# Salvaging diabetic foot through debridement, pressure alleviation, metabolic control, and antibiotics

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## ABSTRACT

There is a fatalist perception of diabetic foot because the argument of "small-vessel disease" prevails. This is the report of a cohort study of patients facing a formal recommendation for major foot amputation to assess how many can be saved with a conventional treatment, defined as debridement, pressure alleviation, metabolic control, and antibiotics. The primary efficacy measurement was the salvage of the limb at the follow-up visit between 25 and 35 days after the first consultation. The secondary efficacy measurement was the subsequent epithelization of the ulcerative lesions, following patients for up to 270 days. The cohort consisted of 105 type 2 diabetic patients; 87 (83%) had severe lesions. A total of 71 patients (68%) required hospitalization. By the intention-to-treat analysis, 89 patients (85%) avoided major amputation. A total of 88 patients were evaluated for complete epithelization, reaching median success by day 120. Overall, 51 patients (49%) underwent minor amputations. It was concluded that there is a high rate of unnecessary major foot amputations, because a diabetic foot can be salvaged across the continuum of severity when patients receive care in a multidisciplinary wound clinic.

Foot disease represents the single most common cause of hospitalization in persons with diabetes; worldwide, about every 30 seconds on average a limb is amputated as a consequence of diabetes.[1,2] When prevention fails, specialized teams may limit the damage, avoiding unnecessary amputations.[3–5] Such teams should include specialized surgeons, internists, microbiologists, nurses, and educators.[6–8] Necrotic tissue removal requires expert knowledge to reduce the risk of amputation and allows a collection of good specimens for microbiological study.[6,9]

Among physicians, a fatalist perception regarding diabetic foot is common because the argument of "small-vessel disease" prevails.[8,10] Nevertheless, there are much more important contributing factors such as neuropathy, trauma, infection, and poor metabolic control.[10–13] Our goal in this study was to evaluate how many patients receiving a recommendation for major amputation could preserve their limbs by following standard care, under the hypothesis that they can be salvaged across the continuum of severity when patients are cared for a multidisciplinary wound clinic. Because it would be ethically unacceptable to randomize patients to amputation or no amputation groups, we designed a longitudinal study in which every included patient had to have a formal proposal for amputation, providing us with a common characteristic to recruit a cohort.

## MATERIALS AND METHODS

### Setting

Clinic "Cabeza de Vaca" is a private center dedicated to the treatment of diabetic feet in Leon, Mexico. About 95% of the patients are self-referred, many of them asking for a second opinion after receiving a major amputation proposal, and about 80% arrive from distant communities. The clinic follows strict policies for asepsis, antisepsis, and sterilization. Every patient with diabetic foot is submitted to a conventional treatment, defined as debridement, pressure alleviation, metabolic control, and administration of antibiotics.

### Subjects

The protocol was approved by the research and ethics committee of the University of Guanajuato School of Medicine. The cohort was recruited from December 2005 to March 2007. Patients were eligible only if they asked us for a second opinion after receiving a recommendation from a physician for transtibial or transfemoral amputation due to foot disease. In addition, patients must suffer from diabetes, a new diagnosis required fasting glucose levels $> 126 \, \text{mg/dL}$ (7 mmol/L). We defined acute infection as the presence of gross purulence, or two or more of the following: hot erythema, lymphangitis, swelling, or induration, severe pain, and fever ($> 38 \, ^{\circ}\text{C}$) or peripheral blood leukocytosis ($> 11,000/\mu\text{L}$).[8,12–14] Vascular compromise was assessed by the absence of a pedial pulse or an ankle/arm index $< 0.8$.[10,14] Wound depth was evaluated with a blunt probe, and severity classified using the University of Texas System (UTS), which uses a matrix of wound grade (depth) on the horizontal axis and wound stage (ischemia or infection) on the vertical axis. Grade 0 means a healed ulcerative lesion. Grades I, II, and III mean ulcers that affect skin, tendons or capsule, and bone, respectively. Within each grade, there are four stages: stage

A means no infection or ischemia, whereas stages B, C, and D mean infection, ischemia, and both, respectively.[14] We classified affected sites according to the affected areas (toes, medial portion of the foot, ankle, and leg), taking initial photographs to measure the ulcer sizes and to have a reference to evaluate their evolution.

After an initial evaluation, we proposed a treatment plan, which required compliance with the follow-up period estimated to achieve total epithelization of the foot. For the selected patients, we ordered basic laboratory work-ups: complete blood count, serum glucose level, creatinine, and blood urea nitrogen. We performed cultures by deep soft tissue biopsy in patients with evidence of infection; we did not take cultures by swabbing or needle aspiration.

### Clinical procedures

Generally, we treated those with mild-to-moderate lesions as outpatients (grades 0 and I of the UTS), whereas we hospitalized those with severe lesions (grades II and III). As needed, an experienced surgeon (F.G.C.V.) performed the debridement and culture collection; he also prescribed empirical antibiotic treatment. After the surgeon removed necrotic tissue in one to five sessions, a team of qualified nurses performed periodical wound cleansing and dressing, using sterile gauze and saline solution. In both hospitalized patients and outpatients, we performed the initial cleansing on a daily basis and, after improvements were observed, twice a week. The internists supervised metabolic control. In patients with poor initial clinical response, the infectious disease specialist reassessed the antimicrobial therapy based on culture results. During the initial care, we required the removal of pressure from the foot, permitting the use of crutches.

After initial care, relatives of patients coming from distant communities received training to perform wound cleansing. We asked all patients with grade II and III lesions to avoid walking for 30–60 days, recommending the use of crutches, off-loading devices or wheelchair for essential activities. We recorded amputation extent with a discrete scale from 0 to 4, as follows: (0) no amputation, (1) partial amputation of toes or metatarsals, (2) complete amputation of toes, (3) transmetatarsal amputation, and (4) transtibial or transfemoral amputation. We considered amputations to be high level if they belonged to extent three or four on this scale.

After processing the biopsy material in a mortar, we performed aerobic cultures. For polymicrobial cultures, we identified the predominant organism. We used biochemical procedures for bacterial identification and the disk diffusion method for antimicrobial susceptibility, according to the standards of the Clinical and Laboratory Standards Institute.[15] We considered the isolates of coagulase-negative staphylococci, *Corynebacterium* spp., and alpha hemolytic streptococci as contaminants.

### Analysis

The primary efficacy measurement was the early salvage of the limb, defined as the avoidance of a high-level amputation (transmetatarsal or higher) and at least 10% of reduction of the ulcer area at the follow-up visit between 25 and 35 days after the first consultation. Ulcer areas were measured by a single evaluator (A.E.M.) using photographs. To evaluate the reduction of the ulcer areas, initial and subsequent pictures were manipulated to equalize the size of the foot according to the angle of the picture on a computer screen (Illustrator® Adobe Systems Inc., San Jose, CA); the area of interest was then measured by an image software package (AutoCAD 2008®, Autodesk Inc., San Rafael, CA). The reduction of the ulcer area was assessed against the initial area. By analysis of variance, we established significant differences among proportions of improvement (dependent variable), with the independent variables being the grade and stage of the lesions according to the UTS. Based on the intention-to-treat approach, we considered patients lost to primary follow-up as if they were submitted to high-level amputation.

The secondary efficacy variable was the complete epithelization of the foot or a superficial ulcer $< 2\,cm^2$,[16] following patients for up to 270 days. To consider attrition, we used the Kaplan–Meier method to evaluate time to achieve the complete epithelization of the limb and the logrank test to compare differences in curves of success.

## RESULTS

### Cohort description

We recruited 105 patients who received recommendation for transfemoral or transtibial amputation. During the recruiting period, we did not include 10 additional patients who fulfilled eligibility criteria but did not accept the treatment plan. Table 1 describes the final cohort, with all patients suffering from type 2 diabetes; three of them (3%) were in a chronic peritoneal dialysis program. Patients came from 70 different medical institutions or medical offices, where they received the amputation recommendation.

Regarding the extent of the lesions, 18 (17%) were light to moderate (grade 0 and I of the UTS), and 87 (83%) were severe (grade II and III); 92 (88%) had received antimicrobials, and 85 (81%) had evidence of infection at the first visit, 47 (45%) of whom were febrile. The toe region was the most commonly affected area as 83 patients (79%) had compromised toes. Overall, 75 patients (71%) had more than one region affected.

We obtained biopsy for culture in 85 patients; in the remaining 20 patients, we did not consider it indicated. Of the 85 cultures, 74 (87%) had a potential pathogen identified. Gram-negative bacilli predominated (51, 69%), with *Escherichia coli* being the most common isolate (27, 37%), followed by other Enterobacteriaceae (24, 32%) and *Pseudomonas* spp. (6, 8%), whereas *Enterococci* were the predominant Gram-positive isolate (18, 24%). Drug-resistance of *E. coli* against ampicillin, trimethoprim-sulfa, gentamycin, ciprofloxacin, and ceftriaxone was 93, 82, 48, 70, and 48%, respectively.

### Clinical evolution

Seventy-one patients (68%) were hospitalized for an average stay of 6.6 days (range: 2–12 days). Of the 18 patients with minor-to-moderate lesions, only 2 (11%) required hospitalization; on the other hand, of the 87 patients with severe lesions, 69 (79%) required hospitalization.

**Table 1.** Descriptive characteristics of a cohort of 105 diabetic patients with diabetic foot who were recommended for transtibial or transfemoral amputation

| Characteristic | Value | |
|---|---|---|
| Men, n (%) | 62 | (59) |
| Women, n (%) | 43 | (41) |
| Age, mean (range) | 62.8 | (31–97) |
| Diabetes evolution in years, mean (range) | 15 | (0–42) |
| Type of diabetes control, n (%) | | |
| Hypoglycemic agents | 81 | (77) |
| Diet only | 5 | (5) |
| Insulin | 19 | (18) |
| Diabetic foot evolution in days, mean (range) | 57.4 | (3–360) |
| Diabetic foot evolution < 15 days, n (%) | 8 | (8) |
| Blood hemoglobin in g/dL, mean (range) | 11.4 | (5.2–17.7) |
| Patients with hemoglobin < 11 g/dL, n (%) | 44 | (42) |
| Serum glucose in mg/dL, mean (range) | 150.9 | (43–450) |
| Patients with serum glucose > 110 mg/dL, n (%) | 65 | (62) |
| Serum creatinine in mg/dL, mean (range) | 1.3 | (0.4–10.9) |
| Patients with serum creatinine > 2 mg/dL, n (%) | 8 | (8) |
| Severity classification, UTS; n (%) | | |
| Grade 0 | 1 | (1) |
| Grade I | 17 | (16) |
| Grade II | 22 | (21) |
| Grade III | 65 | (62) |

UTS, University of Texas System.

**Table 2.** Failures and minor amputations in 105 patients with diabetic foot at the follow-up visit between 25 and 35 days after the first consultation

| Outcome | N | (%) |
|---|---|---|
| Primary failure | 16 | |
| Transtibial amputation | 2 | 13 |
| Transmetatarsal amputation | 6 | 37 |
| No reduction of the ulcer area | 3 | 19 |
| Lost to follow-up | 5 | 31 |
| Minor amputation | 51 | |
| Partial of toes or metatarsals | 45 | 88 |
| Total of toes | 6 | 12 |

well as those including all toes, occurred in patients belonging to grade III of the UTS. Figure 1 shows the evolution of lesions from selected patients. Table 3 shows the distribution according to the UTS classification of the 89 patients with salvaged feet (minus one patient without initial ulcerative lesions) and the epithelization of the ulcerative lesions at the 25–35-day follow-up. As shown, patients with more severe lesions resulted in significantly lower mean healing values.

Grouped by grades of the UTS, the 88 patients whose lesions are described in Table 3 were evaluated for complete epithelialization of ulcerative lesions (from the original cohort, we did not include patients with primary failure and one patient graded 0 who received the amputation proposal for suffering pain from "poor circulation").

Forty-one patients (39%) received initial oral antimicrobial treatment, with 13 patients from the hospitalized group and 28 from the nonhospitalized group. Monotherapy with ceftibuten was the most common prescription (17, 42%) followed in frequency by monotherapy with quinolones (14, 34%). All of the 71 hospitalized patients received antibiotics; in 58 (82%), they were administered intravenously, with the combination of imipenem/clindamycin as the most frequently used treatment (22 patients, 38%), followed in frequency by monotherapy with levofloxacin (10 patients, 17%) and monotherapy with imipenem (seven patients, 12%); 19 patients were treated with combinations of quinolones, clindamycin, and fosfomycin. Initial glycemic control required insulin in 13 hospitalized patients (18%) and in six outpatients (18%).

By the intention-to-treat analysis at the 25–35-day visit, 89 patients (85%) avoided major amputation, and 16 (15%) were considered as primary failures because of major amputation (eight cases, 50%), no improvement of ulcers (three cases, 19%), or lost to follow-up (5 cases, 31%). All of the primary failures belonged to grades II or III of the UTS; the specific salvage rate for these groups was 84%. Overall, 51 patients (49%) underwent minor amputations. Table 2 shows high-level and minor amputations in more detail. All of the high-level amputations, as



**Figure 1.** From top to bottom, the evolution of three selected patients. The left column corresponds to the initial conditions; the right column represents days 120, 270, and 270, respectively. (1) Diabetic foot IIIB (see text for classification); (2) diabetic foot IIIB; and (3) diabetic foot IIIB that underwent transmetatarsal amputation and it was analyzed as a failure, although the patient regained functionality.

**Table 3.** University of Texas Scale classification for 88 patients with salvaged feet and improvement of their ulcerative lesions at the follow-up visit between 25 and 35 days after the first consultation

| | | Grade | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | I | | II | | III | | |
| Stage | $n$ | Epithelialization mean (%) | $n$ | Epithelialization mean (%) | $n$ | Epithelialization mean (%) | | $F, p$ |
| A | 8 | 82 | 2 | 50 | 3 | 43 | | |
| B | 4 | 45 | 15 | 45 | 40 | 40 | | |
| C | 4 | 73 | 3 | 63 | 4 | 30 | | |
| D | 1 | 35 | 0 | | 4 | 28 | | |
| Total | 17 | 68 | 20 | 49 | 51 | 39 | | 10.705, < 0.001 |

Median success for all grades was reached by day 120. By day 210, the success rate was 90% for group I, 100% for group II, and 80% for group III. By day 240, success rate was 90% for group III (Figure 2). Differences in curves of success were not statistically significant (log-rank test, $x^2 = 4.73$, $p = 0.094$).

### Patients lost to follow-up

All the patients lost to follow-up were residents from distant communities. We tried to reach by telephone those lost to primary follow-up. To the best of our knowledge, no patient died as a consequence of foot infection. Of the five patients lost to primary follow-up, we reached three: a 75-year-old female who survived after being submitted to transtibial amputation in her community, a 76-year-old male who healed and regained functionality, and a 65-year-old male who survived after transtibial amputation in his community. We could not reach two additional patients, an 85-year-old female and an 84-year-old female; both were in regular clinical conditions when last seen at the first follow-up visit at 7 days.
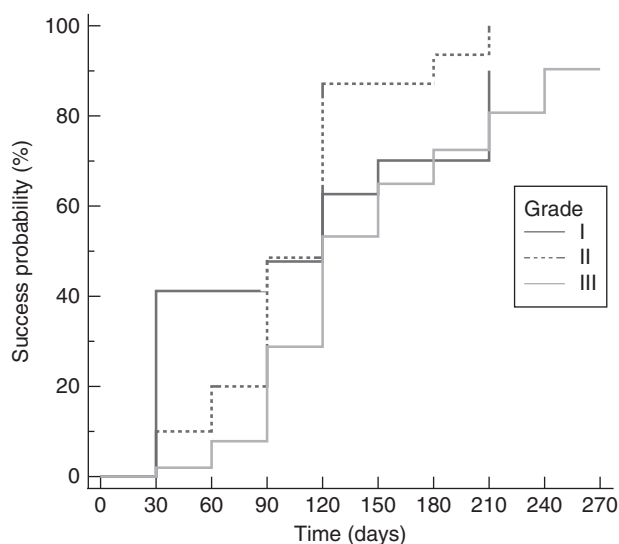


**Figure 2.** Kaplan–Meier analysis of complete ulcer epithelialization in 88 patients with diabetic foot.

## DISCUSSION

Our data show that an organized team, by just following a standard treatment, can save many limbs previously condemned to removal. We infer that there is a critical situation in which unnecessary amputation is a major social burden. Special attention should be given to the enormous psychological, physical, and economic burden to patients, not to mention the high risk of amputation of the remaining foot and death in the immediate years following amputation.[1,2,17,18] Human resources being more important than technical ones, our model of a team following basic principles is reproducible wherever there is a modest healthcare setting. Unfortunately, even in the proper setting, there is often a lack of devoted personnel, with critical tasks relegated to unprepared personnel.[19]

Amputation is frequently recommended as a relatively simple procedure to cover healthcare deficiencies.[9,20] Many patients lost their feet while seeking alternative therapies that did not attend to the fundamentals. Honest scientific efforts toward "adjunctive" therapies are in development, such as the use of recombinant growth factors, larval debridement therapy, skin substitutes, hyperbaric oxygenation, and wound-dressing agents.[21–24] In compliance with our current standard treatment, we do not use these new therapies.[25] In our experience, after 30 days of proper treatment, patients and heath care personnel may notice the trend toward salvage or amputation. Nevertheless, 1 month is not always enough to make a final decision, as chronic ulcers may go for much longer periods without an amputation.

Our salvaging plan is focused on debridement, pressure alleviation, metabolic control, and antibiotics. Accordingly, we recognize potential limitations to our inferences as international practice guidelines may recommend other potentially valuable interventions.[26] First, we often drive the initial selection of antibiotics by costs or availability, as many patients bring their own drugs from previous hospitalizations. Currently, however, no single antibiotic regimen has shown superiority over others.[27] Being aware of the diverse microbiota, we believe that, at least for chronic diabetic foot, the prognosis rests mostly on the surgical debridement, pressure alleviation, and metabolic control. Second, regarding osteomyelitis, we use clinical diagnosis only and we favor surgical resection or curettage of affected areas; in our experience, the medical approach produces disappointing results, in addition to

the prolonged use of antibiotics and high costs. Nevertheless, the treatment of osteomyelitis is a contested topic,[28,29] and medical treatment may theoretically reduce the need for minor amputations. Finally, we do not offer revasculariztion procedures, which could accelerate the recovery and even rescue some feet.[26] Even considering these potential weaknesses, our study is unique because it contains, to the best of our knowledge, the biggest cohort of diabetic feet with a formal amputation proposal in the medical literature. We believe that the poor care that our cohort had received reflects the circumstances in other settings, and that effective care for diabetic foot is no more difficult to perform than poor care.

We conclude that (1) even feet with severe damage can be salvaged with conventional treatment, and (2) there is a high rate of unnecessary major amputation recommendations in settings similar to the one that we report in the present study. If our sample represents, as we think it does, the global population of patients with diabetic foot, there is a serious lack of knowledge regarding the prognosis of patients treated by a team working with elements available almost anywhere. Practitioners of teams treating diabetic foot may benefit by audits to compare their results against expected results.

## ACKNOWLEDGMENT

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