OUTCOME OF SEVERE DIABETIC FOOT ULCERS AFTER STANDARDISED MANAGEMENT IN A SPECIALISED UNIT

A cohort study

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SUMMARY - Objective: The primary objective was to evaluate the efficacy in terms of limb salvage and healing time of standardised multidisciplinary management for high-grade diabetic foot ulcers. The secondary objective was to retrospectively identify the factors that influenced time to healing.

Study design and methods: Over a 2-year period, 157 patients with diabetic foot ulcers were managed in our specialised unit using a standard treatment strategy; 118 were followed until healing or for at least 7 months (range, 7-29) after hospital discharge and form the basis for this study. Predetermined criteria were used to diagnose and manage the lesions. The number of major amputations and the time to healing were the main outcome measures. Univariable and multivariable analyses were done retrospectively to look for factors associated with time to healing.

Results: The limb salvage rate was 97.5% and the healing rate was 50% after 10 months and 70% after 16 months. Factors significantly associated with healing time were arterial disease without bypass surgery \( (p < 0.001) \) and renal replacement therapy \( (p < 0.05) \). Osteomyelitis, as managed in this study, did not increase the healing time \( (p > 0.6) \).

Conclusion: In high-grade diabetic foot ulcers, standardised conservative management with second-line bone-sparing surgery, if needed, yields an acceptable limb salvage rate. With combined medical and surgical treatment, osteomyelitis is not a poor prognosis factor.

Key-words: diabetes, foot ulcers, limb salvage rate, healing time.

RÉSUMÉ - Devenir d’ulcères de pied diabétique sévères après prise en charge standardisée dans une unité spécialisée. Une étude de cohorte.

Objectif : L’objectif principal était d’évaluer l’efficacité, en termes de sauvetage de membre et de temps de cicatrisation, d’une prise en charge standardisée multidisciplinaire d’ulcères de pied diabétique de haut grade. L’objectif secondaire était d’identifier rétrospectivement les facteurs influençant le délai de cicatrisation.

Schéma d’étude et méthodes : Sur une période de 2 ans, 157 patients présentant un ulcère de pied diabétique ont été gérés dans notre unité spécialisée selon une stratégie thérapeutique standardisée ; 118 ont été suivis jusqu’à cicatrisation ou pendant au moins 7 mois (extrêmes 7-29) après la sortie de l’hôpital et forment la base de cette étude. Des critères prédéterminés ont été choisis pour le diagnostic et la prise en charge des lésions. Le nombre d’amputations majeures et le délai de cicatrisation sont les principales variables de jugement. Une analyse uni- et multivariée a été effectuée rétrospectivement pour mettre en évidence des facteurs associés au délai de cicatrisation.

Résultats : Le taux de sauvetage de membre a été de 97.5 % et celui de cicatrisation de 50 % après 10 mois et 70 % après 16 mois. Les facteurs significativement associés au délai de cicatrisation ont été l’artériopathie sans chirurgie de revascularisation \( (p < 0.001) \) et la thérapeutique de suppléance rénale \( (p < 0.05) \). L’ostéite, telle que prise en charge dans cette étude, n’a pas retardé le délai de cicatrisation \( (p > 0.6) \).

Conclusion : En cas d’ulcères de pied diabétique de haut grade, une prise en charge conservative standardisée avec chirurgie minimaliste sur les os de seconde intention, si nécessaire, permet un taux de sauvetage de membre acceptable. En combinant traitement médical et chirurgical, l’ostéite n’est pas un facteur de mauvais pronostic.

Mots-clés : diabète, ulcère de pied, taux de sauvetage de membre, délai de cicatrisation.
In 1992, St. Vincent Declaration set a 5-year target of decreasing by half the leg amputation rate in diabetic patients [1]. Since then, several studies have established the benefits of a multidisciplinary approach to diabetic foot lesions [2-5]. In particular, in patients with severe arterial disease, revascularisation has been shown to improve the limb salvage rate [6-11]. However, the other components of foot ulcer management remain poorly standardised. Thus, the type, indications, and degree of urgency of orthopaedic procedures are not well defined. Surgical resection or immediate extensive resection in patients with sepsis [12, 13] seems associated with lower limb salvage and healing rates than second-line surgery after medical treatment [14] or limited debridement [8, 15, 16]. In addition, amputation, however minor, is associated with an increased risk of further amputation [16]. A similar lack of consensus exists regarding the management of osteomyelitis, with some groups advocating medical treatment only [17], despite evidence that combined medical treatment and conservative surgery decreases the time to healing [18].

Taking these data into account, we developed a standardised treatment strategy for high-grade diabetic foot ulcers. This strategy aimed at optimising the limb salvage rate and healing time by combining first-line medical treatment, revascularisation if needed, and limited second-line orthopaedic surgery. First-line amputation was not used. Osteomyelitis without severe ischaemia was treated by second-line limited bone resection to preserve as many weight-bearing points as possible. When severe arterial disease was present, revascularisation was done as soon as sepsis was controlled by the medical treatment.

We report the limb salvage rate, healing rate, and healing time obtained with this treatment strategy in 118 patients followed up until healing or for at least 7 months. We also retrospectively looked for factors that influenced the time to healing.

**PATIENTS AND METHODS**

**Patients**

Patients admitted to the podiatry unit of the diabetology department at the Pitié Teaching Hospital in Paris, France, are diabetic patients referred to the unit by the diabetology department outpatient clinic, other departments in the hospital (e.g., nephrology or vascular surgery), or other hospitals in the vicinity. Of the 157 patients managed at the podiatry unit between April 1996 and May 1998, 118 (75%) patients were followed up until healing of their ulcer or for at least 7 months after discharge. These 118 patients were included in the study. The 39 other patients were either lost to follow up or managed elsewhere (at the referring department or at other wound healing units).

**Clinical features**

Indications for admission to the podiatry unit were as follows: foot ulcer with evidence of systemic infection, (fever, chills) and/or locally severe lesions (extensive cellulitis, toe or forefoot necrosis, osteomyelitis), i.e., grade 3, 4, and 5 ulcers according to the Wagner classification [19].

The following criteria were used to diagnose complications of diabetes and to classify the patients for management purposes:

- retinopathy: at least 5 microaneurysms by fundoscopy;
- nephropathy: persistent proteinuria ≥ 20 mg/L;
- peripheral neuropathy: insensitivity to the 10-g 5.07 Semmes-Weinstein monofilament at any of six standardized plantar sites (three toes and three metatarsal heads) on either foot [20], on two separate occasions;
- peripheral arterial disease (PAD), with three grades based on clinical findings, the ankle-brachial blood pressure index (ABI, considered interpretable if < 1.3, [22]), and Doppler ultrasound findings. TCPO₂ was not in use at the time of the study. The three grades were as follows: absence of PAD defined as absence of the posterior tibial pulse present, no ischaemic trophic disorders, and ABI ≥ 0.9 [21, 22]; moderate PAD defined as absence of the posterior tibial pulse, ABI between 0.5 and 0.9 [21, 22], and arterial lesions by Doppler ultrasound; and severe PAD defined as absence of the posterior tibial pulse and ABI ≤ 0.5 [21, 22] or, in patients with ischaemic trophic disorders, severe arterial lesions by arteriography.
- osteomyelitis, defined as probing to bone with local infection and suggestive features on weekly bone X-rays [23, 24].

**Treatment strategy (Fig. 1)**

First-line medical treatment was used routinely. If needed, surgery was performed subsequently. In patients with severe arterial lesions, revascularisation was done immediately after arteriography.

**Routine first-line medical treatment**

- unloading of the ulcer from mechanical stress, including strict bed rest (heels unsupported), use of off-loading shoes or wheelchair. The crucial importance of completely relieving the pressure from the ulcer was explained to the patient and family;
- daily local care consisting mainly in drying of oozing or necrotic lesions with a dye such as aqueous fluorescein. Lesions with marked oozing were covered with absorbent dressing. Skin keratosis and slough were removed mechanically in patients without severe arterial lesions. In all other cases, petrolatum gauze was used;
tight glucose control, with insulin therapy if needed;

- standardised antibiotic therapy [25]: empirical antibiotic therapy mainly by amoxicillin-clavulanic acid was started at admission in patients with fever or locally severe lesions (extensive cellulitis, deep ulcer). After 48hr, antibiotics were adapted based on the results of microbiological studies of swabs inserted deep into the ulcer after disinfection of the edges of the lesion. The narrowest spectrum possible was used. Two antibiotics were given in combination in patients with osteomyelitis;

- purulent collections under tension were incised in the wound-care room.

**Surgical management**

In patients meeting our criteria for severe PAD, bypass surgery, if possible, was done as soon as possible. When the necrosis involved only one or two toes, debridement was not performed during the procedure. Medical treatment was continued until drying and auto-amputation of the lesions occurred. In patients with more extensive necrosis, only the necrotic area was debrided during the bypass procedure. The wounds were left open.

In patients with osteomyelitis as defined above, after 10 to 15 days of medical treatment, surgical resection confined strictly to the osteomyelitic site was performed. The procedure usually consisted in removal of a metatarsal head, proximal phalanx, or toe. The change to the outer appearance of the foot was kept to a minimum. When severe PAD was present also, revascularisation was performed before the orthopaedic procedure. In patients with moderate PAD, orthopaedic surgery was done only in the absence of long-distance narrowing or tibio-peroneal artery occlusion by Doppler ultrasound [26].

**Follow up**

After the patient was discharge from the unit, he was followed up by the same foot-care team on an outpatient basis until healing or for at least 7 months (range, 7 to 29 months). The recommended outpatient treatment is described below.

- complete protection of the ulcer from weight bearing until healing was complete. This was achieved using half-shoes (Barouk, Ets Neut, Paris, France) for forefoot ulcers, Sanital shoes (Ets Neut, Paris, France) for heel ulcers, and Orthop USA shoes (Ets Neut, Paris, France) for toe ulcers. The importance of protection from weight bearing was explained to the patient and family at each visit;

- daily topical treatment (petrolatum gauze or alginite) by a nurse at home, until healing was complete;

- in patients with osteitis, two antibiotics adapted based on microbiological studies were given in combination for 2 months;

- visit to the podiatry unit outpatient clinic every 2 weeks, with measurements of ulcer size, radiographs if needed, bacteriological specimen collection, and adaptation of the antibiotics.
The aim of the statistical analysis was to look for factors associated with time to healing. Because some patients failed to achieve healing within the study period, we used survival analysis. Patients who died before healing were censored because death was not related to ulcer or treatment complication.

The analysis was performed in two steps. We first tested the relations between each factor and the time to healing, using the log-rank test for categorical variables and a univariable Cox model for continuous variables. Those factors associated with time to healing at a p level of less than 0.05 in this analysis were included in a stepwise Cox regression model to look for independent associations with time to healing.

When no major amputation was required with a non-unfavourable evolution, the limb was considered as save (limb salvage).

### TABLE I. Main patient characteristics (n = 118).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nb (%)</th>
<th>Mean ± SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>90 (76)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>28 (24)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>64 ± 11 (30-92)</td>
<td></td>
</tr>
<tr>
<td>Type of diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20 (18)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>98 (82)</td>
<td></td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>19.5 ± 10 (1-57)</td>
<td></td>
</tr>
<tr>
<td>Previous foot ulcer</td>
<td>71 (60)</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>90 (75)</td>
<td></td>
</tr>
<tr>
<td>Nephropathy</td>
<td>66 (56)</td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Kidney transplant</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>8.66 ± 1.9 (5.6-15)</td>
<td></td>
</tr>
<tr>
<td>Type of ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathic</td>
<td>30 (25)</td>
<td></td>
</tr>
<tr>
<td>Ischaemic</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>Neuroischaemic</td>
<td>82 (69)</td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>51 (43)</td>
<td></td>
</tr>
</tbody>
</table>

### RESULTS

#### Patient characteristics

The mean length of stay in the podiatry unit, including pre- and postoperative management, was 28 days (range, 6 days to 6 months). Of the 118 patients, 29 required one or more readmission during follow-up.

*Table I* shows the main characteristics of the 118 patients. Mean age was 64 years. Of the 118 patients, 71 (60%) had a previous history of foot ulcer. The ulcer was neuropathic in 30 (25%) patients, ischaemic in 6 (6%), and neuroischaemic in 82 (69%).

#### Surgical procedures, rate of minor amputation, and rate of limb salvage

**Surgical procedures (Table II)**

Of the 51 patients with osteomyelitis, six had severe PAD requiring an arterial bypass procedure (see below). Of the 45 remaining patients with osteomyelitis, 39 had a surgical procedure without major ampu-
tation during the hospital stay, after 14 days of medical treatment on average. 6 patients required readmission during follow-up for a first or second minor surgical procedure (n = 2 and n = 4, respectively). Thus 41/45 ulcers with osteomyelitis in absence of severe PAD required a minor surgical procedure.

Severe arterial lesions were present in 30 patients (including 6 with osteomyelitis). In 6 of these patients, bypass surgery was not feasible and below-the-knee (n = 2) or minor (n = 4) amputation was required. Bypass surgery was performed in the remaining 24 patients. Amputation was required in 12 of these 24 cases and consisted in minor amputation (transmetatarsal or toes) in 11 cases and in above-the-knee amputation in one patient. Six other patients required readmission during follow-up for minor amputation (mummification of the toes or phalanges). The six remaining ulcers were either lateral wounds or areas of dry necrosis that did not require amputation. Thus 24/30 ulcers with severe PAD required minor or major amputation.

Of the remaining 43 ulcers (no osteomyelitis or severe PAD), six required toe amputation and 18 resection of one phalanx.

Follow-up

The 118 patients were followed up until complete healing or for at least 7 months (range, 7-29 months). Of these 118 patients, 29 required readmission, during which orthopaedic surgery was performed in 12 patients (first procedure in 8 and repeat surgery in 4). No major amputations were required after the first admission. Thus, the final limb salvage rate was 97.5% (3 major amputations) and the minor amputation rate was 31% (n = 37).

Ten (8.5%) patients died before healing was achieved. Nine were related to cardiovascular disease. There were no deaths in the intraoperative or immediate postoperative period.
Factors associated with healing time

Figure 2 shows the time-course of the percentage of unhealed ulcers. At 10 and 16 months, the healing rates were 50% and 70%, respectively.

The results of the univariable analysis of factors potentially associated with healing time are reported in Table III. Osteomyelitis, as managed in our study, was not significantly associated with healing time (p > 0.6, NS). The strongest association with healing time was for moderate or severe PAD (p < 0.002). This adverse influence of arterial disease was not apparent, however, when PAD was associated with bypass surgery (p > 0.1, NS), suggesting that bypass surgery allowed a drastic decrease in the adverse influence of PAD on healing process. Thus we compared the healing rate over time in patients with non treated PAD who survived until follow-up completion (n = 56) and in the other patients (i.e., the patients with treated PAD (bypass surgery) and who survived until follow-up completion [n = 22] and the patients with non-ischaemic ulcers [n = 30]). Time to healing of 50% of the ulcers was 13 months in the first group and 6 months in the second, p < 0.001 (Fig. 3).

Neither presence of renal disease nor the serum creatinine level was associated with healing time. Conversely, healing time was significantly longer in the patients who required renal replacement therapy (p < 0.05).

Variables significant (p < 0.05) in the univariable analysis were entered into the multivariable model. Only two factors were independently associated with a longer healing time: PAD not treated by bypass surgery (relative risk for the ulcer to be healed with time: 0.462; 95% confidence interval, 0.292-0.728) and renal replacement therapy (relative risk for the ulcer to be healed with time: 0.393; 95% confidence interval, 0.156-0.982).

DISCUSSION

Some components of the treatment of high-grade diabetic foot ulcers are widely accepted, such as revascularisation in patients with severe arterial disease and the need for tailoring the treatment program to the type of ulcer [27]. However, considerable disagree-
management persists for many other components. Aggressive surgical debridement has been suggested [5, 13, 27-29] to ensure prompt control of wound infection. However, this approach carries a risk of removing noninfected bone segments located within or near the infected site. This is highly undesirable given that previous amputation is associated with an increased risk of further amputation [16]. Even partial amputation of the great toe contributes to the development of foot deformities that increase the risk of ulcer recurrence [30]. Thus, maximum preservation of forefoot integrity has been advocated to decrease the risk of ulcer recurrence [9, 15]. With the same goal, we developed a strategy that emphasises immediate medical rather than surgical treatment of soft tissue sepsis, followed by second-line bone-sparing surgery. Our limb salvage rate (97.5% at 16 months) was comparable to that reported previously [9, 15].

However, because the absence of immediate aggressive surgical wound cleansing might conceivably delay healing, we evaluated not only the limb salvage rate but also the time to healing. Among studies of diabetic foot ulcers similar in severity to those in our population, few have provided details on healing rates and healing time. Using non-conservative management, Nelher et al. [13] obtained a short-term healing rate similar to ours (40% between 4 and 6 months but with a 22% rate of major amputation. The 16-month healing rate in our cohort (70%) was comparable to the long-term healing rate obtained by Eneroth et al. [14] but with a 20% rate of major amputation. Thus, our results suggest that combined medical and surgical treatment of high-grade diabetic foot ulcers with maximum foot preservation may provide a satisfactory limb salvage rate without increasing the healing time as compared to more aggressive management.

A distinctive feature of our management strategy is the strong emphasis placed on full protection from weight bearing started at the same time as the rest of the management program and continued throughout follow-up. Because protection from weight bearing is difficult to quantify, it was not evaluated objectively in our study. However, this factor is known to influence wound healing [5, 28, 31].

A second salient characteristic of our management strategy is the limited surgical resection of osteomyelitic foci after initial medical treatment. This decreased the healing time [18] as compared to medical treatment alone. Our finding that osteomyelitis was not associated with healing time indicates that our management strategy was able to remove the potentially negative effect of infection on wound healing. However, the decision to perform surgery can be difficult to take in patients with moderate arterial lesions (that do not require bypass surgery), because in this situation orthopaedic resection procedures can exacerbate the local ischaemia. None of the non-invasive means of investigating distal arterial vascularisation (transcutaneous oxygen pressure, ABI, Doppler ultrasound) has validated an ischaemic threshold below which an orthopaedic procedure is risk-free. Consequently, in patients with osteomyelitis and moderate arterial lesions, we based surgical decisions on Doppler ultrasound criteria (absence of long-distance narrowing or of tibio-peroneal occlusion) [26]. None of the orthopaedic procedures were followed by ischaemic complications. However, these criteria need to be validated.

Finally, our retrospective analysis of factors that might influence healing time found no effect of age, sex, or diabetes duration [32]. In contrast, healing time was longer in patients with arterial disease, in keeping with earlier reports that this factor increased the risk of major amputation [29] and the time to healing [32, 33].

In conclusion, standardised medical treatment of the infectious component, with complete protection from weight bearing, combined with conservative surgery in patients with osteomyelitis and with revascularisation whenever possible in patients with severe arterial disease provides a satisfactory limb salvage rate without noticeably increasing the time to healing. Emphasis on bone preservation with avoidance of aggressive surgical debridement may decrease the risk of recurrence, although this requires evaluation.

REFERENCES


