Full-Thickness Leg Ulcers: Patient Demographics and Predictors of Healing

Lia van Rijswijk, RN, ET, and the Multi-Center Leg Ulcer Study Group*
Newtown, Pennsylvania

Background. Despite increased knowledge about the immediate and underlying causes of chronic leg ulcers, their management remains a challenge. Some ulcers rapidly respond to treatment whereas others do not, and the decision to reassess the patient and treatment modality is usually based on the clinician's own experience.

Methods. Following diagnosis of the underlying cause of leg ulcers, 181 patients were screened. The use of a hydrocolloid dressing (DuoDERM) was evaluated in the treatment of 61 patients with 72 full-thickness ulcers. Patient characteristics associated with deep wounds as well as patient and wound characteristics predictive of the extent of healing and time required for healing were identified.

Results. Patients with full-thickness ulcers were more likely to be overweight ($P < .001$) and not fully mo-

bile ($P = .016$). During a mean treatment time of 56 days, 54% of the full-thickness ulcers healed. Ulcers were less likely to heal if the patients were men ($P = .02$) or had diabetes mellitus ($P < .003$). A >30% reduction in ulcer area after 2 weeks of treatment was a predictor of both treatment outcome ($P = .016$) and time required for healing ($P = .004$). Odor at baseline and advanced age also were associated with increased time required for healing ($P = .005$ and .017, respectively).

Conclusions. Noninvasive clinical assessments can aid the clinician in predicting treatment outcome and may facilitate the decision to change therapy and evaluate treatment compliance.

Key words. Leg ulcers; predictive value of tests; occlusive dressing; wound healing. (*J Fam Pract 1993; 36:625-632*)

Chronic leg ulcers disrupt the lives of 500,000 to 700,000 patients in the United States and remain a frustrating problem for many clinicians.[1,2] Their failure to heal can be related to the underlying disease, lack of patient compliance, and less-than-optimal treatment. Even when a correct diagnosis has been made and the appropriate treatment instituted, many ulcers require months of treatment. The decision to reassess the patient's condition and change treatment is often based on the individual clinician's experience.[3,4]

Despite the large variety of treatment modalities available today, the average healing rate for leg ulcers is largely unknown, in part because many of the variables that influence healing are unknown or cannot be adequately controlled.[5] The purpose of this study was to identify demographic differences between patients with full-thickness ulcers and patients with partial-thickness ulcers, to assess the response of full-thickness leg ulcers to one change in treatment regimen (dressing type), to evaluate the rate of healing, and to identify patient and wound characteristics associated with a better response to treatment. To reduce the number of variables that might influence the healing rate, only patients who had ulcers with full thickness dermal involvement were enrolled.

ISSN 0094-3509

Methods

Patient Recruitment

After approval to conduct the study was obtained from ethics committees or institutional review boards at each institution, eight clinics screened 181 patients with 221 ulcers. Those with full-thickness leg ulcers were evaluated over a period of 26 months. Informed consent was obtained from all study patients.

The following baseline patient characteristics were obtained: age, sex, weight, weight in relation to height (body build), existence of diabetes mellitus, and number of ulcers. Patients' general health condition, mobility, activity level, and overall skin condition were assessed on 3-point rating scales. General health was rated as excellent (no concomitant disease or condition), good (controlled underlying disease or condition), or poor. Mobility was defined as full, restricted, or very restricted, and activity level was assessed as mostly ambulatory, ambulatory part of the time, or immobile. Overall skin condition was rated as healthy (well hydrated, good turgor, no disease), poor (poor turgor, dry skin), or dehydrated/rashes (marked dehydration or concomitant skin condition). Wound depth was assessed as superficial, partial-thickness (some dermal involvement), or full-thickness (dermal involvement down to but not exposing or involving bone or tendon). The underlying cause of the ulcer (venous stasis ulceration, arterial disease, mixed venous and arterial, trauma, or systemic disease) was established using standard clinical assessment as well as Doppler flow and laboratory studies.[3,4]

Baseline assessments of the full-thickness wounds included determining how long the ulcer had existed (history), which treatments were used, and, if possible, what clinical response to previous treatment was observed. Since not all ulcers had been measured regularly before the start of the study, a 5-point clinical assessment rating scale was used to record response to previous treatment (deteriorated, no change, mild or moderate improvement, marked improvement, or healed). Finally, the location of the ulcer was recorded.

Baseline assessments that were made each time the dressing was changed included: assessment of ulcer depth, presence of necrosis and granulation tissue, condition of the ulcer margin, odor emanating from the wound, and amount of drainage. Pain was assessed on a 3-point rating scale (no pain, some pain, very painful). In addition, the maximum wound diameter was recorded and ulcers were traced on metric paper to quantify reduction in ulcer size and reepithelialization.

Treatment

The ulcers were cleansed with 3% hydrogen peroxide and rinsed with a saline solution. The surrounding skin was dried, and the hydrocolloid dressing DuoDERM Hydroactive Dressing (ConvaTec, A Bristol-Myers Squibb Company, Princeton, NJ) was applied, extending at least 1.5 in. beyond the ulcer margin. Concomitant treatments (bed rest, elevation, and compression) were used only if used before study enrollment. The dressing was left in place until nonadherent or for a maximum of 5 days. Patients were studied until healed or for a period of 2 months. Use of the dressing could be extended for an additional 4 months, provided that the ulcer's response to treatment was encouraging. At the final evaluation, the investigator was asked to rate treatment effectiveness, using the same 5-point rating scale used to evaluate response to previous treatment, and the overall level of patient comfort during the study.

Statistical Analysis

All patients who were enrolled in the study were included in the data analysis. A 40-10 Optomax Image Analyser (Optomax Inc, Hollis, NH) was used to measure the ulcer areas from the tracings to quantify reduction in ulcer diameter. Tracings made on the first day of the study served as the baseline. Subsequent tracings were made weekly. If more than one evaluation was made during the week, the last measurement was used. To compensate for initial differences in wound size, the following formula was used to calculate percent reduction from baseline:

$$\% \text{ reduction} = 100 \times (\text{baseline} - \text{current size}) / \text{baseline}$$

Measurements of ulcers in patients with more than one ulcer were averaged and classified as healed only if all ulcers were healed. Consequently, the number of patients with healed ulcers for all analyses derived from the tracings was lowered. To compare means among patients with healed and unhealed ulcers, t tests were used. The chi-square test for independence and the Mantel-Haenszel test for trend were used to compare qualitative characteristics and ordered qualitative characteristics of the healed and unhealed patients. To adjust for possible confounding caused by associations among the various prognostic factors, a stepwise logistic regression analysis was performed to analyze the proportion of patients healed. The distribution of healing times (ie, the percentiles) was estimated using the Kaplan-Meier product limit estimators for patients grouped by clinical, wound, and demographic characteristics. The Kaplan-Meier method of estimating healing curves and the logrank test

can be used even though not all patients had healed when the study was completed.[6] The time taken for ulcers to heal 80% and 50%, as well as time required for 100% healing were analyzed. Cox proportional hazards model, including all prognostic factors for time required for 100% healing, was used to assess the independent predictive value of each prognostic factor of time required for healing.[7] All tests were performed at the .05 level of significance using the Statistical Analysis System (SAS Institute, Cary, NC).

Results

Patient Characteristics

Of the 181 patients screened, 61 patients with 72 full-thickness leg ulcers were enrolled in the study. The other 120 patients had 149 partial-thickness ulcers. Although these patients were not enrolled in the study for treatment, patient characteristics were compared with those of the patients with full-thickness leg ulcers to identify any significant differences between the two groups. The mean age of the patients with partial-thickness leg ulcers was 67 years (±14.4 SD, SE 1.33) compared with 66 years (±14.6 SD, SE 1.87) for patients with full-thickness leg ulcers. In both groups women outnumbered men 2:1. Most patients (99 [83%] of those with partial-thickness ulcers and 48 [79%] of those with full thickness) had only one ulcer. The mean weight of patients with partial-thickness ulcers was similar to the weight of patients with full-thickness ulcers (69.8 kg [±17.8 SD] and 73.2 kg [±17.6 SD], respectively). However, 83 (69%) patients with partial-thickness leg ulcers were of normal weight in relation to height (body build), and 34 (28%) patients were overweight, compared with 28 (46%) patients with full-thickness leg ulcers who were of normal weight and 29 (48%) who were overweight (P = .01). No difference between the patient groups with respect to diabetes mellitus was observed. Twelve patients (20%) with full-thickness ulcers and 27 (23%) with partial-thickness ulcers had diabetes. Excellent general health was reported for 10% of patients with full-thickness leg ulcers compared with 20% of patients with partial-thickness ulcers (P = .004). Those with partial-thickness ulcers were more likely than those with full-thickness ulcers to have unrestricted mobility (67% and 43%, respectively, P = .01). Also, 78% of patients with shallow ulcers enjoyed unrestricted activity compared with 59% of patients with deep ulcers (P = .05). Finally, dehydrated skin and rashes, were reported in 54 patients, 46 (38%) of whom had shallow ulcers and 8 (13%) of whom had deep ulcers (P = .001). Stepwise logistic

Table 1. Characteristics of Patients with Full-Thickness vs Partial-Thickness Leg Ulcers, by Stepwise Logistic Regression Analysis

Characteristic	Odds Ratio (95% CI)	P Value*
Skin dehydrated or with rashes	0.188 (0.062–0.571)	.003
Overweight	3.43 (1.672–7.046)	.001
Restricted mobility	2.54 (1.188–5.456)	.016

*Likelihood ratio statistic = 30.804, P < .001.
CI denotes confidence interval.

regression analysis showed that patients with full-thickness ulcers were less likely to have dehydrated skin and rashes (P = .003), but were 3.4 times more likely to be overweight (P < .001). Also, patients with deep ulcers were 2.5 times more likely to have restricted mobility (P = .016) (Table 1).

Full-Thickness Ulcer History

Of the 61 patients with full-thickness ulcers, 26 (43%) had ulcers that had existed for less than 6 months, and 17 (28%) had ulcers that had existed for more than 2 years. In the majority of ulcers (41 [67%]), the underlying cause was venous insufficiency. Eleven ulcers were diagnosed as having a mixed venous and ischemic origin, and three were directly related to trauma. Six patients with ulcers secondary to systemic disorders (cryoglobulinemia, sickle cell anemia, and rheumatoid vasculitis) were also enrolled in the study.

A wide variety of cleansing agents (eg, saline, povidine iodine solution, absorbent beads), debridement techniques (eg, surgical, wet-to-dry, enzymes), dressings (eg, gauze, nonadherent gauze, zinc paste bandages) and supportive measures (eg, compression bandages) had been used before patients were enrolled in the study. Compression bandages had been used as part of the previous treatment regimen in 31 (75%) of the ulcers that were secondary to venous insufficiency. Results of previous treatments were rated as deterioration in 33 (54%) and no change in 14 (23%). Previous treatments had resulted in marked improvement in one ulcer.

Response to Treatment

During a median study treatment time of 47 days (mean 56.2, range 5 to 254), 39 full-thickness ulcers (54%) healed and 11 (15%) were rated as markedly improved based on the same 5-point rating scale that was used at study enrollment. The mean healing time for ulcers that healed was 54 days. Eleven ulcers healed within 30 days following study enrollment. Sixteen healed between 31 and 60 days, and the remaining five ulcers took >60 days to heal. Four patients were discontinued from the study

because their ulcers responded poorly to treatment, including one instance of contact dermatitis, one case of maceration of the surrounding skin as a result of prolonged contact with wound exudate, and two instances of an increase in wound size. Study discontinuation did not occur for reason of a clinical infection in any of the 72 wounds studied.

Subsequent analysis of baseline patient characteristics showed that patient sex significantly influenced treatment outcome: men were less likely to heal than women ($P = .007$). The mean body weight of patients whose ulcers did not heal was 6 kg higher than the mean weight of patients whose ulcers did heal ($P = .03$) (Table 2). Patients with ulcers secondary to a systemic disease were also less likely to heal than patients who had venous, mixed venous and ischemic, or traumatic ulcers ($P = .02$). Diabetes was also a risk factor. Full-thickness ulcers healed in only 3 of the 12 patients with diabetes, whereas they healed in 28 (60%) of 47 patients without diabetes ($P = .03$). A list of all wound assessments at baseline as a function of treatment outcome is given in Table 3. Neither initial ulcer size nor the presence or absence of granulation or necrotic tissue influenced treatment outcome. However, ulcers of patients with a baseline assessment of no odor emanating from the wound were more likely to heal compared with ulcers that exhibited strong odor at baseline assessment ($P = .02$). Also, ulcers with large amounts (> 5 mL/day) of wound exudate at baseline were less likely to heal ($P = .009$). Using the ulcer tracings, the mean area at baseline for all ulcers combined was 9.72 cm^2 (SD $\pm$ 11.62 cm^2). Although a trend was observed between baseline area and treatment outcome, the difference was not significant. Nine of the 27 largest ulcers (>13.3 cm^2) did not heal, whereas 4 did ($P = .2$).

During the study, the mean percent reduction in ulcer area was 57%. Stepwise logistic regression analysis showed that patient sex, diabetes, and percent of reduction in area after 2 weeks were independent predictors of treatment outcome. Women were 10 times more likely to heal than men ($P = .03$), and patients without diabetes were 9 times more likely to heal ($P = .02$). Finally, patients who exhibited at least a 30% reduction in ulcer area were twice as likely to heal ($P = .01$) (Table 4).

Time Required for Healing

The median time for ulcers to reduce in area by 50% was 31 days (mean 36.0, SE 3.1). The median times to reach 80% and 100% healing were 40 days (mean 51, SE 5.3) and 64 days (mean 83, SE 10.8), respectively (Figure 1). Healing time was significantly increased if moderate or strong odor was present at baseline. The median healing times (100% curve) ranged from 45 days (mean 55, SE

Table 2. Baseline Characteristics as a Function of Treatment Outcome in 61 Patients with Full-Thickness Leg Ulcers

Characteristic	Not Healed	Healed	P Value*
Age, y (mean $\pm$ SD)	67 ($\pm$ 13)	65 ($\pm$ 13)	NS
Weight, kg (mean $\pm$ SD)	76 ($\pm$ 20)	70 ($\pm$ 20)	.035
Sex, %			
Male	52	19	
Female	48	81	.007
Number of ulcers per patient, %			
1	80	87	
2	17	13	
3	3	0	NS
Diabetes, %			
Yes	32	10	
No	68	90	.032
General health condition, %			
Excellent	10	10	
Good	59	59	
Poor	31	31	NS
Leg mobility, %			
Full	35	50	
Restricted	48	41	
Very restricted	17	9	NS
Body build, %			
Normal	41	50	
Overweight	48	47	
Underweight	11	3	NS
Activity, %			
Ambulatory	55	63	
Ambulatory part time	34	34	
Immobile	11	3	NS
Overall skin condition, %			
Healthy	59	56	
Poor	24	35	
Dehydrated/rashes	17	9	NS
Ulcer etiology, %			
Venous	62	72	
Venous/ischemic	17	19	
Traumatic	0	9	
Other (systemic)	21	0	.023
Duration, %			
<6 months	39	50	
6 months–1 year	11	19	
1–2 years	14	9	
>2 years	36	22	NS
Response to previous treatments, %			
Deteriorated	45	63	
No change	24	25	
Mild/moderate improvement	31	9	
Marked improvement	0	3	NS

*Student's t test was used to calculate for age and weight; chi-square test was used for all other variables.
SD denotes standard deviation; NS, not significant.

Table 3. Baseline Wound Characteristics as a Function of Treatment Outcome in 72 Full-Thickness Leg Ulcers

Characteristic	Not Healed, %	Healed, %	P Value*
Baseline area			
0–2 cm	19	33	
2–4 cm	28	28	
>4 cm	53	39	NS
Ulcer margin			
Clean/well delineated	44	28	
Scaling	34	50	
Necrotic	22	22	NS
Granulation tissue			
Entire ulcer bed	12	8	
Some present	73	56	
None present	15	36	NS
Necrotic tissue			
None present	51	53	
Obvious	46	44	
Thick eschar	3	3	NS
Pain			
None	12	6	
Some pain	48	58	
Very painful	40	36	NS
Wound exudate			
None	0	28	
<5 mL/d	81	61	
>5 mL/d	19	11	.009
Odor			
None	58	89	
Recognizable	29	11	
Strong	13	0	.027

*Chi-square test.
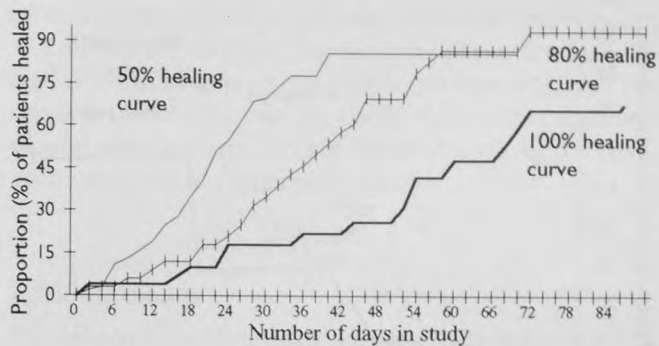NS denotes not significant.

Figure 1. Kaplan-Meier estimates of ulcer healing times: 50%, 80%, and 100% curves for all patients. Median time for 50% healing, 31 days; 80% healing, 40 days; and 100% healing, 69 days.

days, respectively, for wounds with >5 mL exudate per day ($P = .04$ for 50% healing and $P = .03$ for 80% healing). An increase in baseline area was associated with an increase in time required for healing, but the overall differences were not significant ($P = .1$). When baseline areas were grouped into two groups instead of four (<13.3 cm^2 and ≥ 13.3 cm^2), the difference in time required for healing was marginally significant ($P = .047$), with median times to 100% healing of 57 days (mean 75, SE 11.5) for the smaller ulcers and 121 days (mean 97.5, SE 13.2) for the largest ulcers. Percent reduction in ulcer size afer 2 weeks of treatment did influence the time for 50%, 80%, and 100% healing. Ulcers that exhibited a >30% reduction healed significantly faster compared with all other groups ($P = .0001$) (Figure 2). Finally, increased age was associated with an

8.2) for wounds with no odor to 163 days (mean 131.5, SE 17.6) for wounds with some odor ($P = .003$). The median healing time for patients whose ulcers had a strong odor at baseline could not be calculated because none of these ulcers healed.

Increased amounts of wound exudate at baseline also appreciably increased the time to reach 50% or 80% healing and ranged from a median of 21 and 29 days, respectively, for wounds without exudate, to 26 and 53

Table 4. Predictors of Treatment Outcome (Healed vs Not Healed) in 61 Patients with Full-Thickness Leg Ulcers

Characteristic	Odds Ratio (95% CI)	P Value
No diabetes mellitus vs diabetes mellitus	9.40 (1.414–62.51)	.003
Female vs male	10.12 (2.184–46.95)	.020
>30% reduction in ulcer area after 2 weeks*	2.37 (1.174–4.799)	.016

*Compared with all others (grouped as <−29%; −29 to <0%; 0 to 30%; and >30%).
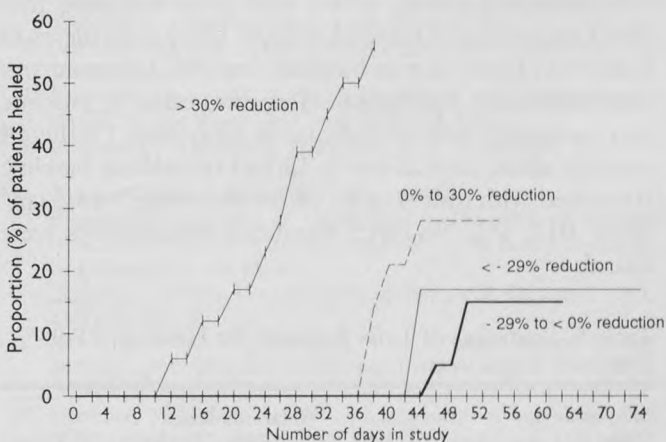CI denotes confidence interval.

Figure 2. Time until complete healing by percent reduction in ulcer area after 2 weeks of treatment. Median values: >30% reduction, 37 days; 0 to 30% reduction, 67 days; −29% to <0% reduction, N/A (the median time until healing could not be calculated for this group since fewer than 50% of patients healed); and <−29% reduction, 163 days ($P = .0001$, logrank statistic).

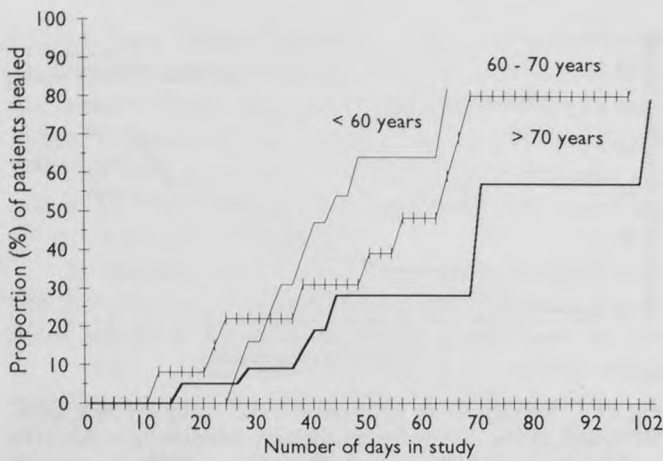Figure 3. Time until complete healing by patient age group. Median values: aged <60 years, 45 days; aged 60 to 70 years, 64 days; and aged >70 years, 71 days ($P = .04$, logrank statistic).

increase in time required for healing. Ulcers in patients over 70 years of age took longer to heal than patients who were younger. This difference was also marginally significant ($P = .047$) (Figure 3).

Based on the stepwise Cox proportional hazards models, the best combination of predictor variables for healing time were young age, absence of odor at baseline, and percent reduction in ulcer area. Age >70 years reduced the likelihood of reaching 100% healing (odds ratio = 0.27) ($P < .002$), and odor at baseline was also associated with a reduction in the proportion of patients whose ulcers healed ($P = .005$). Ulcers that exhibited a >30% reduction in area after 2 weeks of treatment were 2.2 times more likely to heal ($P = .004$) (Table 5).

Cross tabulations of sex and odor indicated that ulcers in men were somewhat more likely than ulcers in women to have odor at baseline, but the difference was not statistically significant. However, odor at baseline was associated with an increase in ulcer area. Of the 14 smallest ulcers (≤ 3.25 cm^2), 13 had no odor at baseline compared with only 4 of 11 ulcers that were >13.3 cm^2 ($P = .017$, χ^2). No other significant relationships were found.

Table 5. Predictors of Time Required for Healing of Full-Thickness Leg Ulcers

Variable	Hazards Ratio (95% CI)	P Value*
>70 years of age vs <70 years	0.27 (0.0926–0.7923)	.017
Odor at baseline	0.18 (0.0577–0.6026)	.005
Ulcer area reduced by >30% after 2 weeks	2.26 (1.296–3.955)	.004

*Likelihood ratio statistic = 30.80, P < .001.
CI denotes confidence interval.

At the final evaluation, healing progress was rated as slower than for previous treatments in 11 ulcers (15%) and faster in 61 ulcers (85%). Most patients (53 [87%]) reported decreased pain with this treatment modality. Time spent caring for the ulcer decreased for 66 of 72 ulcers (92%) compared with the patients' previous treatment modality.

Discussion

We have tried to identify clinical guidelines that may predict ulcer severity (depth) as well as treatment outcome and time required for ulcers to heal after the cause of the ulcer has been classified. Our population appeared typical of other leg ulcer patient populations studied, with a female to male patient ratio of 2:1 and a mean age >65 years.[1,8] The role of compromised venous return and the ensuing cascade of events in the development of ulcers has been well documented.[9–11] Most patients have partial-thickness ulceration. In our population, patients with deep ulcers were more likely to be overweight and have restricted mobility. Patients with shallow wounds, however, were more likely to have dehydrated skin or rashes or both, suggesting, in addition to the underlying origin of the condition, a more "superficial" problem. Immobility has been implicated as a factor in delayed healing, but its relationship to ulcer depth has not been previously evaluated.[2] Following one of the first reports on the use of "nontraditional" dressings on chronic ulcers, many studies have confirmed the value of maintaining a moist wound environment.[12–15] Chronic wounds with their underlying disease and varying depth present a unique challenge, however, when studying the effect of any treatment.

We restricted our population to one treatment change in patients with full-thickness ulcers only in order to provide some uniformity in the results obtained. The results obtained were encouraging: healing was observed in 54% of patients and a mean percent reduction in ulcer area of 57% after 56 days of treatment of full-thickness leg ulcers that had been refractory to previous treatments. Clinically, the vast majority of ulcers (85%) healed faster than with previous local wound treatment modalities. When reepithelialization and contraction were quantified and the percent reduction in ulcer area was analyzed as a function of treatment time and outcome, marked differences were observed after as little as 2 weeks of treatment. Percent reduction in area after 2 weeks of treatment, particularly in ulcers that showed a 30% or greater reduction, was predictive of both treatment outcome and time required for healing. Similar findings were reported by Cherry et al[4] based on their many years of clinical

experience. Cordts and coworkers[16] found that the effect of treatment on chronic leg ulcers was most pronounced during the first 4 weeks of their study. Finally, the effect of reduction in wound area on treatment outcome has recently been reported for full-thickness pressure ulcers.[17] The clinical implication of this finding is that if a full-thickness leg ulcer does not exhibit a measurable reduction in area during the first 2 to 4 weeks of treatment, extra efforts to diagnose and treat additional causes of tissue breakdown appear warranted.

Patient and ulcer characteristics were also found to predict both treatment outcome and time required for healing. Women were more likely to heal than men, and the presence of diabetes mellitus negatively influenced treatment outcome. Delayed wound healing in patients with metabolic disorders is a well-known documented phenomenon, but why women are more likely to develop ulcers, yet heal better, is not as well understood.[18,19] An increased incidence of leg ulcers in women could be the result of pregnancy and subsequent deep venous thrombosis.[11,20] With respect to healing, some practitioners may argue that compliance remains a challenge in treatment of male patients. With respect to time required for healing, increased age, odor at baseline, and percent reduction in ulcer area were independently predictive.

In their leg ulcer prevalence study encompassing a population of 238,000, Baker and coworkers[20] found a significant increase in the prevalence of ulcers in patients >60 years of age. Older age was also found to be a prognostic factor for time required for leg ulcer healing by Skene et al.[21] In our study, an increase in baseline area was marginally associated with an increase in time required for healing. Some authors have found, using the same proportional hazards models, that baseline area was a predictor of time required for healing.[21,22] Cordts et al found that baseline ulcer measurement correlated with reduction in ulcer area; however, others have not found any effect of baseline area on time required for healing.[16,23,24] Unfortunately, comparison of the various results obtained is hampered by the fact that, in most studies, superficial as well as deep chronic wounds are analyzed together.

In our study of full-thickness leg ulcers only, odor was more predictive of treatment outcome than baseline area, but these factors did correlate with one another. Odor at baseline had not been assessed previously. The larger the area the more intense the odor; thus it seems that using baseline area as a predictive factor warrants further investigation. Additional studies of partial-thickness ulcers using other treatment modalities are necessary to confirm our findings. In future controlled clinical studies, patient sex, presence of diabetes mellitus, odor, baseline area, and percent reduction in ulcer area should be considered as well as all other standard confounding variables in the analysis. The majority of our findings not only confirm what practicing clinicians have observed but serve as a reminder that regular clinical assessments and wound measurement remain valuable tools in the management of these recalcitrant wounds.

References

1. Callam MJ, Ruckley CV, Harper DR, Dale JJ. Chronic ulceration of the leg: extent of the problem and provision of care. BMJ 1985; 290:1855–6.
2. McDonagh PF. Hemodynamic concepts underlying the etiology and treatment of chronic venous edema and ulcers. Wounds 1991; 3:182–90.
3. Falanga V, Eaglstein WH. A therapeutic approach to venous ulcers. J Am Acad Dermatol 1986; 14(5 Pt 1):777–84.
4. Cherry GW, Ryan TJ, Cameron J. Blueprint for the treatment of leg ulcers and the prevention of recurrence. Wounds 1991; 3:2–15.
5. Clark RA. Cutaneous tissue repair: basic biologic considerations. I. J Am Acad Dermatol 1985; 13 (5 Pt 1):701–25.
6. Kaplan E, Meier P. Nonparametric estimation from incomplete observation. J Am Stat Assoc 1958; 53:457–81.
7. Cox DR. Regression models and life tables (with discussion). J R Stat Soc Br 1972; 34:187–220.
8. Baker SR, Stacey MC, Jopp-McKay AG, et al. Epidemiology of chronic venous ulcers. Br J Surg 1991; 78:864–7.
9. Burnand K, Whimster I, Naidoo A, et al. Pericapillary fibrin the ulcer-bearing skin of the leg: the cause of lipodermatosclerosis and venous ulceration. BMJ 1982; 285:1920–2.
10. Burnand KG, Clemson G, Gaunt J, et al. The effect of sustained venous hypertension in the skin capillaries of the canine hind limb. Br J Surg 1981; 69:41–4.
11. Phillips TJ, Dover JS. Leg ulcers. J Am Acad Dermatol 1991; 25(Pt 1):965–87.
12. Alper JC, Welch EA, Ginsberg M, et al. Moist wound healing under a vapor permeable membrane. J Am Acad Dermatol 1982; 8:347–53.
13. Friedman SJ, Daniel Su WP. Management of leg ulcers with hydrocolloid occlusive dressing. Arch Dermatol 1984; 120:1329–36.
14. Varghese MC, Balin AK, Carter DM, Caldwell D. Local environment of chronic wounds under synthetic dressings. Arch Dermatol 1986; 122:52–7.
15. Mulder G, Walker A. Preliminary observations on clotting under three hydrocolloid dressings. J R Soc Med 1989; 82:739–40.
16. Cordts PR, Hanrahan LM, Rodriguez AA, et al. A prospective, randomized trial of Unna's boot versus DuoDERM CGF hydro-

active dressing plus compression in the management of venous leg ulcers. J Vasc Surg 1992; 15:480–6.

17. Van Rijswijk L. Full-thickness pressure ulcers: patient and wound healing characteristics. Decubitus 1993; 6:16–23.

18. Das SK. Wound healing, operative incisions and skin grafts. In: Hardy JD, ed. Hardy's textbook of surgery. 2nd ed. Philadelphia: JB Lippincott, 1988:106–12.

19. Goslen JB. Wound healing for the dermatologic surgeon. J Dermatol Surg Oncol 1988; 14:959–72.

20. Baker SR, Stacey MC, Jopp-McKay AG, et al. Epidemiology of chronic venous ulcers. Br J Surg 1991; 78:864–7.

21. Skene AI, Smith JM, Dore CJ, et al. Venous leg ulcers: a prognostic index to predict time until healing. BMJ 1992; 305:1119–21.

22. Kikta MJ, Schuler JJ, Meyer JP, et al. A prospective randomized trial of Unna's boots versus hydroactive dressing in the treatment of venous stasis ulcers. J Vasc Surg 1988; 7:478–83.

23. Colgan MP, Dormandy JA, Jones PW, et al. Oxpentifylline treatment of venous ulcers of the leg. BMJ 1990; 300:972–5.

24. Stewart AJ, Leaper DJ. Treatment of chronic leg ulcers in the community: a comparative trial of Scherisorb and Iodosorb. Phlebology 1987; 2:115–21.