Prognostic Value of the Clinical Examination of the Diabetic Foot Ulcer

David Edelman, MD, David M. Hough, MD, Katrina N. Glazebrook, MD,
Eugene Z. Oddone, MD

OBJECTIVE: To determine the value of the history, physical examination, and magnetic resonance imaging (MRI) in predicting successful primary healing of a foot ulcer in a diabetic patient.

DESIGN: Prospective cohort study.

SETTING: Durham (NC) Veterans Affairs Medical Center.

PATIENTS: Sixty-four consecutive diabetic patients with 78 dermal ulcers through the full thickness of the skin and at or distal to the malleoli of the ankle.

MEASUREMENTS AND MAIN RESULTS: A structured clinical history and physical examination were performed by two examiners, a physician participating in the study and the referring physician. Fifty of these patients with 63 ulcers underwent MRI. Patients were followed prospectively for 6 months after enrollment to ascertain healing of the ulcer, amputation, and death. During the 6-month follow-up period, 8 (13%) of the patients died. Seventeen (22%) of the ulcers were amputated, 17 (22%) of the ulcers failed to heal, and 36 (47%) healed primarily. Univariate predictors of healing at 6 months included age less than 65 years, diagnosis of diabetes within the last 15 years, painless ulcer, palpable ankle pulse, ankle-brachial index greater than 0.5, and the physician's assessment of the overall likelihood of osteomyelitis. In a multivariable logistic regression model, predictors of healing included the presence of an audible pulse on Doppler examination ($p = .01$) and a painless ulcer ($p = .04$). The diagnosis of osteomyelitis on MRI did not predict healing in these patients.

CONCLUSIONS: Foot ulcers in patients with diabetes frequently have poor outcomes; fewer than half the patients in this study healed their ulcers within 6 months. The vascular components of the clinical examination are the best predictors of healing in patients with a diabetic foot ulcer.

KEY WORDS: foot ulcer; clinical examination; magnetic resonance imaging (MRI); lower extremity amputation; peripheral vascular disease.

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Patients with diabetes suffer between 500,000 and 1 million dermal ulcers of the foot annually in the United States.¹ The incidence of diabetic foot ulcer is comparable to that of stroke. Patients with diabetes and a foot ulcer require more than 50,000 lower extremity amputations annually, and the direct annual costs associated with these amputations exceed \$1.1 billion.² Quality of life is poor for the patient with a chronic foot ulcer³; it is still worse after an amputation.⁴ Because intensive multi-specialty intervention improves healing in these ulcers,^{5,6} physicians should be able to rapidly identify patients with ulcers at high risk for adverse outcomes so as to initiate concentrated action.

One means to rapidly identify diabetic patients with foot ulcer at high risk of an adverse outcome is the clinical examination. A prospective cohort study identified individual elements of the history and physical examination associated with poor outcomes.^{7,8} However, no study has assessed the relative importance of the various components of the examination.

Another means for identifying high-risk ulcers is to assess the patient for osteomyelitis underlying the ulcer. The approach to the diagnosis of osteomyelitis has changed with the advent of highly sensitive and specific radiographic diagnostic tests, including magnetic resonance imaging (MRI).⁹⁻¹² Although osteomyelitis in the bone underlying the ulcer is considered a strong predictor of poor outcomes for the diabetic foot ulcer,¹³ no study using a standardized diagnostic approach to osteomyelitis has assessed this association.

We sought to determine the relative values of the clinical examination and MRI in predicting healing of the diabetic foot ulcer. We also sought to determine which elements of the history and physical examination are the best predictors of successful primary healing.

METHODS

Patients

Outpatients and inpatients with diabetes mellitus and a foot ulcer at the Durham Veterans Affairs (VA) Medical Center were enrolled between November 1994 and March 1996. Patients were recruited from outpatient clinic, emergency department, and inpatient settings. We attempted to enroll consecutive patients by having nurses contact us at their intake interview. The emergency department log also was reviewed daily for cases of foot ulcer. We enrolled all patients we could identify who had diabetes and one or more foot ulcers, regardless of severity. Patients were eligi-

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Address correspondence and reprint requests to Dr. Edelman: Durham Veterans Affairs Medical Center, Ambulatory Care (11C), 508 Fulton St., Durham, NC 27705.

ble if they had both a diagnosis of diabetes mellitus and a wound through the full thickness of the dermis at or distal to the malleoli of the ankle. Patients with lacerations and puncture wounds were excluded. Other exclusions were the previous diagnosis of osteomyelitis underlying this ulcer; previous MRI or bone biopsy of this ulcer; and the inability to tolerate MRI. The study was approved by the Institutional Review Board of the Durham VA Medical Center. We enrolled only patients who provided written, informed consent.

Examination Protocol

At enrollment, patients received a 13-item structured clinical history and a 16-item structured physical examination from one of the physicians involved in the study. Historical components included patient characteristics (age, race, gender, smoking status), diabetes-specific information (medication, duration of diabetes), ulcer-related information (duration of ulcer, previous amputation, fever, chills or sweats, painful ulcer), and vascular history (claudication). Physical examination components included general examination (leg, width, depth, location of ulcer), signs of infection (crepitus, necrosis, purulence, erythema, induration, visible bone in the ulcer), and vascular examination (dorsal pedal and posterior tibial pulses, cyanosis, edema). Pulses were graded as present or absent. The examination also included ankle-brachial index (ABI).¹⁴ Finally, the physician assessed (as low, moderate, or high) the overall likelihood of osteomyelitis underlying the ulcer. Patients also received a similar structured examination from the physician primarily responsible for their care at the point of enrollment (e.g., their primary care physician). Each examiner was blinded to the other examination.

An MRI was scheduled for the patient at the time of enrollment; MRI was scheduled usually within 1 week and always within 2 weeks of enrollment unless the patient insisted on a later date ($n = 2$). Results of MRI were communicated to the patient's physician by a study physician. The treatment plan for the patient was always determined by the physician responsible for the patient's care.

MRI Protocol

All MRIs were read by two radiologists (DMH and KNG) who were blinded to the clinical examination and each other's readings. Each radiologist rated the study as positive or negative for osteomyelitis or abscess, indeterminate, or inadequate for interpretation. When there was disagreement between the two radiologists ($n = 10$), a consensus was reached by discussion. The technical MRI protocol is available from the authors on request.

Outcome Measures

A healed ulcer was defined as complete wound closure assessed during a visit with a study physician (DE)

6 months after enrollment. Only one physician assessed outcomes. Ulcers were classified as being healed by primary intention, or not; the latter category included non-healing ulcers, amputations, and deaths. In addition, the total number of outpatient visits and inpatient hospital days was measured by the electronic medical record; utilization outside the Durham VA Medical Center was assessed by patient or patient's representative report (there were two reported hospitalizations outside the Durham VA Medical Center).

Data Analysis

Observer Agreement. We used Spearman correlation coefficients to assess observer agreement in measurement of continuous variables. We quantitated interobserver agreement of discrete variables using the kappa (κ) score. Kappa and its 95% confidence intervals (CIs) were calculated by the method outlined by Fleiss.¹⁵ When there were more than two categories, a weighted κ was calculated. In interpreting κ , the following would be a standard assessment of the quality of agreement: 0–0.2, poor; 0.2–0.4, fair; 0.4–0.6, moderate; 0.6–0.8, substantial; >0.8, near-perfect.¹⁶

Predictive Analysis and Modeling. The ulcer was the unit of analysis except in descriptions of the baseline demographics of the patients. In all analyses, we compared ulcers that had healed at 6 months with ulcers that had not healed. Univariate analysis was performed by χ^2 when assessing discrete independent variables (Fisher's Exact Test was used when appropriate), or by Wilcoxon Rank-Sum Test when assessing continuous independent variables. To simplify presentation, continuous variables were also dichotomized about their median and analyzed as discrete variables. Discrete variables with more than two outcomes were dichotomized in whichever way maximized their level of significance.

To model the multivariables for the probability of healing, we identified univariate predictors of healing ($p < .1$) and entered them into a logistic regression model. The modeling strategy used was previously described for the clinical examination for sinusitis.¹⁷ Briefly, the univariate predictors were entered into a logistic model and independent predictors were identified by stepwise regression. In all analyses, backward elimination yielded results identical to those of stepwise regression.

To avoid bias in the examinations of patients enrolled late in the study, we did not analyze the data until the last subject was enrolled. We performed all analyses with the SAS statistical analysis system (SAS Institute, Inc., Cary, NC).

RESULTS

Patient Data

We enrolled 64 patients with 78 ulcers in the study. Median patient age was 66 years (range 43–81 years);

Table 1. Prevalence of the Components of the History and Physical Examination of the Ulcers at Enrollment

Component	Number of Ulcers*, (%)
Element of history	
Painful ulcer	44 (56)
Claudication (affected leg)	26 (33)
Never been seen by physician before enrollment	22 (28)
Prior lower extremity amputation	20 (26)
Fever, chills or sweats	10 (13)
Smoking status	
Ex-smokers	41 (53)
Smokers	19 (24)
Never smoked	18 (23)
Median days since patient noticed ulcer (interquartile range)	33 (14–153)
Physical findings	
Leg	
Right	48 (62)
Left	30 (38)
Location	
Metatarsal heads	28 (36)
Toes	28 (36)
Other	22 (28)
Ankle-brachial index (n = 53)	
Above 0.9	22 (42)
0.5–0.9	13 (25)
Below 0.5	18 (34)
Induration	68 (87)
Edema	62 (80)
Erythema	62 (80)
Necrosis	58 (74)
Purulence	52 (67)
Present dorsal pedal pulse	42 (54)
Present posterior tibial pulse	33 (42)
Cyanosis	26 (33)
Visible bone in ulcer	7 (9)
Crepitus	3 (4)
Median width in largest dimension (interquartile range)	20 mm, (11–28 mm)
Median depth (interquartile range)	3 mm, (2–5 mm)
Physician estimate of likelihood of osteomyelitis	
Low	22 (28)
Moderate	28 (36)
High	28 (36)

*Total number of ulcers was 78.

median time since diagnosis of diabetes was 15 years (range 1–54 years). One woman was enrolled in the study. African-American enrollees had 27 (35%) of the 78 ulcers, and the rest of the patients were white. Forty-eight (62%) of the ulcers were in patients who used insulin; 24 (31%) in patients who took oral hypoglycemic agents, and 6 (7%) in patients who were diet-controlled. The distribution of the elements of the baseline clinical examination of the 78 ulcers is shown in Table 1.

Ulcer Characteristics

The baseline clinical examinations of the ulcers are summarized in Table 1. A majority (56%) of ulcers were painful; 33% of the ulcers were in patients who had claudication of the affected leg. The median ulcer was 20 mm wide and 3 mm deep. The vast majority of ulcers had signs of infection such as induration (87%), erythema (80%), necrosis (74%), or purulence (67%). Signs of vascular compromise were less common but still present in a majority of ulcers; 58% of the ulcers were in patients who had ABI <0.9. The study physician assessed the probability of underlying osteomyelitis as “high” in 36% of cases.

Observer Agreement

In order to determine if the clinical examination was reproducible enough to be useful as a prognostic tool for ulcer healing, we measured interobserver variability for most components of the examination. We measured agreement between the study physician and the referring physician (Table 2). Agreement for the various physical findings and historical elements varied widely, from near-perfect for width of the ulcer to poor for crepitus. The overall likelihood of osteomyelitis had worse agreement than any individual component of the examination.

Table 2. Interobserver Agreement for the Elements of the Clinical History and Physical Examination of the Diabetic Foot Ulcer*

Element	κ or ρ (95% CI)
Clinical History	
Smoking status	0.86 (0.79, 0.94)
Claudication (affected leg)	0.45 (0.25, 0.65)
Painful ulcer	0.44 (0.26, 0.62)
Fever, chills or sweats	0.34 (0.09, 0.59)
Physical examination	
Leg	0.92 (0.83, 1.00)
Width of ulcer	0.83 (0.55, 1.00)
Depth of ulcer	0.64 (0.36, 0.92)
Edema (affected leg)	0.53 (0.37, 0.70)
Palpable dorsal pedal pulse (affected leg)	0.48 (0.23, 0.72)
Palpable posterior tibial pulse (affected leg)	0.38 (0.20, 0.57)
Visible bone in ulcer	0.35 (0.07, 0.62)
Cyanosis (affected leg)	0.34 (0.13, 0.57)
Erythema	0.30 (0.09, 0.52)
Purulence	0.28 (0.07, 0.48)
Necrosis	0.22 (0.04, 0.41)
Induration	0.20 (0.03, 0.37)
Crepitus	0.16 (−0.07, 0.56)
Likelihood of osteomyelitis	0.13 (−0.03, 0.30)

*Data are shown as κ values (for categorical variables) or Spearman correlation coefficients (for continuous variables) with 95% confidence intervals in parentheses.

FIGURE 1. Flow chart of diabetic patients with foot ulcers.

MRI Assessment

A summary of patient recruitment, enrollment, and use of MRI is shown in Figure 1. Of the 92 ulcers on 77 willing and eligible patients, only 42 patients (55%) with 50 ulcers (54%) completed a diagnostic MRI that could be interpreted for the study. In two cases a patient did not complete MRI because it could not be done promptly; in all other cases the patient failed to complete the study for reasons relating to the severity of the ulcer or global medical condition.

Magnetic resonance imaging outcomes, and their clinical correlates, are shown in Table 3. Only 50 (64%) of the ulcers had a conclusive diagnosis by MRI. For 22 of the remaining 28 ulcers, MRI was nondiagnostic or was not available because the patient was taken to the MRI suite

but did not tolerate the procedure. For the other 6 ulcers, either the patient required amputation within 48 hours of enrollment and therefore missed MRI ($n = 4$), or there were nonmedical reasons for not receiving MRI ($n = 2$, breakdown of the magnet). Of the 50 ulcers for which there was a conclusive diagnosis, 29 (58%) were diagnosed with osteomyelitis.

Clinical Outcomes

Of the 78 ulcers, 36 (47%) healed by primary intention. Of the remaining 40 ulcers for which we obtained 6-month data (2 were lost to follow-up), 17 ulcers remained open, 13 ulcers were amputated in patients who survived the 6-month follow-up, 3 patients with 4 ulcers died after amputation, and 5 patients with 6 ulcers died without amputation. Of the 62 patients with complete follow-up, 42 (68%) were hospitalized 97 times for all causes during the 6-month follow-up period; only 2 of the 97 hospitalizations were not at the Durham VA Medical Center. Median time during the 6-month follow-up period spent in the hospital was 23 days.

Factors Associated with Primary Healing

Table 4 shows the association between primary healing at 6 months and the individual history, physical examination, and radiographic characteristics. The characteristics that predicted failure of healing were age of the patient greater than 65 years, history of amputation, pain in the ulcer, absence of posterior tibial pulse, ABI <0.5 , absence of audible posterior tibial pulse by Doppler, or moderate or high likelihood of osteomyelitis (as opposed to low likelihood). All other characteristics, including presence of osteomyelitis on MRI, did not significantly predict primary healing of the ulcer at 6 months. Because of the possibility that some unmeasured patient characteristic might cause confounding when more than one ulcer per patient was analyzed, we repeated the analysis using only the largest ulcer on each patient. The same seven examination characteristics were significant in this analysis.

In a multivariable logistic regression model, the two factors that retained predictive ability were the absence of an audible posterior tibial pulse on Doppler examination (odds

Table 3. Radiographic, Clinical, and Utilization Outcomes for Enrolled Ulcers

Outcome	Number (% of Category of MRI Diagnosis)		
	MRI Diagnostic of Osteomyelitis ($n = 29$)	MRI Negative for Osteomyelitis ($n = 21$)	No MRI or MRI Nondiagnostic ($n = 28$)
Healed	13 (45)	12 (57)	11 (39)
Nonhealed	6 (21)	4 (19)	7 (25)
Amputation	9 (31)	2 (10)	6 (21)
Death*	2 (7)	2 (10)	6 (21)
No follow-up	0	1 (5)	1 (4)

*Numbers do not add correctly because three patients with four ulcers died after amputation.

Table 4. Univariate Analysis of Value of the Clinical History, Physical Examination, and MRI Findings in Predicting Primary Healing of Ulcers at 6 Months*

Element	Relative Risk (95% CI)
Clinical history	
Prior lower extremity amputation	2.20 (1.29, 3.76)
Painful ulcer	1.68 (1.07, 2.65)
Age ≥ 65	1.68 (1.07, 2.65)
Evaluated prior to enrollment	1.63 (0.61, 4.32)
Diabetes ≥ 15 years	1.50 (0.97, 2.31)
Self-described as white race	1.37 (0.85, 2.21)
Ulcer present more than a month	1.03 (0.66, 1.59)
Current smoker	1.00 (0.61, 1.64)
Claudication (affected leg)	0.93 (0.59, 1.46)
Using insulin	0.88 (0.57, 1.37)
Fever, chills or sweats	0.73 (0.36, 1.50)
Physical examination	
Inaudible posterior tibial pulse by Doppler	2.44 (1.36, 4.39)
Ankle-brachial index <0.5	1.79 (1.00, 3.24)
Likelihood of osteomyelitis medium or high	1.78 (1.10, 2.89)
Absent posterior tibial pulse by palpation	1.61 (1.01, 2.56)
Crepitus	1.97 (0.89, 4.39)
Edema	1.51 (0.83, 2.75)
Necrosis	1.43 (0.84, 2.44)
More than 20 mm wide	1.42 (0.92, 2.21)
Absent dorsal pedal pulse	1.36 (0.88, 2.09)
Ulcer on toe (vs proximal)	1.34 (0.87, 2.07)
Purulence	1.29 (0.65, 2.09)
Cyanosis	1.28 (0.83, 1.99)
Erythema	1.16 (0.66, 2.04)
Visible bone in ulcer	1.10 (0.54, 2.24)
Induration	1.06 (0.52, 2.17)
Ulcer on left leg	1.03 (0.66, 1.60)
More than 3 mm deep	1.03 (0.66, 1.60)
MRI diagnostic or indeterminate for osteomyelitis	1.33 (0.79, 2.22)

*Relative risks are presented as they would affect risk of an adverse outcome (nonhealing, amputation, death).

ratio [OR] 8.46; 95% CI 1.54, 46.5) and the presence of pain at the site of the ulcer (OR 3.69; 95% CI 1.03, 13.2) ($c = 0.742$). When we excluded the elements of the examination that require the use of a Doppler, prior amputation (OR 6.45; 95% CI 1.86, 22.4) and pain (OR 2.85; 95% CI 1.04, 7.81) are significant after adjusting for all other factors ($c = 0.741$). We again analyzed the data using only the largest ulcer on each patient. In this case the only variable that retained significance was absence of a pulse on Doppler examination. When we excluded the elements of the examination that require the use of a Doppler ultrasound, the results were the same as in the analysis of all ulcers.

DISCUSSION

We have demonstrated that the most important clinical predictors of failure to heal a diabetic foot ulcer are those that reflect poor blood supply to the wound, pain at the site of the ulcer, and absence of an audible posterior tibial pulse on Doppler examination. In addition, we have shown that there is fair-to-moderate agreement among examiners for most aspects of the diabetic foot examination, including those elements that are predictive of outcome. The κ values for the components are similar to those typically reported for the clinical history and physical examination.¹⁸⁻²²

Our findings support the classic paradigm for the pathogenesis and healing of the diabetic foot ulcer, which suggests that although neuropathic changes cause these ulcers, vascular disease leads to nonhealing.²³ Several other components of our clinical examination have been shown in another cohort to be risk factors for nonhealing in unadjusted analysis.^{7,8,24} Many of these components of the examination were significant univariate risk factors for nonhealing in this study as well. However, multivariate analysis demonstrates that vascular insufficiency is the dominant risk for poor healing.

A surprising result is that the MRI diagnosis of osteomyelitis did not predict failure to heal. However, given that the treating clinicians were given the results of the MRI, positive MRI might have led to aggressive therapy for those patients with osteomyelitis, reducing the difference in outcomes between patients with normal and abnormal MRI results. For example, 26 of 29 patients with MRI diagnostic of osteomyelitis were given antibiotics either of a duration appropriate for that disease (either 6 weeks' intravenous or 12 weeks' oral therapy²⁵⁻²⁷) or from diagnosis until amputation or death. This is a higher proportion than those who had an MRI negative for osteomyelitis ($p = .009$).

Thus, it is possible that the diagnosis of osteomyelitis on MRI might play an important role in determining patient therapy and therefore outcome in these patients. However, given that for 46% of the ulcers for which MRI was considered no MRI diagnosis was obtained, and given the question about the study's predictive value, we suggest that MRI may not be of primary importance in management of the diabetic foot ulcer. This conclusion is consistent with the results of a recent decision analysis.¹

A potential limitation of this study is the fact that clinical information from the presentation is used in determining management, which presumably affects outcome. The effect of this bias on the association between the baseline clinical examination and outcome is uncertain. One possibility is that specific elements of the clinical examination, especially those related to vascular disease, may have led the treating physician to take a more aggressive approach to the ulcer. Thus, ulcers that would otherwise have failed to heal may have healed with this more aggressive therapy, and the power of these factors to predict failure to heal will appear diminished. Another

possibility is that poor vascular supply to the ulcer may have been assumed by surgeons to destine the patient to amputation, and may have led them to amputate more quickly. This would cause the absence of good vascular supply to appear to be a more powerful predictor of poor outcome than it really is. However, the absence of an audible pulse on Doppler examination remains a significant predictor of nonhealing even if all amputations and deaths are removed from the analysis, despite reduced power owing to a smaller sample size. This suggests the prognostic value of the vascular examination extends beyond its ability to predict the patients on whom surgeons will perform amputations.

The application of these findings to populations other than ours must be approached with caution. The adverse outcome rate in our study is higher than in a Swedish cohort of diabetic foot ulcers.¹³ Whether this reflects process of care or severity of ulcer at presentation is unknown. It is also striking that in our cohort, the median time between recognition of the ulcer and presentation was 33 days. In a cohort of patients from both VA hospitals and HMO settings the median time between recognition of the ulcer and presentation was only 7 days.²⁸ However, the significance of this difference is uncertain; in that study, as in ours, the time to presentation was not a predictor of adverse outcome.

Clinicians utilize a wide variety of approaches to the management of the diabetic foot ulcer, which are often not justified by the scientific data.²⁹ At baseline, all ulcers should receive prompt and thorough local wound care and appropriate antibiotic therapy. Despite the absence of studies suggesting that clinical findings should lead to specific interventions, it is not unreasonable to suggest that patients with a high risk of adverse outcome should be managed more aggressively, while conservative management with close follow-up may be acceptable for patients with a lower likelihood of adverse events.

In that context, our findings suggest a simple clinical approach to assessing the odds of healing for the diabetic patient at initial presentation with a foot ulcer, shown schematically in Figure 2. If Doppler ultrasonography is available to the examiner, this assessment for posterior tibial pulse is performed first. Absence of a pulse confers an extremely high risk of nonhealing, amputation, or death. As such, patients with no audible pulse might be managed more aggressively. A possible consideration would be rapid referral to a local specialist in diabetic foot care or to a vascular surgeon. In a retrospective study, prompt revascularization of the dysvascular diabetic patient with a foot ulcer reduced amputation rates.³⁰ In the presence of an audible pulse on Doppler, if the ulcer is painless the odds of healing are greatly enhanced beyond baseline and more conservative management might be attempted. From a pragmatic perspective, it is important to consider the possibility that Doppler ultrasonography is not available to the primary care provider. If no Doppler is available, a patient with a previous amputation of either

With Doppler.

Without Doppler

FIGURE 2. Algorithmic approach to the diabetic foot ulcer. Likelihood ratios for adverse outcomes (death, amputation or nonhealing) are presented for each of the states.

foot at any level is at increased risk of an adverse outcome and, again, might be considered for referral to a specialist. If the patient has never had an amputation, a painless ulcer may again be managed conservatively; a painful ulcer in a patient who has never had an amputation again suggests that the ulcer is at baseline risk.

There are many clinical approaches to the diabetic foot ulcer, but there is no evidence at this time for a single best management strategy. The vascular supply of the affected limb is probably the most important factor in predicting healing of the diabetic foot ulcer, and all measures should be taken promptly to save the foot. Furthermore, in clinical trials for methods of treating ulcer, patients should be stratified by the adequacy of blood supply to their leg. Further research is necessary to determine conclusively which vascular interventions, if any, provide improved outcomes for patients with poor blood supply to the foot with an ulcer.

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