic tissue). It should be tested first on the patient's hand, so the patient knows what to expect. The patient may respond, "Yes," upon detecting the monofilament and then indicate where it was perceived. If e4 sites are imperceptible, this is diagnostic of the loss of protective sensation (Figure 3).^{9,10}

Loss of pressure sensation typically occurs later than does loss of vibratory sensation. Therefore, it is useful to use calibrated tuning forks or vibration perception threshold meters (biothesiometers). The biothesiometer allows the clinician to raise volume on the device, increasing the amplitude until the patient feels the vibration. The vibration perception threshold is measured in volts. If vibratory sensation is perceived at a level in excess of 25 V, that patient has about 7-fold greater risk of foot ulceration.⁶ Again, combining

modalities (vibration perception threshold monitors plus monofilament testing) increases the diagnostic yield—particularly sensitivity without losing specificity—although if only 1 method must be selected, vibration testing is probably preferable because of its rapid results, ease of use, and less subjectivity involved in its interpretation compared with the Semmes-Weinstein monofilament test.

The second question that is important for determining ulcer risk is, "Is there a deformity causing high pressure?" The most common means of acquiring foot ulcers is exposure to pressure. This may be via constant exposure to low pressure, a single event causing exposure to high pressure, or most commonly, the moderate pressure repeated in the 3000 to 10 000 steps that many patients take every day. Correcting a foot deformity has been demonstrated to reduce dynamic foot pressure and reduce the odds of developing ulcerations.¹¹ It also is known that limited joint mobility is a significant factor associated with increased plantar pressure (eg, <15 degrees of dorsiflexion at the hallux), and can lead to foot ulceration in the patient with diabetes.

The final assessment question that, if answered affirmatively, indicates increased risk of ulceration is whether there is a history of previous ulcers or amputation. In fact, if the patient has a prior history, it is likely that all of the prerequisites are in place to produce another ulcer, and the patient has a 10-fold greater risk for a subsequent ulcer.⁸

CONCLUSION

It cannot be emphasized strongly enough that careful history and physical examination are imperative to the prevention of ulcers and amputations in the patient with diabetes. In the words of Professor Lindsay, who died in Belfast more than a century ago but whose wisdom still applies, "For every 1 mistake made for not knowing—10 are made for not looking."

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Figure 3. 10-g Semmes-Weinstein Monofilament*

- 10-g Semmes-Weinstein monofilament testing
- "Yes-no" method of administration
 - Administered at 10 sites on each foot



*Data from from Armstrong et al. *Arch Intern Med*. 1998;158:289-292.*

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