Background: Infected foot wounds in patients with diabetes are the most common reason for diabetes-related hospital admission in the United States. Nonhealing foot wounds are the major precipitant of lower-extremity amputation in the diabetic population.

Hypothesis: The null hypothesis was that there would be no difference in proportion of healing with or without use of a foot-level mechanical compression device.

Design: Twelve-week, double-blind, randomized, controlled trial.

Setting: A university teaching hospital and related clinics.

Patients: One hundred fifteen patients with diabetes, 74% male, with foot infections requiring incision and debridement.

Intervention: All patients received either a functioning or placebo (nonfunctioning) foot compression device (Kinetic Concepts Inc, San Antonio, Tex). Patients and investigators were blinded to the functionality of the device.

Primary Outcome Measure: Proportion of wound healing in each group.

Results: There was a significantly higher proportion of healing in the active group than in the placebo group (39 [75%] of 52 patients vs 23 [51%] of 45; \( \chi^2 = 6.0; P < .02; \) odds ratio, 2.9; 95% confidence interval, 1.2-6.8). In the placebo group, there was no difference in proportion of healing between those identified as compliant (≥50 hours of use per week) vs noncompliant (\( P = .10 \)). In patients receiving active units, more patients in the compliant subgroup experienced wound healing (\( P < .03 \)). When compared as a whole, there was a significant trend toward an increasing proportion of healing from the placebo-noncompliant to the placebo-compliant to the active-noncompliant to the active-compliant groups (\( \chi^2_{\text{trend}} = 8.3; P < .005 \)).

Conclusions: Edema reduction achieved in this study by way of a pump and wrap system may increase the proportion of wound healing in patients after debridement of foot infections in patients with diabetes. Furthermore, the data suggest a potential association between increased compliance with use of the device and an increased trend toward wound healing.

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WOUNDS ON THE SOLE of the foot are one of the most common complications of diabetes mellitus and a major cause of disability and morbidity.\(^1\) Infected foot wounds in persons with diabetes are the most common reason for diabetes-related hospital admission in the United States,\(^2\) with approximately 90% of all lower-extremity amputations in patients with diabetes resulting from failure of these wounds to heal.\(^3\) This faulty healing of the diabetic neuropathic wound is secondary to the 2 often-coexisting factors: infection and vascular disease. Patients with vascular disease comitant with an infected ulceration are up to 90 times more likely to suffer a high-level amputation than are lower-risk subjects.\(^4\)

Even without overt structural macrovascular disease, large foot wounds in persons with diabetes, such as those commonly encountered after debridement of gas gangrene, polymicrobial infections, or necrotizing fasciitis, often present a major challenge to the clinician. Interstitial edema is frequently present in these patients, both preoperatively and postoperatively, and can retard or complicate healing, particularly in the presence of other comorbid conditions. Resultant increased oncotic pressure in postcapillary venules impairs arteriograde delivery of vital nutrients to the area, thus prolonging...
PATIENTS AND METHODS

In this double-blind, randomized, placebo-controlled clinical trial, we identified and enrolled 115 patients with diabetes who had foot infections requiring incision and debridement (Figure 1). Descriptive statistics for this population are summarized in Table 1. All patients were diagnosed as having diabetes mellitus on the basis of the criteria set forth by the World Health Organization, which include treatment with insulin or an oral hypoglycemic agent, 2 random glucose measurements greater than 11.1 mmol/L (200 mg/dL), or a fasting glucose level greater than 7.8 mmol/L (140 mg/dL). We excluded patients with diagnosed active congestive heart failure, end-stage renal disease, or a serum creatinine level greater than 177 µmol/L (>2.0 mg/dL) on the day of hospital admission. We also excluded any subjects who received a lower-extremity bypass graft within the period of study.

Subjects underwent a systematic neurovascular examination. We evaluated vibration perception threshold with a biothesiometer (Biomedical Instrument Corp, Newbury, Ohio). Tissue perfusion was assessed with a transcutaneous oxygen tension monitor (Radiometer, Westlake, Ohio). Edema was monitored by measuring circumference of the forefoot at a point 1 cm proximal to the first and fifth metatarsal heads both at the initiation of the trial and at complete healing or at the 12-week study end point, whichever came first. Subjects with transmetatarsal amputations had their foot measured at a point 1 cm proximal to the residuum of the amputation.

All patients received either a functioning or placebo pulsatile pneumatic foot compression system (Kinetic Concepts Inc, San Antonio, Tex). This system includes a wrap that goes around the foot and a pneumatic pump that intermittently fires bursts of air through tubing to the wrap. The wrap contains a bladder that is rapidly inflated to approximately 160 mm Hg for 2 seconds to empty the veins of the foot. This cycle is repeated every 20 seconds. Patients and investigators were blinded to the functionality of the device. The device was applied by a medical technician who was the only member of the investigational team aware of the device's status. This individual did not partake in the discussion or analysis of the data. We randomized patients by means of a computerized table. Since all patients who participated in this project had moderate to severe peripheral sensory neuropathy, they were not generally able to feel whether they were receiving substantial compression therapy. In the placebo device, all lights, audible alerts, and programming indicators were functional and identical to and indistinguishable from those of the active device. The placebo foot wrap that was applied to the foot, however, was fenestrated so as not to inflate and impart compression. Both active and placebo units were programmed to download the total time that they were used, and this was checked on a weekly basis to monitor compliance. The enrolling technician instructed the patient and/or the patient's caregivers as to appropriate use of the device, which consisted of approximately 8 hours of use per day.

Wounds were measured by means of a computerized planimetric video wound measurement system (ViRGE Videometer, Winnipeg, Manitoba). All were graded by the University of Texas Diabetic Wound Classification System. Weekly wound care was standardized and consisted of thorough sharp debridement of the site with a scalpel blade to remove all wound debris, necrotic tissue, fibrin, eschar, and nonviable tissue. Undermining of the wound was eliminated as much as possible by trimming or clipping the overhanging edge. The wound was dressed with a standard moist gauze dressing. Patients were instructed to cleanse their wound twice a day with sterile isotonic sodium chloride solution and then blot the wound dry while using disposable gloves. Wound care instructions were reviewed at every visit to ensure patient compliance with the study protocol. On discharge from the hospital, all patients were off-loaded in a removable cast walker (DH Pressure Relief Walker, Center Orthopaedics, Camarillo, Calif) to reduce pressure over the wound site. Patients were, as is common practice, instructed to limit weight bearing on the affected limb even with the off-loading device in place.

Outcomes were evaluated weekly up to the 12-week study end point. These included proportion of complete wound healing and compliance. Wounds were considered healed when complete epithelialization occurred. Compliance was defined as use of the device for 50 or more hours weekly. This was monitored by downloading the period of time the devices were used weekly. We used a χ² test with odds ratio and 95% confidence interval to compare all dichotomous variables in this study. This included the proportion of patients whose wounds healed in each treatment arm. In addition, we used log-rank Kaplan-Meier survival analysis to compare time to healing between both treatment groups. Furthermore, we used a χ² test for trend (χ² trend) to assess the prevalence of healing on the basis of compliance with edema-reduction therapy. We used a t test for independent samples to compare continuous variables in both groups. We prospectively defined the course of study as an 18-month period of enrollment or the enrollment of 100 wounds, whichever came first.

A total of 18 patients did not complete the study and were therefore not assessed in the final analysis. Eleven of these patients complained of pain during use of the device (5 in the active group and 6 in the placebo group). Five subjects did not return for their initial follow-up appointments after hospital discharge and refused to continue (1 in the active group and 4 in the placebo group). Two patients (1 in the active group and 1 in the placebo group) developed dorsal irritation thought to be related to the device and were therefore dropped from the study. Thus, a total of 97 subjects (52 in the active group and 45 in the placebo group) completed the study.

or even reversing the normal wound-healing process. Any effort to decrease interstitial edema may decrease this postcapillary oncotastic pressure, provide a more stable conduit for nutrient flow, and therefore promote more rapid healing. However, if such a patient is unable to maximize his or her physiological capacity to peruse the lower extremity, then certainly the ability of a large foot wound to heal will be compromised.

At the present time, pneumatic foot compression devices are indicated for prophylaxis of deep venous thrombosis after orthopedic trauma, hip and knee arthroplasties, and numerous other types of surgery where patients...
are at high risk for venous thrombosis.\textsuperscript{6-10} The mechanism of action of pneumatic pedal compression devices appears to be at least 3-fold: enhancing fibrinolysis and venous outflow, and thereby reducing edema.\textsuperscript{7,11-13}

Through the use of aggressive edema reduction by a variety of means, we have improved the outcome of many lower-extremity wounds after debridement of limb-threatening infections. However, we are unaware of any reports in the medical literature discussing the potential clinical utility of this modality. Therefore, the purpose of this randomized, double-blind study was to evaluate the proportion of healing of foot infections in subjects with diabetes undergoing aggressive edema reduction with the use of intermittent pneumatic foot compression after foot-level debridement.

**RESULTS**

There was no significant difference between any of the recorded descriptive characteristics of the patient populations in the active or placebo groups (Table 1 and Table 2). Overall, as expected, larger wounds (\(>5.0 \text{ cm}^2\)) were less likely to heal than were smaller wounds (16 [47\%] of 34 vs 46 [73\%] of 63; \(\chi^2 = 4.0; P < .05;\) odds ratio, 2.4; 95\% confidence interval, 1.0-5.8). Whereas there was no significant difference in foot circumference on initial enrollment between active and placebo groups (28.3 ± 3.2 cm vs 28.1 ± 4.3 cm; \(P = .93\)), the active group appeared to have a significantly greater degree of edema reduction as gauged by foot circumference at the study end point (23.8 ± 1.9 cm vs 25.7 ± 2.7 cm; \(P < .001\)).

There was a significantly higher proportion of healing in the active group than in the placebo group (39 of [75\%] 52 patients vs 23 [51\%] of 45; \(\chi^2 = 6.0; P < .02;\) odds ratio, 2.9; 95\% confidence interval, 1.2-6.8). There was also a significant difference in survival distribution (time to healing) between groups (Kaplan-Meier log-rank = 4.2; \(P = .04\)) (Figure 2).

Interestingly, there was not an appreciable difference in wound size, time of use, or proportion of noncompliance (<50 hours of use per week) between groups with the numbers available.

In the placebo group, the same number of patients achieved wound healing whether they were characterized as compliant or noncompliant (\(P = .10\)). In patients receiving active units, more patients healed in the compliant subgroup than in the noncompliant subgroup (\(P = .03\)). When compared as a whole, there was a significant trend toward an increased prevalence of healing progressing from placebo-noncompliant to placebo-compliant to active-noncompliant to active-compliant.

![Figure 1. Trial profile.](image)

![Figure 2. Kaplan-Meier survival analysis for edema reduction (Kaplan-Meier log rank = 4.2; \(P = .04\)).](image)

### Table 1. Descriptive Characteristics\textsuperscript{*}

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Active ((n = 52))</th>
<th>Placebo ((n = 45))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>49.3 ± 10.3</td>
<td>51.8 ± 10.2</td>
</tr>
<tr>
<td>Sex, No. (%) M</td>
<td>38 (73)</td>
<td>34 (76)</td>
</tr>
<tr>
<td>Ethnicity, No. (%)†</td>
<td>45 (87)</td>
<td>35 (78)</td>
</tr>
<tr>
<td>MA</td>
<td>6 (12)</td>
<td>8 (18)</td>
</tr>
<tr>
<td>W</td>
<td>1 (2)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Duration of diabetes, y</td>
<td>12.5 ± 8.7</td>
<td>12.7 ± 11.3</td>
</tr>
<tr>
<td>Glycosylated hemoglobin level, %</td>
<td>9.7 ± 1.9</td>
<td>9.2 ± 2.5</td>
</tr>
<tr>
<td>Vibration perception threshold, V</td>
<td>39.1 ± 11.3</td>
<td>41.9 ± 9.8</td>
</tr>
<tr>
<td>Transcutaneous oxygen tension, mm Hg</td>
<td>42.0 ± 13.9</td>
<td>50.8 ± 23.2</td>
</tr>
<tr>
<td>Wound size, cm²</td>
<td>6.7 ± 9.6</td>
<td>7.5 ± 15.7</td>
</tr>
</tbody>
</table>

\textsuperscript{*}Unless otherwise indicated, data are given as mean ± SD. MA indicates Mexican American; W, non-Hispanic white; and AA, African American.

†Because of rounding, percentages may not all total 100.

### Table 2. Location of Incision, Drainage, and Debridement of Diabetic Foot Infection

<table>
<thead>
<tr>
<th>Treatment Group, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
</tr>
<tr>
<td>Hallux and first ray</td>
</tr>
<tr>
<td>Lesser digits and rays</td>
</tr>
<tr>
<td>Midfoot</td>
</tr>
<tr>
<td>Hindfoot</td>
</tr>
</tbody>
</table>

(16 [47\%] of 34 vs 46 [73\%] of 63; \(\chi^2 = 4.0; P < .05;\) odds ratio, 2.4; 95\% confidence interval, 1.0-5.8). Whereas there was no significant difference in foot circumference on initial enrollment between active and placebo groups (28.3 ± 3.2 cm vs 28.1 ± 4.3 cm; \(P = .93\)), the active group appeared to have a significantly greater degree of edema reduction as gauged by foot circumference at the study end point (23.8 ± 1.9 cm vs 25.7 ± 2.7 cm; \(P < .001\)).
Debris is restricted by excessive edema around the capillary bed. These fibrin cuffs might prevent the passage of oxygen into the tissue. The impaired wound healing in the presence of edema has also been ascribed to plugging of capillaries by leukocytes. The white blood cell activation can be induced by an inflammatory stimulus or in conditions of impaired blood flow in the lower extremity. This might be an important factor in surgery in persons with diabetes, since vasculopathy is quite prevalent in this population. It may therefore be inferred that any residual edema may further complicate an already compromised wound healing course.

Since its first descriptions in 1869 and numerous times since then, the venous foot pump has been recognized as a potentially powerful and clinically relevant physiological entity. In addition to the aforementioned relatively straightforward effects on mitigation of edema and stasis, it has been established that rapid pressure gradients increase blood flow into the limb. This has been thought to be secondary to diminished venous-side resistance. In addition to increased macro-vascular arterial inflow, increased microcirculatory vasodilation may also be promoted through intermittent foot compression. This is mediated by endothelium-derived relaxing factor (nitric oxide). Tangelder and coworkers reported that, in response to pressure changes, nitric oxide is produced by postcapillary venules; the nitric oxide then diffuses locally to effect vasodilation in neighboring capillary beds. On the basis of this process, it may be inferred that intermittent foot compression delivered in the immediate perioperative period may be beneficial to both functional microvascular and macrovascular flow in subjects such as those with diabetes, who are at high risk for vascular impairment and subsequent wound failure.

In conclusion, this study indicates that edema reduction accomplished by way of intermittent pulsatile foot compression may be a useful adjunct in improving the prevalence of wound healing after incision and drainage of foot infections in persons with diabetes. We believe that consistent attention to edema control over a prolonged period until healing coupled with appropriate patient education and attentive local wound care may ultimately play a role in curtailing the unnecessarily high prevalence of high-level extremity amputations in persons with diabetes mellitus.

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