Outcome of Ischemic Foot Ulcer in Diabetic Patients Who Had no Invasive Vascular Intervention

T. Elgzyri [a,*], J. Larsson [b], J. Thörne [c], K.-F. Eriksson [d], J. Apelqvist [a]

[a] Department of Endocrinology, Skåne University Hospital, Malmö, Sweden
[b] Department of Orthopaedic Surgery, Skåne University Hospital, Lund, Sweden
[c] Department of Surgery, Helsingborg's Hospital, Helsingborg, Sweden
[d] Vascular Department, Skåne University Hospital, Malmö, Sweden

WHAT THIS PAPER ADDS

This is, to our knowledge, the first prospective interdisciplinary study of diabetic patients with ischemic foot ulcers, considered not feasible for revascularization followed and treated to outcome. The study examines outcome and factors that are strongly related to outcome in these patients. The study showed that these patients are not excluded from healing without major amputation. Factors strongly related to outcome were co-morbidity, severity of PAD, and extent of tissue destruction. Findings in this study reinforce the need for a classification system considering factors at the decision making for vascular intervention.

Objective/background: There is limited information regarding outcome in patients not available for revascularisation. Our aim was to identify factors related to ulcer healing in diabetic patients with severe peripheral arterial disease who were not available for revascularisation.

Methods: Diabetic patients with a foot ulcer, consecutively presenting at a multidisciplinary foot centre with systolic toe pressure $<$45 mmHg or an ankle pressure $<$80 mmHg were prospectively included. Patients who received revascularisation were excluded. All patients had continuous follow-up until healing or death.

Results: Out of 602 patients (median age: 76 years) included in this study, 50% healed either primarily (76%) or with a minor amputation (24%). Seventeen percent of patients healed after major amputation and 33% died unhealed. By regression analysis, rest pain, impaired renal function, ischemic heart disease, cerebral vascular disease, extent of tissue destruction, and ankle pressure $>$50 mmHg affected the outcome of the ulcers.

Conclusion: Diabetic patients with ischemic foot ulcers not available for revascularisations are not excluded from healing without major amputation. Factors strongly related to outcome were co-morbidity, severity of peripheral arterial disease, and extent of tissue destruction. Our findings reinforce the need for a classification system considering these factors at decision-making for vascular intervention.

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INTRODUCTION

The diabetic foot ulcer is a heterogeneous disease that continues to be a major problem for the patient and for the healthcare system. Besides the risk of complications, such as infection or amputation,[1] diabetic foot ulcer disease has a major effect on patients' economical and social life.[2] Major amputations of lower extremities have been shown to predict reduced quality of life[3] and re-amputation,[4] as well as mortality,[5] in diabetic patients with foot ulcer.

Peripheral arterial disease (PAD) and concurrent co-morbidities have been shown to be significant predictors of ulcer healing in diabetic patients.[6–11] PAD is considered to be the most important limiting factor for healing of ischemic diabetic foot ulcers.[1,12,13] The majority of studies on ischemic foot ulcer include both diabetic and non-diabetic patients, and examines the rate of limb salvage improvement after revascularization, rather than ulcer healing as an outcome.[14] There are few studies that examine foot ulcer and PAD in diabetic patients only.[6,15,16] One study on patients with critical limb ischemia, without vascular interventions, showed that 54% of legs survived at 1 year.[17] However, to our knowledge, there are no studies that examine factors that affect ulcer healing in diabetic patients with ischemic foot ulcer in the absence of invasive vascular intervention. The aim of this study was to examine the outcome and identify factors related to healing of foot ulcers in diabetic patients with severe PAD not receiving revascularization.

* Corresponding author. T. Elgzyri, Department of Endocrinology, Skåne University Hospital, Lund University, 20502 Malmö, Sweden.
E-mail address: targ.elgzyri@med.lu.se (T. Elgzyri).

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MATERIALS AND METHODS

Study population

Consecutively presenting patients with diabetes and ischemic/neuroischemic foot ulcer (Wagner grade 1–5, at or below the ankle) admitted to a multidisciplinary foot centre between 1984 and 2006 ($n = 1151$; Fig. 1) were treated and followed up according to a standardized protocol until healing or death. The patients' data were prospectively recorded. The study was approved by the local ethics committee. In 602 patients no revascularization (angioplasty or reconstructive vascular surgery) was performed. These 602 patients were included in the present study. All patients continued with conservative treatment at the diabetic foot clinic according to their programme.

Inclusion criteria

Individuals with diabetes mellitus and foot ulcer, and a systolic toe pressure <45 mmHg, a systolic ankle pressure <80 mmHg, or, in the case of non-measurable pressure levels, non-palpable foot pulses with an ulcer Wagner grade 4–5 or rest pain. All patients fulfilled Fontaine grade 4.[18]

Study design

Patients were followed and treated according to a preset standardized protocol by a multidisciplinary team both in and out of hospital until healing with or without amputation was achieved, or until the patient died with an unhealed ulcer. All lesions were assessed and documented by the same team. Outpatient treatment was carried out in collaboration with primary healthcare and home nursing services. Physical examination of the foot was performed at inclusion and regularly during the study by the multidisciplinary team.

The core team consisted of a diabetologist, an orthopedic surgeon, an orthotist, a podiatrist, and a registered nurse educated in diabetes. Vascular investigation was carried out according to a prescheduled programme by a vascular surgeon integrated in the team on a regular basis. Systolic toe and ankle blood pressure was measured using strain gauge and Doppler techniques at the vascular laboratory.[19]

All data were recorded on standardized case record forms; these forms were both computerized and transformed into files. At study entry data were collected on previous management, referral, patient characteristics, comorbidities, ulcer characteristics, and laboratory investigations.

Each patient was represented by one lesion below the ankle. Patients with several concurrent lesions were represented by the one with the worst outcome. Patients with three or more ulcers on the same foot were classified as having multiple ulcers. The most superficial ulcer included was a full thickness skin ulcer penetrating into the subcutaneous layer. The Wagner grade at inclusion and the maximal Wagner grade reached were recorded. Minor gangrene describes Wagner grade 4; major gangrene describes Wagner grade 5.

The patients were treated as outpatients, but in the case of deep infection associated with septic condition, foot surgery, amputations, or exacerbation of inter-current disease they were treated as inpatients under the supervision of the foot team.

Patients were offered medical, surgical, and topical treatment, as well as offloading as needed.[6] All patients were followed up by the team according to protocol until a final outcome: primary healing, healing after minor or major amputation, or death unhealed.

Angiography

Angiography was performed at the discretion of a vascular surgeon according to a written programme that was jointly agreed upon. A retrograde aorto-femoral angiography, routinely visualizing distal vessels, as well as the pedal arch, was performed if the medical condition allowed and if informed consent was given. The catheter was placed as far distally as possible, and delayed and magnified lateral foot views were routinely obtained. This study includes patients who did not have an angiography or were not available for further vascular intervention following angiography.

Exclusion criteria for angiography were:

- medical condition not allowing angiography
- extensive gangrene (Wagner grade 5)
- major amputation performed prior to angiography
- subjective life expectancy of the patient <6 months
- signs of ulcer healing before angiography could be performed
- lack of walking capacity prior to occurrence of ulcer, restitution not expected
- informed consent for angioplasty refused.

All patients undergoing angiography were treated according to a programme regarding hydration and choice of pharmaceutical drugs to avoid renal failure.[20] All reasons for not performing vascular intervention after angiography were registered. Only one reason for each patient, the one most conclusive for the decision, is mentioned. All patients were treated with acetylsalicylic acid or clopidogrel, used since 1998, if no contraindication was present.

Statistics

Values are given as median and range. Comparisons between groups were made using the Mann–Whitney or chi-square test. Statistical significance was defined as a p-value <.05. The simultaneous influence of possible risk factors on a binary outcome (primary healing or minor amputation vs. major amputation or unhealed) was investigated by means of backward logistic regression analysis where all variables with a p-value <0.15 were included in the final model. Survival curves were plotted using Kaplan–Meier analysis and statistical significance was determined by log-rank test. Statistical analysis was performed using SPSS statistics 20 (SPSS, Chicago, IL, USA).