

Variability in Activity May Precede Diabetic Foot Ulceration

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OBJECTIVE — To evaluate the role of activity in the development of neuropathic foot ulceration in individuals with diabetes.

RESEARCH DESIGN AND METHODS — We evaluated the first 100 consecutive individuals with diabetes (95.0% male, aged 68.5 ± 10.0 years with concomitant neuropathy, deformity, and/or a history of lower-extremity ulceration/partial foot amputation) enrolled in an ongoing prospective longitudinal activity study. Subjects used a high-capacity continuous computerized activity monitor. Data were collected continuously over a minimum of 25 weeks (or until ulceration) with daily activity units expressed as means \pm SD.

RESULTS — Eight subjects ulcerated during the evaluation period of 37.1 ± 12.3 weeks. The average daily activity was significantly lower in individuals who ulcerated compared with individuals who did not ulcerate (809.0 ± 612.2 vs. $1,394.5 \pm 868.5$, $P = 0.03$). Furthermore, there was a large difference in variability between groups. The coefficient of variation was significantly greater in the ulceration group compared with the no ulceration group (96.4 ± 50.3 vs. $44.7 \pm 15.4\%$, $P = 0.0001$). In the 2 weeks preceding the ulcerative event, the coefficient of variation increased even further ($115.4 \pm 43.0\%$, $P = 0.02$), but there was no significant difference in average daily activity during that period ($P = 0.5$).

CONCLUSIONS — The results of this study suggest that individuals with diabetes who develop ulceration may actually have a lower overall activity than their counterparts with no ulceration, but the quality of that activity may be more variable. Perhaps modulating the “peaks and valleys” of activity in this population through some form of feedback might prove to reduce risk for ulceration in this very-high-risk population.

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D iabetic foot ulcers and related maladies continue to be among the most common serious diabetes-related sequelae, affecting some 68 per 1,000 individuals with diabetes per annum in the U.S. (1,2). The pathologic process leading to the vast majority of foot ulcerations is a consistent one. In the face of neuropathy, pressure multiplied by repetitive moderate stress leads to inflam-

mation and subsequent autolysis of soft tissue overlying bony prominences (3,4).

Prevention of diabetic foot ulcerations has mainly involved modulating pressure. This has been attempted externally through the use of protective shoes and insoles (5–7) or internally through surgery or physical therapy (8–10). Attention to the other factor at play, namely repetitive stress (daily activity), has only

recently been given attention. This is largely because measuring daily activity has been rather problematic before the recent use of advanced pedometers/accelerometer technology. These newer technologies have begun to bear fruit, however. Using activity monitoring systems, it has been suggested that much of the activity of individuals at the highest risk for ulceration or reulceration is performed in the home (without wearing their protective shoes) (11) and that individuals with active ulcers may only use their pressure off-loading devices for one-third of daily activity (12).

If pressure and activity combine to produce many neuropathic diabetic foot wounds, reason would dictate that among high-risk patients, those who were most active would develop ulceration. To our knowledge, there are no long-term studies evaluating this hypothesis. Therefore, the purpose of this longitudinal observational study was to evaluate whether individuals who develop diabetes-related neuropathic foot ulceration had different activity profiles than individuals at similar risk who do not develop ulceration.

RESEARCH DESIGN AND METHODS

— We evaluated the first 100 consecutive individuals with diabetes and concomitant neuropathy, deformity, and/or a history of lower-extremity ulceration/partial foot amputation enrolled in an ongoing prospective longitudinal activity study. Neuropathy (loss of protective sensation) was defined as a vibration perception threshold >25 V using the VPT meter (Xilas Medical, San Antonio, TX) (13,14). All patients received a standardized diabetic foot evaluation and were allocated physician-approved footwear at the time of enrollment. This footwear included over-the-counter comfort shoes with pressure-relieving insoles or prescriptive depth inlay shoes, depending on the patient's specific foot characteristics as determined by the clinician during the initial and subsequent examinations (15). Patients were classified using the International Diabetes Federation Working Group on the Diabetic Foot Risk Classification and were either category 2 (neu-

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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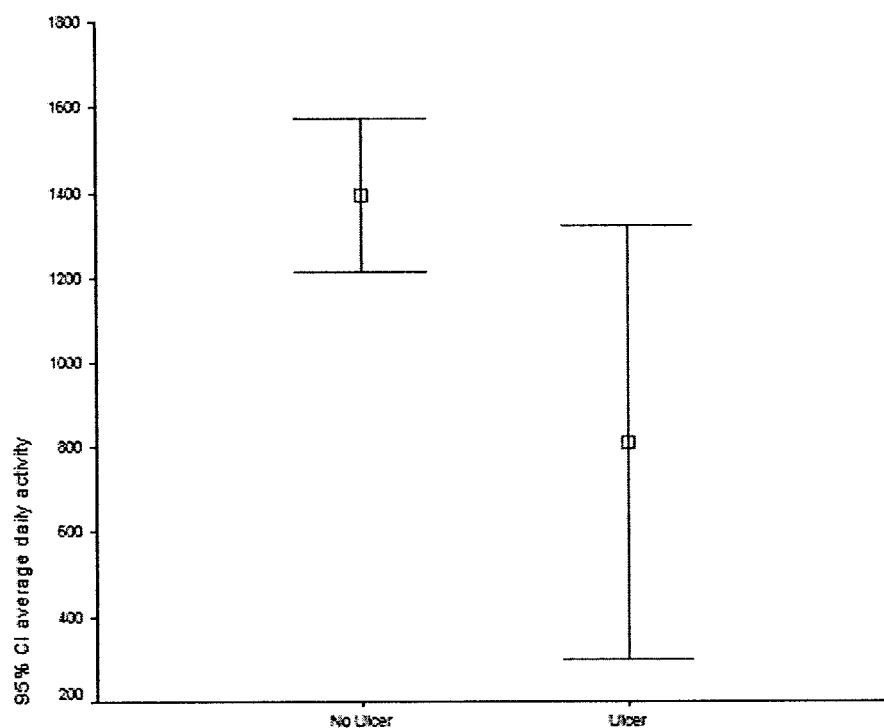


Figure 1—Activity of individuals who developed ulcers compared with those who did not. Data measured in activity units. Bars refer to SD. $P < 0.05$ using nonparametric test.

ropathy/deformity) or category 3 (history of previous ulcer) (16). Patients with concomitant peripheral vascular disease (as defined by nonpalpable pulses and/or an ankle brachial systolic pressure index < 0.80) were excluded from enrollment.

All patients were dispensed a high-capacity computerized accelerometer/pedometer (Biotrainer Pro; IM Systems, Boston, MA). This waist-mounted device is designed to measure the number of steps taken over a period of time. It also records the time of day each step occurred, allowing the identification of clusters of activity. It has an ~ 100 -day memory capacity. The mechanism in the device has been previously calculated to be 96% for brisk walking, 92% for slow walking, 96% for ascending stairs, and 98% for descending stairs (17). This device is the approximate size and weight of a normal waist-mounted step counter. All devices were calibrated by a clinician, who instructed the enrolled participants as to appropriate operation of the devices. The patient was instructed to wear the device at all times during the day and night during the course of the trial. They were followed every 2–3 months for regular preventative foot care visits, at which time the data collected from the devices were

downloaded and the batteries were changed. These downloaded data were

then recorded as activity per day. Patients were followed in this manner for a minimum of 25 weeks (37.1 ± 12.3 weeks) or until ulceration.

The coefficient of variation (CV) was calculated for each subject as the SD of daily activity divided by the mean daily activity and multiplied by 100 to express as a percentage. For analysis of both daily activity and the CV of that activity between individuals who developed ulcers during the study period compared with those who did not, we used a Mann-Whitney U test. For those who developed an ulcer, we evaluated both the difference in activity and the CV of that activity and compared the entire study period to the final 2 weeks preceding ulceration. This was evaluated using a Wilcoxon's signed-rank test for paired samples. All data were expressed as means \pm SD (18).

RESULTS— Of the subjects enrolled, 8% ulcerated during the mean 37.1 ± 12.3 -week follow-up period. All ulcers occurred in the subjects' plantar forefoot. Average daily activity was significantly lower in individuals who ulcerated compared with those who did not (809.0 ± 612.2 vs. $1,394.5 \pm 868.5$, $P = 0.03$) (Fig. 1). Interestingly, there was a large

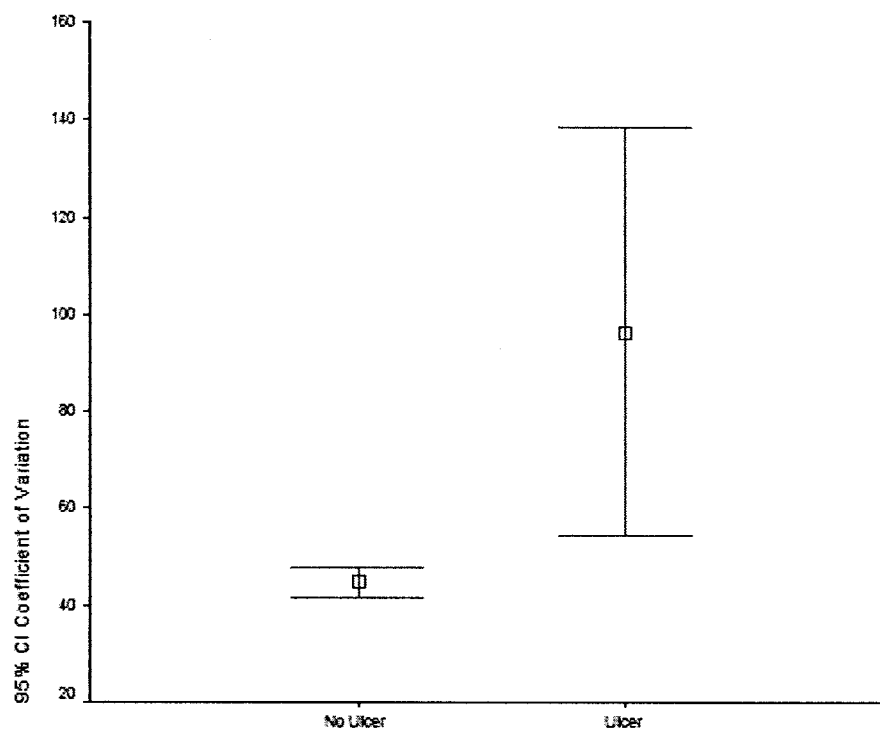


Figure 2—Variability of activity between groups. Bars refer to SD. $P < 0.05$ using nonparametric test.

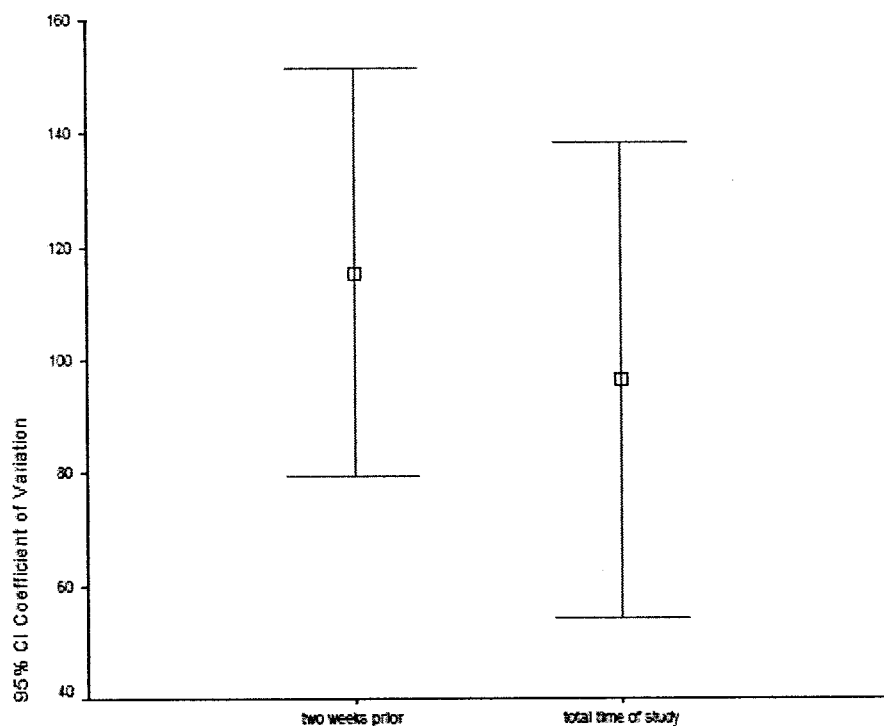


Figure 3—Variability of activity immediately preceding ulceration. Individuals who ulcerated had a higher degree of activity variability in the 2 weeks immediately preceding neuropathic diabetic foot ulceration. Bars refer to SD. $P < 0.05$ using paired nonparametric test.

difference in variability between groups. The CV was significantly greater in the ulceration compared with the no ulceration group (96.4 ± 50.3 vs. $44.7 \pm 15.4\%$, $P = 0.0001$) (Fig. 2). Furthermore, in the 2 weeks preceding the ulcerative event, the CV increased even further ($115.4 \pm 43.0\%$, $P = 0.02$), but there was not a significant difference in average daily activity during that period ($P = 0.5$) (Fig. 3).

We also tested for potential differences between individuals in foot-risk category 2 vs. 3 (Table 1). Foot-risk category 2 refers to individuals with neurop-

athy and deformity but no history of ulceration. Foot-risk category 3 refers to individuals who have a history of foot ulceration. In this study, there was not a significant difference in either activity ($P = 0.9$) or CV ($P = 0.2$) in these two groups. Individuals with a previous history of ulceration (but who did not ulcerate in the study period) were more active than those who developed an ulcer ($1,515.7 \pm 1,083.4$ vs. 809.0 ± 612.2 , $P = 0.05$). Patients who did not ulcerate also had a lower CV compared with their counterparts (45.7 ± 16.2 vs. $96.4 \pm 50.3\%$, $P = 0.001$).

CONCLUSIONS— The results of this study suggest that individuals with diabetes who develop ulceration may actually have a lower overall daily activity than their nonulcerated counterparts, but the quality of that activity may be more variable. This variability may become even more acute in the days leading up to frank skin breakdown. To our knowledge, this is the first study in the medical literature evaluating these specific criteria.

We were surprised to find that individuals developing ulcers were apparently less active than those who did not

suffer ulceration. Many investigators, including ourselves, have long postulated that the formula for neuropathic diabetic foot ulceration included pressure \times cycles of repetitive stress (3,11,12,19–21). While this may still be the case, the data in the present study seem to suggest that there may also be a temporal component to the formula (as to when the stress is applied). In other words, the pattern of activity of individuals who ulcerated in the present study appeared to be characterized by periods of inactivity punctuated by relatively sudden pulses of activity taken over a short time frame.

Perhaps the skin in individuals at highest risk is less able to withstand repetitive stress. Furthermore, perhaps that skin, if not stressed consistently, may be at even higher risk for damage. Matrix reorganization of skin and soft tissue structures have been shown to be compromised by nonenzymatic glycosylation of tissue proteins (22). Attempting to quantify this characteristic, Klaesner et al. (23), using a novel force displacement apparatus, reported that plantar tissues were indeed significantly stiffer in individuals with diabetes, peripheral neuropathy, and a history of foot ulceration than in their nonneuropathic counterparts. In an elegant follow-up study to Klaesner et al., Maluf and Mueller (24) evaluated activity and plantar pressure over a 7-day period in 10 individuals with a history of ulceration. Using a product of pressure multiplied by activity, they reported significantly less daily activity and stress (46 and 41%, respectively) to the plantar foot in individuals with recent ulceration history than in individuals without a history of ulceration. While they were not able to assess the variability of that activity over an extended period of time or actually capture activity leading up to an ulcerative event, their results seem to closely correlate with those of the present study. They concluded that “changes in weight-bearing activity following plantar tissue injury in patients with diabetes may influence plantar tissue adaptation and the risk of ulcer recurrence.” Interestingly, our study did not show a difference in activity over the several-month monitoring period between individuals at moderate risk (neuropathy/deformity) and high risk (history of ulceration). However, both of these groups were more active and less variable in their activity compared with subjects who ulcerated during the study.

Table 1—Descriptive characteristics

	Study population
n	100
Age (years)	68.5 ± 10.0
Sex (% male)	95.0
Duration of diabetes (years)	13.7 ± 9.3
Foot risk category 2 vs. 3 (%)	68/32
BMI (kg/m^2)	30.0 ± 3.0

Data are means \pm SD.

While this might imply that variability of activity may show promise as a potential predictive factor in predicting diabetic foot ulceration, further work is clearly necessary to confirm or refute this initial finding.

We believe that the trends reported in both our study and that of Maluf and Mueller may point to a unique opportunity for proactive preventative intervention. Perhaps modulating the “peaks and valleys” of activity in this population through some form of feedback might prove to reduce the risk for ulceration in this very-high-risk population. This may be accomplished through intelligent activity monitors designed to identify deleterious variations in activity and to notify the patient and/or his/her provider. It also could help train the patient into a healthy pattern of safe, consistent activity that could balance the clearly positive cardiovascular and metabolic benefits of walking (25), while mitigating the dangers of excessive weight bearing in that same high-risk population.

A shortcoming of this study may be our failure to evaluate patient compliance with preventive foot care, such as self-inspection and the use of protective shoes and insoles. In general, many studies tend to take a myopic view of risk factors and focus on physiology without considering professional or self-care practices as a risk factor or a means to modify, reduce, or eliminate risk factors. Therapeutic shoes and insoles are a prime example of an intervention strategy that can substantially reduce the risk of reulceration. The patients who developed ulceration may be taking more of their daily steps at home when they “feel safe” not using special, protective shoes (11,26). There are a number of studies that demonstrate significant pressure reduction on the sole of the foot with padded insoles and shoes (15,27–29). In clinical practice, this type of approach often shows a >50% reduction in reulceration among high-risk patients (5,6,30,31) While patients in this study all received physician-approved therapeutic/comfort footwear, there was no monitoring for use or adherence to the protective regime.

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