

Prevention of Lower-Extremity Amputation in Diabetic Patients

Major advances in limb salvage have resulted from a multidisciplinary approach to treatment.

BY ROBERT G. FRYKBERG, DPM, MPH

Seven percent of the US population was estimated to have diabetes in 2005 — representing a total of 20.8 million people. Of this number, 6.2 million were unaware that they had the disease. There are 1.5 million new cases of diabetes yearly, and the direct medical costs associated with diabetes total \$92 billion. The indirect costs of diabetes, including disability, work loss and premature mortality, are responsible for \$40 billion. Diabetes was the sixth leading cause of death in United States in 1999.^{1,2}

The major complications of diabetes include microvascular disease, protein glycosylation, macrovascular disease, immunopathy and lower-extremity amputation (LEA), according to the Centers for Disease Control and Prevention.^{3,4} Of the major lower-extremity complications, ulceration, infection, peripheral arterial disease, LEA and Charcot foot, are among the most common.^{5,6}

Diabetic patients have a 15% lifetime risk of having ulceration resulting from multifactorial etiology. An ulcer may be neuropathic, ischemic or neuroischemic in its pathophysiology, and it is a precursor to amputation in 80% to 85% of cases.^{4,7}

RISK FACTORS

Risk factors for diabetic foot ulceration can be classified as intrinsic or extrinsic. Intrinsic factors are

- peripheral neuropathy (sensorimotor and autonomic),
- microvascular and macrovascular disease,
- immunopathy,
- structural deformity,
- limited joint mobility,
- nephropathy,
- age,
- duration of diabetes,
- visual acuity and

- previous ulceration.
- Extrinsic risk factors for diabetic foot ulceration are
- minor mechanical trauma (eg, high plantar pressure, shoe pressure and high impact),
 - callus,
 - thermal injury,
 - chemical burns,
 - *bathroom* surgery (cutting corns or calluses with a razor blade, etc.),
 - occupational hazards,
 - living alone,
 - cigarette smoking,
 - poor knowledge of diabetes and
 - psychological factors.

The important components implicated in the pathway leading to foot ulceration are as follows: peripheral neuropathy in 78% of foot ulcers, minor trauma in 77%, deformity in 63%, edema in 37%, peripheral ischemia in 35%, callus in 30% and infection in 1%.⁷

The North-West Diabetes Foot Care Study examined the incidence and risk factors for ulcerations in close to 10,000 patients.

The North-West Diabetes Foot Care Study examined the incidence and risk factors for ulcerations in a community-based cohort of 9,710 patients with 2-year follow-up.⁸ The average incidence of ulceration was 2.2% in this population. The investigators found that the risk factors for foot ulcer were baseline ulcer present (relative risk [RR] 5.5), past ulcer history (RR 3.05), abnormal neuropathy

thy disability score $\geq 6/10$ (RR 2.32), loss of protective sensation (LOPS) to monofilament testing (RR 1.80) and reduced pulses (RR 1.80).

Patients with diabetes can be considered to have a relatively compromised biology that predisposes them to ulceration. Impairments can be in the form of macrovascular disease such as ischemia, or in microvascular disease, consisting of microneurovascular, vasomotor and endothelial dysfunction. These are closely associated with autonomic neuropathy (often recognized by anhidrosis).

While sensory neuropathy leaves the patient insensitive, motor neuropathy effects include the “intrinsic minus” foot, claw toes and high plantar pressures. Furthermore, patients with immunopathy (neutrophil dysfunction) have an increased susceptibility to infection (Figure 1).

LONG-TERM PROGNOSIS

The long-term prognosis for patients with foot ulcers was analyzed by Apelqvist and colleagues.⁹ In their study of 468 diabetic patients with healed foot ulcers, they found a 1-year recurrence rate of 34%, a 3-year rate of 61% and a 5-year rate of 70%. The recurrence rate of foot lesions was slightly higher in patients who had undergone an amputation. Among patients with previous primary healing, the cumulative amputation rates were 3%, 10% and 12% after 1, 3 and 5 years of follow-up, compared with 13%, 35% and 48% among those who previously healed after amputation.

People with diabetes make up about 7% of the population. More than 60% of the nontraumatic LEAs in this country are performed on diabetic patients. The average cost of an amputation is \$24,000 to \$40,000. Despite the concerted efforts of various public health and awareness campaigns aimed at reduction, these rates are rising (Figure 2).^{3,4}

AMPUTATION RATES

Amputation rates are particularly elevated in men, the elderly, blacks and Hispanics. American Indians have the highest risk of amputation, and diabetic nephropathy increases the risk threefold.^{4,10} Foot ulcers are the major risk factor for subsequent amputation, as 80% to 85% of diabetic LEAs are preceded by ulceration (Figure 3).^{11,12}

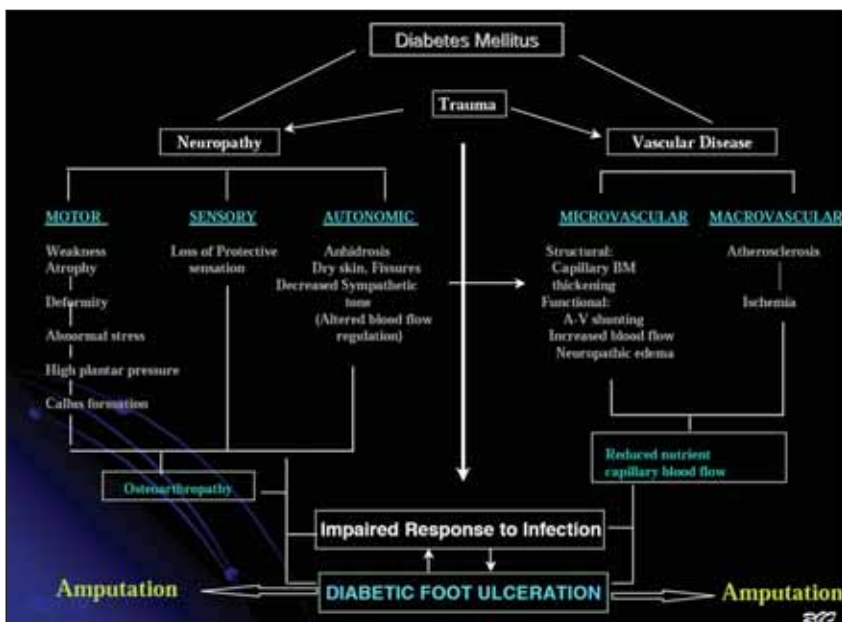


Figure 1. This flow chart illustrates the various factors that cause diabetes to lead to diabetic foot ulceration and possibly amputation.

Pecoraro and colleagues looked at the cumulative proportion of amputation due to individual causes in 80 consecutive initial LEA¹¹

- ischemia 46%,
- infection 59%,
- neuropathy 61%,
- faulty wound healing 81%,
- ulceration 84%,
- gangrene 55% and
- minor trauma 81%.

Adler et al looked at a group of 776 veterans who were followed for a median of 3.3 years.¹³ They evaluated the relative risk of various factors for LEA

- peripheral vascular disease and absent pulse (RR 3.0),
- LOPS 10-g monofilament (RR 2.9),
- foot ulcer history (RR 2.5) and
- prior amputation (RR 3.4).

Other studies suggest that 50% of patients undergoing initial major LEA will require contralateral amputation within 2 years, and 50% will die within 3 years following an initial major LEA.¹⁴

Perioperative mortality rates among patients having LEA averaged 5.8% in the period from 1989 to 1992.^{15,16} Studies have shown that, generally, survival is poor in patients with diabetes following LEA: 1-year mortality rates range from 11% to 41%, and 5-year rates range from 39% to 68%. Often cardiac and renal complications cause death.

In a retrospective database review from 1990 to 2001,

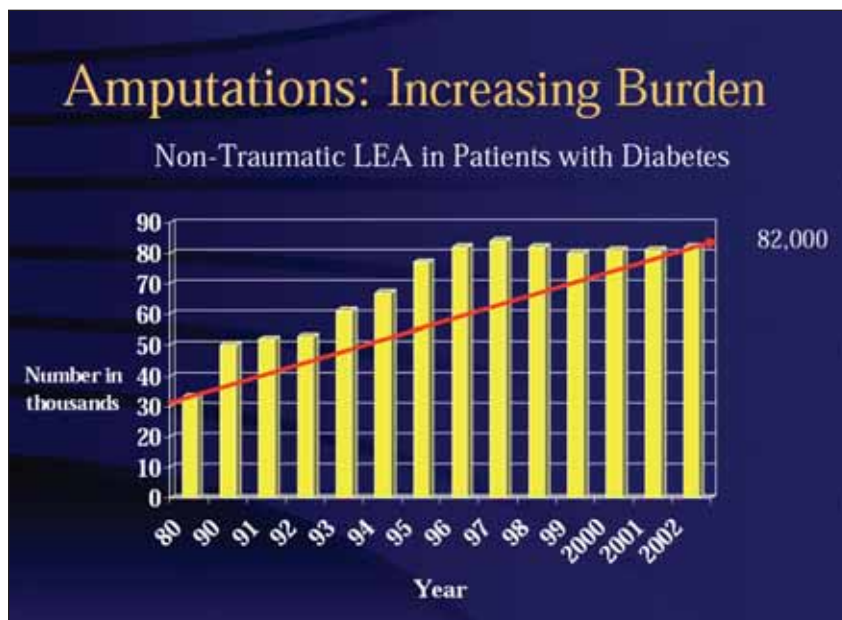


Figure 2. The burden of LEA continues to rise. (Data courtesy of the CDC.)

Aulivola and colleagues looked at 959 consecutive major LEAs in 788 patients.¹⁷ Of this group, close to 81% were diabetic, 704 had below-the-knee amputations and the rest were above the knee. The mean age was 66.7 years, and 57.2% of the group were men. The actuarial overall survival rate at 1 year was 69.7%; at 5 years it was 34.7%.

CAUSES OF LEA

The primary causes of diabetic LEA are fulminant infection, gangrene, unrecognized ischemia, nonreconstructable ischemia, inadequate assessment and massive tissue loss.^{11,13,18}

The causal pathway to amputation is made up of suffi-



Figure 3. Foot ulcers are the major risk factor for subsequent amputation.

cient causes and component causes.¹¹ Sufficient causes invariably produce the effect and are restricted to the minimal number of component causes required for causation. Component causes are not sufficient in themselves to cause amputation, and removal or blocking them renders the action of other components insufficient.

If we are to avoid amputations, we must better understand how to prevent them. We need to know the underlying pathophysiology. We also have to aggressively manage ulceration, infection, gangrene and ischemia. We have to work at the primary and secondary prevention of all complications.

The basic tenets of limb salvage include patient assessment, medical management/stabilization,

appropriate wound care, treatment of infection, treatment of ischemia, foot-sparing surgery and prevention.

PRIMARY PREVENTION

Primary prevention of foot ulceration is the ultimate key to limb salvage. Components of prevention include¹⁹

- education of patients and providers,
- protective footwear,
- regular preventive foot care,
- prophylactic foot surgery and
- multidisciplinary management with aggressive treatment of foot lesions.

The *Five Ps* of prevention are podiatric care (or periodic foot care), protective shoes, pressure reduction, prophylactic surgery and preventive education. Podiatric care includes regular physician visits. At these visits, foot exams should be performed with risk factors evaluated. Early detection of ulcers or preulcerative lesions is vital. Physicians should also provide prophylactic foot care such as debridement of calluses and nail cutting. Aggressive management of foot lesions, with debridement, off-loading and wound care, is critical as well as individualized risk assessment for each patient.

Protective footwear includes therapeutic shoes (extra depth, custom molded) athletic footwear and special modifications as necessary (pedorthic consultation).^{20,21}

To reduce pressure, we recommend performing some type of plantar pressure assessments. Various methods include the computerized F-scan (eg, Tekscan, Boston),

Emed (Novel GmbH, Munich, Germany), pedobarograph systems, as well as the traditional Harris mat or newer Pressurestat methods (Bailey Instruments, Manchester, UK). Pressure-reducing insoles can be either prefabricated or custom molded.

Prophylactic foot surgery in the carefully selected patient can correct structural deformities such as hammertoes, bunions and Charcot foot. In high-risk patients, it can help prevent recurrent ulcers especially if the intervention is performed at an opportune time.

Preventive education should include both the patient and the health care provider. Patient education should consist of teaching daily foot care and inspection, seeking early care for new lesions and behavioral change. Physicians need to know what risk factors to look for in their patients, what the causal pathways are, and they must always examine both feet of all patients, as well as provide appropriate management given the level of patient risk.

MULTIDISCIPLINARY APPROACH

The most successful way to manage the high-risk diabetic foot is with a multidisciplinary approach. Several studies have found that there are improved outcomes and healing with decreased rates of major LEA and reduced lengths of hospital stay through the use of a team approach (Figure 4).

A study by Holstein et al found a 75% reduction in the incidence of major amputations coincided with a sevenfold increase in revascularization procedures and an establishment of multidisciplinary diabetic foot clinic.²²

CONCLUSION

Major advances in limb salvage and amputation have resulted from a multidisciplinary management approach, improvements in podiatric care, the education of providers and patients, vascular surgery with extreme distal bypass and innovations in wound care. ■

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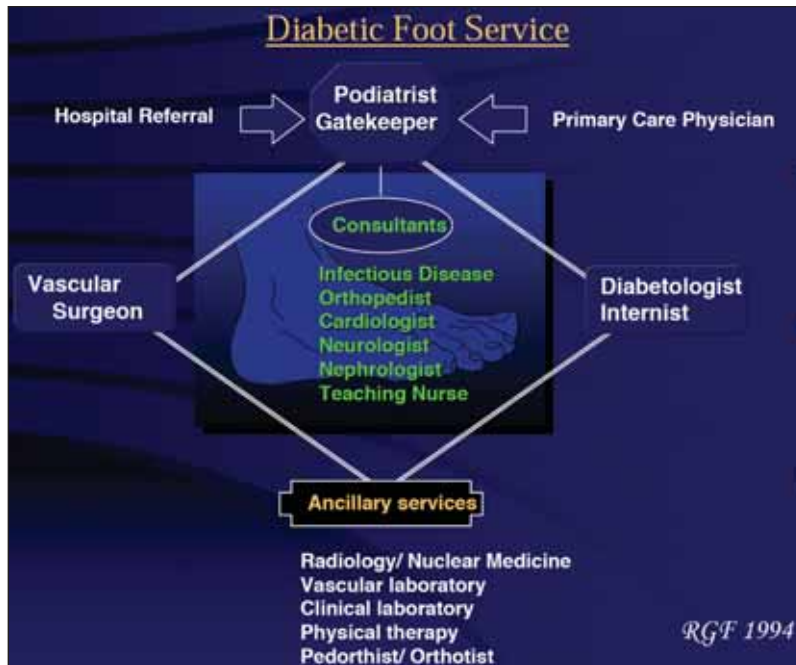


Figure 4. Several studies have found improved outcomes through the use of a team approach to podiatric care.

1. Frykberg RG. Prevention of lower extremity amputation in diabetes. Presented at the American Professional Wound Care Association National Conference 2006. April 6 to 8, 2006. Philadelphia.
2. National Institute of Diabetes & Digestive & Kidney Diseases Statistics 2005. Available at diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm#7. Accessed April 26, 2006.
3. Diabetes in America, 2nd Ed, 1995. Published by the National Diabetes Data Group of NIH's National Institute of Diabetes & Digestive & Kidney Diseases.
4. CDC Diabetes Surveillance. 1999. Available at www.cdc.gov/diabetes/statistics/surv99/chap1/mortality.htm. Accessed April 26, 2006.
5. Frykberg RG, Armstrong DG, et al. Diabetic foot disorders: A clinical practice guideline. *J Foot Ankle Surg.* 2000;39(suppl 1).
6. CDC Diabetes Surveillance. 1997. (Not available online.)
7. Reiber GE, Vileikyte L, Boyko EJ, et al. Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care.* 1999;22:157-162.
8. Abbott CA, Carrington AL, Ashe H, et al. North-West Diabetes Foot Care Study. *Diab Med.* 2002;19:377-384.
9. Apelqvist J, Larsson J, Agardh CD. Long-term prognosis for patients with foot ulcers. *J Intern Med.* 1993;233:485-491.
10. Young BA, Maynard C, Reiber G, Boyko EJ. Effects of ethnicity and nephropathy on lower-extremity amputation risk among diabetic veterans. *Diabetes Care.* 2003;26:495-501.
11. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care.* 1990;13:513-521.
12. Apelqvist J, Ragnarson-Tennvall G, Larsson J, Persson U. Long-term costs for foot ulcers in diabetic patients in a multidisciplinary setting. *Foot Ankle Int.* 1995;16:388-394.
13. Adler AI, Boyko EJ, Ahroni JH, Smith DG. The independent effects of peripheral vascular disease, sensory neuropathy, and foot ulcers. *Diabetes Care.* 1999;22:1029-1035.
14. Bodily KC, Burgess EM. Contralateral limb and patient survival after leg amputation. *Am J Surg.* 1983;146:280-282.
15. Reiber GE. National Institute of Diabetes & Digestive & Kidney Diseases Statistics book chapter. Available at diabetes.niddk.nih.gov/dm/pubs/america/pdf/chapter18.pdf. Accessed April 26, 2006.
16. Larsson J, Agardh CD, Apelqvist J, Stenstrom A. Long-term prognosis after healed amputation in patients with diabetes. *Clin Orthop Relat Res.* 1998;350:149-158.
17. Aulivola B, Hile CN, Hamdan AD, et al. Major lower extremity amputation: outcome of a modern series. *Arch Surg.* 2004;139:395-399.
18. American College of Foot and Ankle Surgery. Clinical Practice Guidelines. Available at www.aefas.org/pubresearch/cpg/diabetic-cpg.htm. Accessed April 26, 2006.
19. ADA Consensus Development Conference 1999.
20. Lavery LA, Vela SA, Fleischli JG, Armstrong DG, Lavery DC. Reducing plantar pressure in the neuropathic foot. A comparison of footwear. *Diabetes Care.* 1997;20:1706-1710.
21. Uccioli L, Faglia E, Monticone G, et al. Manufactured shoes in the prevention of diabetic foot ulcers. *Diabetes Care.* 1995;18:1376-1378.
22. Holstein P, Ellitsgaard N, Olsen BB, Ellitsgaard V. Decreasing incidence of major amputations in people with diabetes. *Diabetologia.* 2000;43:844-847.