

Vigilance Needed to Reverse Amputation Epidemic

BY ERIK L. GOLDMAN
Contributing Writer

WASHINGTON — The United States has one of the highest diabetes-associated limb amputation rates of any industrialized country, but many of these expensive and debilitating operations could be prevented through more aggressive early treatment of minor wounds, ulcerations, and infections.

Among people with diabetes in the United States, 7/1,000 lose a limb each year, compared with 5.5/1,000 in Germany, 3.5/1,000 in the Netherlands, 2.7/1,000 in the United Kingdom, and 1.2/1,000 in Denmark.

According to the International Working Group on the Diabetic Foot, the prevalence of limb amputation among diabetics ranges between 0.2% and 4% worldwide.

Between 50% and 85% of all lower-extremity amputations could be prevented, said Vickie R. Driver, D.P.M., at a health care congress sponsored by the Wall Street Journal and CNBC. "Eighty-five percent of all amputations are preceded by foot ulcers that have been allowed to progress. Lower-extremity ulcers and infections need to be seen as medical emergencies, and we need to treat them early and aggressively."

Intensive patient education and a concentrated limb-sparing effort by cross-disciplinary medical teams using a wide range of surgical and medical interventions can greatly reduce amputation rates, according to a retrospective study by Dr. Driver and her colleagues at Madigan Army Medical Center in Tacoma, Wash.

From 1999, when Madigan introduced a comprehensive Limb Preservation Service, to 2003, amputations went from 9.9/1,000 leg ulcer patients to 1.8/1,000, an 82% decrease. This was despite an overall increase in the number of diabetic patients entering the medical center (Diabetes Care 2005;28:248-53).

There is no single "magic bullet" therapy that will spare amputations, emphasized Dr. Driver, who is now director of clinical research in foot care, endovascular, and vascular services at Boston Medical Center. Treatment of advanced nonhealing wounds takes a combination of diligent monitoring of the feet and legs; aggressive treatment of any injury or infection, however minor it may seem at the time; careful debridement for more advanced ulcers; and application of a wide range of state-of-the-art therapies. Patients as well as physicians need to understand that in the context of diabetes, even a relatively insignificant injury can presage severe problems down the road.

Specialized matrix dressings like Promogran and wound-healing gels like Regranex, which contain growth factors to stimulate healing, definitely have a place in the management of diabetic leg ulcers, though neither of these alone is universally effective, Dr. Driver said.

She had high praise for vacuum-assisted closure (VAC), a relatively new form of negative-pressure wound therapy (NPWT) that involves targeted application of subatmospheric pressure to a wound. VAC is used in conjunction with specialized dressings such as GranuFoam.

"This is used for wounds that are very deep. It has three main benefits: It removes fluid from the wound, it pulls the edges of the wound together, and it stimulates new growth," Dr. Driver said. A 12-week study at 18 U.S. centers randomized 162 patients with severe advanced foot ulcers to treatment with VAC (n = 77) or moist wound therapy (n = 85) using state-of-the-art dressings. After 112 days, 43 of the VAC-treated patients (56%) showed 100% wound closure, compared with 33 of those treated with

moist dressings (39%).

There was also a marked decrease in the need for subsequent surgeries or amputations (43 procedures in the VAC patients vs. 120 procedures in the moist wound therapy patients). The average total cost to achieve healing was \$25,954 for VAC vs. \$38,806 for moist wound care, a difference of \$12,852 (Lancet 2005;366:1704-10).

A subsequent study pitted VAC against advanced moist wound therapy (AMWT), which included hydrogels and alginates, in 342 diabetic patients with severe foot ulcers.

At 12 months' follow-up, 73 of the VAC patients (43%) achieved complete wound closure, compared with 48 of the AMWT patients (29%). A total of 105 VAC patients (62%) reached the 75% closure mark, compared with 85 (51%) of the AMWT group (Diabetes Care 2008;31:631-6).

The patients treated with VAC also had fewer amputations (6 vs. 11) and fewer acute care admissions, all of which contributed to a markedly lower total cost of care.

VAC, Regranex, Promogran, and many of the other cutting-edge wound-healing therapies are not cheap, but when properly applied they can greatly reduce the overall cost of caring for diabetes-associated ulcerations. Left unchecked, those costs can be tremendous, and the total price mounts rapidly as ulcers persist. Of total expenditures on leg ulcers—and Medicare spends between \$1.5 billion and \$2 billion annually—70%-80% is for hospitalizations, not ambulatory care or medications.

According to data from Medicare, the average cost for managing a patient with a noninfected foot or leg ulcer

is \$775 per month. That increases to \$2,048 per month if the patient develops cellulitis. If he or she goes on to develop osteomyelitis, the cost averages \$3,798 per month.

In analyzing data from her experience at Madigan Army Medical Center, Dr. Driver said she found that wound depth directly correlates with number of outpatient visits. Patients with ulcers extending down to the tendon or joint capsule had an average of 30 office visits per quarter, compared with 9 per quarter for those with epithelialized wounds. Further, having an extensive and deep leg ulcer carried 40% odds of hospitalization for any and all causes within the next 3 months.

In a seminal but underreported 2004 study, researchers in the Netherlands showed that an optimal foot care program aimed at identifying and treating minor foot/leg injuries, when added to an intensive glycemic control program, could markedly reduce total cost of care per quality-adjusted life-year for people with diabetes. Foot care plus glycemic control programs had a total cost per quality-adjusted life-year of roughly \$25,000. Intensive glycemic control alone had an average cost of \$32,057 (Diabetes Care 2004;27:901-7).

Electrical Stimulation a Promising Adjunct

High-voltage, pulsed electrical stimulation is an effective adjunct to multidisciplinary attempts at limb salvage in diabetic patients with complex lower extremity wounds, results from a small study demonstrated.

Of 45 wounds in 30 patients, 78% of the wounds healed in a mean of 14 weeks using the electrical stimulation system, Dr. Jeremy J. Burdge reported at the annual meeting of the Wound Healing Society. Dr. Burdge, a plastic and reconstructive surgeon who practices in Columbus, Ohio, and his associates evaluated the efficacy of high-voltage electrical stimulation in patients who failed to improve despite multidisciplinary treatment approaches. More than half (57%) of the patients in the study were men; their mean age was 66 years. The mean age of wounds was 25 weeks, and the mean surface area was 7.8 cm². Most wounds were located on the foot (51%) and heel (28%). The mean number of electrical stimulation treatments per wound was 23 and 35 (78%) of the wounds healed in a mean of 14 weeks.

Dr. Burdge had no conflicts to disclose.

—Doug Brunk

Irrespective of Weight, Exercise Benefits Men With Diabetes

BY MICHELE G. SULLIVAN
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SAN FRANCISCO — Even moderate physical fitness appears to confer a significant survival benefit on men with type 2 diabetes, no matter what their body weight, according to Roshney Jacob-Issac, Ph.D.

Her retrospective study, presented at the annual meeting of the Endocrine Society, found an inverse association between mortality and increasing fitness, with normal- and overweight men gaining even more survival benefits as they reached the highest fitness levels. Although obese men did not reap any extra survival benefit with the top fitness level, moderate fitness decreased their overall risk of death by 52%.

"Increasing physical fitness has a sur-

vival benefit in diabetes regardless of body mass index," said Dr. Jacob-Issac of the Veterans Affairs Medical Center, in Washington. "For this reason, we suggest that moderate physical activity be advocated for all patients with diabetes."

Her retrospective study examined the link between all-cause mortality and exercise capacity in 2,690 men with type 2 diabetes, all of whom were referred for exercise tolerance testing at VA centers in Washington, D.C., or Palo Alto, Calif. Nearly half of the men (1,196) were obese; 1,088 were overweight, and 406 had a normal BMI.

The study did not include any men who, during testing, had a positive stress test, unstable symptoms, or a left bundle branch block; it also excluded anyone with

an implanted pacemaker or impaired chronotropic response.

Peak work load, which was determined via a stress test, was estimated in metabolic equivalents (METs). One MET is the energy expenditure at rest, or an oxygen consumption of 3.5 mL/kg a minute. Based on peak workload, individuals were categorized as low fit (5 or fewer METs), moderately fit (5.1-8 METs), or highly fit (more than 8 METs). All-cause mortality was assessed at a mean of 7 years.

There were 762 deaths (172 in the normal-weight group, 334 in the overweight group, and 256 in the obese group). After adjusting for age, cardiac medications, and cardiovascular disease risk factors, Dr. Jacob-Issac found a strong, graded relationship between increasing fitness and

decreasing mortality in all three groups.

In normal weight men, moderate fitness conferred a 40% reduction in the risk of death and high fitness conferred a 60% risk reduction, compared with low fitness. In overweight men, the risk reduction was 40% for moderate fitness and 65% for high fitness, compared with low fitness.

In obese men, moderate fitness conferred a 52% reduction in the risk of death, but being highly fit conferred no additional protection. This might be because of the very small number of men who were both obese and highly fit, Dr. Jacob-Issac noted.

A separate analysis concluded fitness level was a better predictor of mortality than age, BMI, hypertension, or dyslipidemia.

Dr. Jacob-Issac reported no conflict of interest related to the study.