ORIGINAL RESEARCH Prognosis of the outcome of severe diabetic foot ulcers with multidisciplinary care

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Background: Approximately 2-4% of individuals worldwide with diabetes mellitus have foot ulcers. This study aims to assess the factors affecting the outcomes of severe foot ulcers in diabetic individuals.

Methods: An analytical prospective cohort study was conducted from March 1st, 2015, to March 1st, 2017. A total of 34 individuals was selected. The study included patients with foot ulcers below the ankle who were at risk of amputation. All tests used a <5% level of significance and confidence interval of 95%. A Pearson's chi-squared test and binary multiple regression were performed to assess the factors related to healing.

Results: Only 11.7% of the individuals required amputation; ulcers classified as 2/B according to the University of Texas Diabetic Foot Ulcer Classification System healed before the 1/B ulcers. Neuropathic ulcers were the most prevalent (58.8%); 61.8% healed after 1 year. Most of the individuals were overweight, 47.1% had reduced glomerular filtration rates, and 78.8% had glycated hemoglobin >7%. Body mass index and osteomyelitis were the two significant variables in logistic regression.

Conclusions: In this study, osteomyelitis was the main complication related to the risk of amputation, and elevated body mass index and osteomyelitis were the significant factors that induced a slower healing time.

Keywords: diabetes mellitus, diabetic foot, diabetes complications, multidisciplinary care

Introduction

The worldwide incidence of foot ulcers in individuals with diabetes mellitus is approximately 2-4%; the cumulative incidence throughout life is 25%, and the prevalence is 4–10%.^{1,2} Additionally, people with diabetes are 15 to 40 times more likely to require lower-leg amputation compared to the general population.³

Neuropathy and peripheral artery disease are the main underlying diseases that may result in foot ulcers, which are a common complication of infection.^{4,5} Foot ulceration that results in amputation hinders the quality of life while increasing morbidity and mortality; in addition, the treatment is expensive.⁶ The lifetime risk for foot ulceration in people with diabetes is 15-25%.

In Brazil, which has a population of 7.12 million individuals with type II diabetes, an estimated 484,500 individuals present with ulcers, of whom it is estimated that approximately 81,000 require amputation each year and many will progress to death.5

Foot ulcers are considered chronic and their progress and healing depend on the correlation of several factors, such as age, the presence of infection, necrosis, peripheral artery disease, other comorbidities, deficient immune responses, and

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social factors such as self-care.^{7,8} In light of the increased prevalence of diabetes in Brazil and the consequent increase in complications, including the risk of ulceration, that require management in which nurses play a key role, this study aims to assess the factors influencing the outcomes of foot ulceration in diabetic individuals.

Methods

Design, setting, and patient characteristicsDesign, setting, and patient characteristics

An analytical prospective cohort study was conducted from March 1st, 2015, to March 1st, 2017, in a center specializing in diabetic foot care, in Brasília, Brazil. The study included individuals with type II diabetes who were over 18 years old and had foot ulcers below the ankle that were classified under the Texas classification as either serious or infected, with a risk of osteomyelitis/amputation, proceeding from emergency or primary care. The following were excluded: individuals with venous ulcers, multiple ulcers, cancer, or neurological diseases and/or who were taking corticosteroids or immunosuppressants.

Data collection and measures

A total of 41 individuals was selected for the study, of whom 4 abandoned treatment and 3 died, leaving 34 individuals. In this work, a simple random sampling scheme, without replacement, was used to estimate populational proportions. The sample size was calculated with a sampling error of 5%. While the annual incidence of total ulcers in the population was 4%, we estimated a rate of 2% at this specialized level and calculated a sample size of 32 patients.

These patients were treated by a multidisciplinary team made up of an endocrinologist, neurologist, nutritionist, nurse and psychologist. Ulcers were evaluated according to the recommendations of the International Consensus on Diabetes, which uses the Texas Ulcer Classification as a standard. In this consensus, the ulcers were evaluated according to depth, vascular insufficiency, and infection.⁹

Protective plantar sensation was evaluated using Semmes-Weinstein monofilament testing (10 mg), vibration sensation with a 128-Hz tuning fork, thermal sensation with the handle of a tuning fork, and the Achilles reflex with a rubber hammer. To identify the risk of Peripheral Artery Disease, the Ankle-Brachial Index (ABI) was calculated using a manual continuous wave Doppler. The evaluation of the ulcer was undertaken by the researcher and by trained nurses. Frequent debridement of nonviable tissue was undertaken by the nurses. Surgical interventions were only used in deep ulcers. Ulcer monitoring was carried out weekly in this center, with medication review, tissue evaluation and photographs.

The ulcers were also classified as neuropathic (absence of protective plantar sensation) ischemic (ABI below 90, or absence of a pulse), or neuro-ischemic.¹⁰ Infection was diagnosed based on IWGDF⁴ recommendations after considering the clinical characteristics and markers such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR). All the patients had a plain radiograph of the foot and, in the event of suspected osteomyelitis, magnetic resonance imaging was undertaken, although the Probe-to-Bone test was used for diagnosis of osteomyelitis.⁴ Regarding management of the ulcer, negative pressure therapy was used in individuals whose ulcers were deeper and with exudate. The patients were followed over a two-year period, although the cutoff period for assessment of healing or amputation was 1 year. Healing was defined as the restoration of tissue over 2 consecutive evaluations. Other clinical findings were also studied, such as weight and waist circumference. The reference parameters for BMI were classified as normal (18.50-24.99), overweight (≥25.00), pre-obese (25.00–29.99), obese (>30.00), obese class I (30.00-34.99), obese class II (35.00-39.99), and obese class III (≥ 40.00).^{11,12} The Cockcroft-Gault equation was used to estimate glomerular filtration.¹³

Multidisciplinary approach

All clinical patients referred to the Referral Center for diabetes and diabetic foot care were classified as a priority because they were considered to be at potential risk of amputation.

Usually, these patients came from primary care and emergency care.

All of the involved professionals had more than 5 years of experience in that health unit.

The first analysis was performed by the physicianendocrinologist and the nurse, who assessed the risk of amputation of the patient.

The evaluation was comprehensive and involved performing screening tests for the diagnosis of neuropathy, diagnosis of peripheral arterial disease, as well as ulcer management, including cleaning and debridement, treatment, classification by the Texas scale, blood tests and X-rays or RNM of the foot.

Subsequently, the patients were referred to the nutritionist and psychologist. The nutritionist performed the nutritional diagnosis and orientation in an individualized way, recorded the anthropometric measures, and calculated the Body Mass Index (BMI).

The psychologist carried out the psychotherapeutic and psychoeducational accompaniment, stimulating adherence to the treatment.

Referrals to other specialists, such as social service, vascular surgery, etc., were performed as needed.

The evaluations of each professional were shared through the electronic medical record.

Subsequently, the team discussed the patient's clinical data and adopted behavior to elaborate the plan of care, respecting the patient's reality, expectations, and preferences for better adherence to treatment, which were focused on self-care.

Health education was carried out in a monthly group format with ulcer patients, with at least ten meetings planned annually.

While the contents were not predetermined, they were discussed previously with the patients and their families, to motivate more protagonism and adherence to treatment.

The contents were varied and included the prevention of complications, measures of promotion, self-care, counting of carbohydrates, and prevention of depression, among others.

The management of and approach to the ulcer were performed weekly, the nutritional evaluation was performed monthly, and the psychological follow-up was performed bimonthly.

After being discharged because the ulcers healed, the patients returned monthly to the diabetic-foot outpatient clinic because they were classified as being at high risk of reulceration.

If the final outcome was amputation, the patient was referred to the vascular surgery outpatient clinic because they were post-surgical and needed to be followed by another team.

Despite the weaknesses that the center's service presents, we can highlight positive factors, such as the patient's immediate acceptance into the center, team expertise, regular and multiprofessional follow-up, permanent health education with active participation of the patients and families, that were determining factors for amputation avoidance (Figure 1).

Data analysis

The study was divided into data description, tests of association and multiple logistic regression. The level of significance used in this study was 5%. The quantitative variables are presented as minimum values, maximum values, means and standard deviations (Table 2). The chisquared test with a Monte Carlo simulation was used to assess possible associations between the Texas scale, osteomyelitis and healing (<1 year and >1 year). The variable of healing time did not present with a normal distribution per the Kolmogorov-Smirnov statistical test (*p*-value <0.001), so the nonparametric Kruskal-Wallis test was used to compare the healing time in each Texas scale category (Figure 2). Finally, multiple binary logistic regression was undertaken (Table 4).

Ethical considerations

This work was approved by the ethics committee of the Health Sciences Education and Research Foundation, Brazil, under Certificate n. 943,133. This work was conducted in accordance with the Helsinki Declaration, and all participants signed a written informed consent form.

Results

The study started with 41 individuals, but 4 left during the study follow-up, and 3 passed away; the final sample had 34 individuals (Table 1).

The most frequent ulcers encountered were those classified as 2/B according to the Texas classification, which are infected wounds with exposure of the tendon and capsules, although 64.7% of the patients did not have osteomyelitis. In 90.6% of the cases, antibiotics were used due to the high prevalence of infection. A minority of the patients required amputation and 45.5% had reulceration at a different location of the foot. Neuropathic signs, such as dry skin, fissures, mycoses, and deformities, were prevalent on all patients. There was a greater prevalence of overweight (41.2%) and class II obesity (20.6%), and 47.1% of the patients presented with a slightly reduced glomerular filtration rate.

The quantitative variables are presented with the minimum, maximum, mean, and standard deviation (Table 2).

The mean healing time was 10 months and 21 days. The GFR was mildly decreased in 47.1% of the patients; the mean GFR was 88.24. In 53.1% of the patients, the hemoglobin level was below the reference values, which is a sign of anemia. The mean glycated hemoglobin was

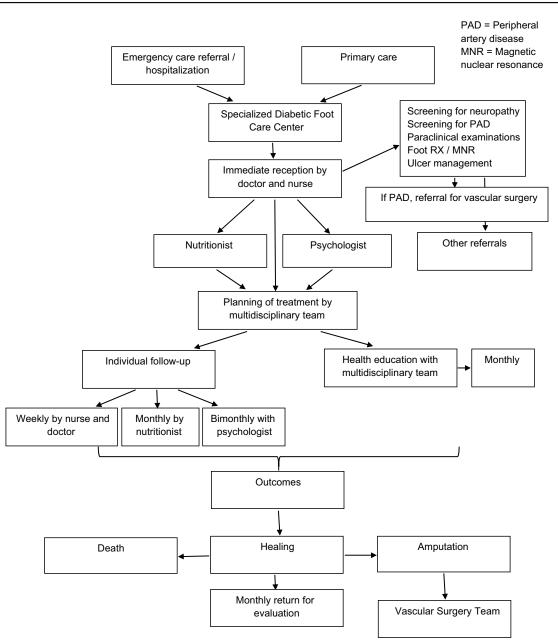
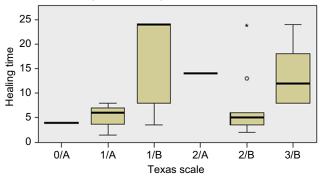
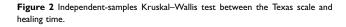


Figure 1 Flowchart of multidisciplinary approach.



Independent-Samples Kruskal-Wallis Test



8.13%, and 78.8% of the patients had a glycated hemoglobin level above the mean normal value for glycated hemoglobin (7%). However, most of the patients had desirable total cholesterol (61.3%), desirable triglycerides (60.7%), and optimal LDL (60.7%), but low HDL (70.4%), because they were already undergoing treatment.

The deformities investigated were cavus foot, Charcot foot, valgus foot, and claw toes; 47.6% of the individuals did not have any deformity, 26.4% had claw toes, 11.76% had Charcot foot, and 14.7% had valgus foot and other deformities. Overall, 90.1% of the individuals were treated with antibiotics, while 88.2% had mixed microbiota. The

| Table I Sociodemographic and clinical variables of the individuals with foot ulcers in a referral center for diabetes in Brasilia, Brazil, |
|--|
| 2015–2017 (Total sample, N=34) |

| Variable | n | n Absent % Variable | | Variable | n | Absent | % | |
|-----------------------|------------------|---------------------|------|--|----|---------------------------------------|------|--|
| Work | rk Osteomyelitis | | | | | | 1 | |
| Active | 20 | 0 | 58.8 | Yes | 12 | 0 | 35.3 | |
| Retired | 14 | | 41.2 | No | 22 | | 64.7 | |
| Schooling | | | | Previous ulcer | | | | |
| Elementary | 17 | 0 | 50 | Yes | 21 | 0 | 61.8 | |
| High School | 15 | | 44.1 | No | 13 | | 38.2 | |
| Higher Ed. | 2 | | 5.9 | Healing | | | | |
| Lives alone | | | | <1 year | 13 | 0 | 38.2 | |
| Yes | 4 | 0 | 11.8 | >l year | 21 | | 61.8 | |
| No | 30 | | 88.2 | Debridement | | | | |
| Comorbidities | | | | Yes | 33 | 0 | 97.1 | |
| Yes | 31 | 0 | 91.2 | No | 1 | | 2.9 | |
| No | 3 | | 8.8 | Amputation | | | | |
| Previous amputation | | | | Yes | 4 | 0 | 11.7 | |
| Yes | 9 | 0 | 26.5 | No | 30 | | 88.3 | |
| | | | | Reulceration | | | | |
| | | | | Yes | 15 | 1 | 45.5 | |
| | | | | No | 18 | | 54.5 | |
| No | 25 | | 73.5 | Use of antibiotics | | | | |
| Previous examination | | | | Yes | 30 | 1 | 90.1 | |
| Yes | 16 | 0 | 47.1 | No | 3 | | 9.09 | |
| No | 18 | | 52.9 | Dry skin, fissures, callosity | | | | |
| Place of the ulcer | | | | Yes | 28 | 0 | 82.4 | |
| Calcaneus | 1 | 0 | 2.9 | No | 6 | | 17.6 | |
| Dorsum | 2 | | 5.8 | Mycosis | | | | |
| Metatarsus | 13 | | 38.2 | Yes | 16 | 0 | 47.1 | |
| Toes | | | 32.3 | No | 18 | | 52.9 | |
| Midfoot | 7 | | 20.6 | Deformities | | | | |
| | | | | Yes | 18 | 0 | 52.9 | |
| Use of insulin | | | | No | 16 | | 47.1 | |
| Yes | 16 | 0 | 47.1 | Loss of protective plantar sensitivity | | | | |
| No | 18 | | 52.9 | | | | | |
| Smoking | | | | Yes | 30 | 0 | 88.2 | |
| Yes | 4 | 0 | 11.8 | No | 4 | , , , , , , , , , , , , , , , , , , , | 11.8 | |
| No | 30 | ľ | 88.2 | BMI | | | | |
| Use of alcohol | | | 00.2 | Normal | 6 | 0 | 17.6 | |
| Yes | 111 | 0 | 32.4 | Overweight | 14 | , , , , , , , , , , , , , , , , , , , | 41.2 | |
| No | 23 | ľ | 67.6 | Class I obesity | 6 | | 17.6 | |
| Ulcer classification | 25 | | 07.0 | Class II obesity | 7 | | 20.6 | |
| Without complications | 3 | 0 | 8.8 | Class III obesity | Í | | 2.9 | |
| Neuropathic | 20 | ľ | 58.8 | Glomerular filtration rate | | 0 | 2.7 | |
| Neuroischemic | | | 32.4 | Normal | 12 | 0 | 35.3 | |
| ABI | 1 | | 52.4 | Slightly reduced | 16 | | 47.1 | |
| Ischemic | 111 | 0 | 32.3 | Moderately reduced | 3 | | 8.8 | |
| Normal | 10 | ľ | 29.4 | Severely reduced | | | 2.9 | |
| Calcification | 13 | | 38.2 | Renal Insufficiency | 2 | | 5.9 | |
| Texas classification | 13 | | 30.2 | | | | 3.7 | |
| 0/A | | 0 | 2.9 | | | | 1 | |
| 0/A 1/A | | | | | | | 1 | |
| | 4 | | 11.8 | | | | 1 | |
| I/B | 8 | | 23.5 | | | | | |

(Continued)

Table I (Continued).

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| Variable | n | Absent | % | Variable | n | Absent | % |
|----------|----|--------|------|----------|---|--------|---|
| 2/A | I | | 2.9 | | | | |
| 2/B | 13 | | 38.2 | | | | |
| 3/B | 7 | | 20.6 | | | | |

Notes: ABI was categorized as ischemia (<0.90), normal (0.90–1.30), and calcification (>1.30); BMI was classified as normal (18.50–24.99), overweight (\geq 25.00), pre-obesity (25.00–29.99), obesity (>30.00), class I obesity (30.00–34.99), class II obesity (35.00–39.99), and class III obesity (\geq 40.00); GFR (ml/min/1.73 m²) was categorized as normal (\geq 90), slightly reduced (60–89), moderately reduced (45–59), severely reduced (15–29), and renal Insufficiency (<15). **Abbreviations:** ABI, ankle-brachial index; BMI, body mass index; GFR, glomerular filtration rate.

| Variables | Minimum | Maximum | Mean | Standard deviation |
|------------------------------|---------|---------|--------|--------------------|
| Age | 31.00 | 80.00 | 58.85 | 11.19 |
| Time since diagnosis (years) | 0.67 | 35.00 | 15.64 | 9.83 |
| Healing time (months) | 1.50 | 24.00 | 10.21 | 7.88 |
| Initial BMI | 21.61 | 45.71 | 29.18 | 6.19 |
| Final BMI | 21.00 | 45.62 | 29.92 | 5.86 |
| Waist circumference | 73.00 | 140.20 | 101.79 | 17.17 |
| ABI | 0.00 | 2.50 | 1.18 | 0.51 |
| GFR | 12.60 | 211.50 | 88.24 | 45.57 |
| Hemoglobin | 8.70 | 28.50 | 12.88 | 3.49 |
| Red blood cells | 8.30 | 315.00 | 45.50 | 49.78 |
| Platelets | 122.00 | 785.00 | 290.34 | 118.20 |
| HbAlc | 4.50 | 10.70 | 8.13 | 1.37 |
| Total cholesterol | 88.00 | 264,00 | 178.29 | 45.77 |
| CRP | 0.40 | 24.00 | 5.01 | 5.88 |
| Triglycerides | 70.00 | 334.00 | 143.43 | 69.12 |
| LDL | 17.00 | 209.00 | 93.86 | 51.37 |
| HDL | 28.00 | 245.00 | 57.70 | 42.50 |

Table 2 Clinical and laboratory data of individuals with foot ulcers in a referral center in Brasilia, Brazil, 2015–2017

Abbreviations: BMI, body mass index; ABI, ankle-brachial index; GFR, glomerular filtration rate; HbAIc, glycated hemoglobin; CRP, C-reactive protein; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

most common medications used were carbamazepines, including ertapenem and meropenem, in addition to cipro-floxacin associated with clindamycin. Only 11.7% of the individuals took antibiotics for gram-positive organisms (cephalexin and benzetacil).

Although most of the patients (23) had an increase in BMI during the study, there was no significant statistical difference between the initial and final values (p-value=0.060); the test used was the Wilcoxon test for paired samples.

The chi-square test was used to assess the association of the Texas scale with osteomyelitis and healing (<1 year and >1 year); there was no statistically significant correlation (osteomyelitis, *p*-value=0.074; healing, *p*-value=0.081). This means that the Texas scale was not different for groups with or without osteomyelitis and with healing times <1 year or >1 year. The healing time was also compared based on all levels of the Texas scale (Figure 2). This analysis showed that there was a statistically significant difference in the healing time between at least two levels of the Texas scale (p-value=0.036). There was a significant difference between patients with 1/B and 2/B ulcers (p-value=0.048), in which the healing time was significantly higher for the patients classified as 1/B in relation to those classified as 2/B. There was no significant difference among the other groups.

The relationship of several variables with amputation (yes or no) and healing (<1 year and >1 year) was also investigated, and the odds ratio was calculated. The Pearson chi-square test was used to evaluate the association between the variables. Only osteomyelitis and amputation had a statistically significant association (p-value=0.023), which means that patients with osteomyelitis required significantly more amputations. No patient with osteomyelitis

| | Healing (<i or="" year=""></i> | l year) | Amputation (yes or no) | | |
|--|---------------------------------|---------|------------------------|---------|--|
| Variables | Odds ratio | p-value | Odds ratio | p-value | |
| Lives alone | - | 0.260 | - | 1.000 | |
| Previous amputation | 0.376 | 0.397 | 1.048 | 1.000 | |
| Osteomyelitis | 0.268 | 0.158 | - | 0.023 | |
| Previous ulcer | 0.343 | 0.267 | - | 0.290 | |
| Mycosis | 1.061 | 0.934 | 1.231 | 1.000 | |
| Deformities | 0.779 | 0.724 | 0.271 | 0.550 | |
| Loss of the protective plantar sensitivity | 0.500 | 0.974 | - | 1.000 | |
| Glycated hemoglobin | 0.833 | 1.000 | 0.818 | 0.872 | |

Table 3 Factors associated with risk of healing (<1 year and >1 year) and amputation (yes or no) among individuals with foot ulcers ina referral center in Brasilia, Brazil, 2015-2017

required amputation; therefore, the odds ratio was not calculated (Table 3).

After the selection of variables, 2 explicit and significant variables remained: BMI and osteomyelitis. The odds ratio for BMI was 1.113, while for osteomyelitis it was 0.107. We can interpret this as meaning that with each increase in one unit of BMI, the patient presents with a 1.113 higher probability of their ulcer taking more than one year to heal. Osteomyelitis (categorical variable) was divided as yes (1) or no (2). Therefore, patients without osteomyelitis (2) presented with 0.107 times greater chance of taking more than one year to heal the foot, which means mathematically the inverse; that is, patients with osteomyelitis (1) had a 1/0,107=9.34 higher

 Table 4 Logistic regression analysis of the healing response (<1 year and >1 year) in individuals with foot ulcers in a referral center in Brasilia, Brazil, 2015–2017

| Logistic regression | with all varia | | | - | - | | | |
|----------------------|----------------|------------|-------|----|-------|-----------------------|-------------------|--------|
| | В | SE | Wald | df | Sig. | Exp(B) | 95% CI for EXP(B) | |
| | | | | | | | Lower | Upper |
| Age | -0.010 | 0.058 | 0.032 | 1 | 0.859 | 0.990 | 0.883 | 1.110 |
| Lives alone | 42.526 | 29,228.190 | 0.000 | 1 | 0.999 | 2.94*10 ¹⁸ | 0.000 | |
| Amputation | -0.604 | 1.816 | 0.111 | 1 | 0.739 | 0.546 | 0.016 | 19.192 |
| TEXAS classification | 0.623 | 0.574 | 1.178 | 1 | 0.278 | 1.865 | 0.605 | 5.749 |
| Osteomyelitis | -1.127 | 1.319 | 0.730 | 1 | 0.393 | 0.324 | 0.024 | 4.297 |
| BMI | 0.190 | 0.110 | 2.982 | 1 | 0.049 | 1.210 | 1.065 | 1.502 |
| Previous ulcer | 0.319 | 1.464 | 0.047 | 1 | 0.828 | 1.375 | 0.078 | 24.263 |
| Mycosis | -0.363 | 1.227 | 0.087 | 1 | 0.767 | 0.696 | 0.063 | 7.705 |
| Deformities | -0.770 | 1.420 | 0.294 | 1 | 0.588 | 0.463 | 0.029 | 7.490 |
| LPPS | 20.868 | 24,173.348 | 0.000 | 1 | 0.999 | 1.15*10 ⁹ | 0.000 | |
| ABI | 0.007 | 1.707 | 0.000 | 1 | 0.997 | 1.007 | 0.035 | 28.597 |
| Ulcer classification | 0.163 | 1.705 | 0.009 | 1 | 0.924 | 1.176 | 0.042 | 33.279 |
| HbAlc | -0.376 | 0.437 | 0.741 | 1 | 0.389 | 0.687 | 0.292 | 1.616 |
| Constant | -107.242 | 79,617.266 | 0.000 | 1 | 0.999 | 0.000 | | |
| Backward stepwis | e regression | | | | | | | |
| | В | SE | Wald | df | Sig. | Exp(B) | 95% CI for EXP(B) | |
| | | | | | | | Lower | Upper |
| Osteomyelitis | -2.238 | 0.899 | 6.193 | 1 | 0.013 | 0.107 | 0.018 | 0.622 |
| BMI | 0.107 | 0.048 | 5.010 | 1 | 0.025 | 1.113 | 1.013 | 1.222 |

Abbreviations: BMI, body mass index; LPPS, loss of protective sensation; ABI, ankle-brachial index; HbA1c, glycated haemoglobin; B, beta; SE, standard error; Wald, wald test; Sig., statistical significance; Exp(B), exponential beta; CI, confidence index.

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probability of their foot ulcer taking more than a year to heal in relation to those without osteomyelitis.

Discussion

This study, conducted in a referral center, shows that despite adverse situations hindering self-care, such as low education level, deep ulcers and decompensated diabetes, it is possible to avoid amputations when care is provided by a multidisciplinary team specialized in the care of the foot. Only 12.1% of the patients required amputation in association with osteomyelitis. The multidisciplinary approach is a key factor in decreasing reulceration and thus reducing the amputation rates, as previous studies have demonstrated.^{14,15} In 61.8% of the cases, the healing time was longer than 1 year. The average healing time was 10 months and 21 days, and 45.5% of the patients had reulceration in this period. Reulceration has been reported previously,^{16,17} and its incidence varies from 42% to 77.03%, regardless of the use of adequate shoes.^{17,18} Other studies suggest that individuals with peripheral neuropathy and previous ulceration present with a rise in plantar pressure when compared with patients with neuropathy but with no history of ulceration, which may explain the reulceration.¹⁹

The most frequent site of ulcers in this study was the metatarsus, followed by the toes. In the TEXAS classification, 2/B ulcers, with exposure of the tendon and capsules, were the most common infection. The healing time was significantly higher for the patients with more superficial ulcers without exposure of the tendon and capsules (Texas 1/B) when compared to more severe cases, such as 2/B. This may be due to foot discharge, a key point in self-care, since individuals with superficial ulcers may not take the necessary rest and continue to wear inappropriate shoes. On the other hand, individuals with larger ulcers presented better diabetes selfcare management and rest because of their higher risk of amputation. The more severe ulcers (2/B and 3/B) were treated with vacuum therapy since patients had more exudate. Previous research has demonstrated the efficacy of this therapy in chronic foot ulcers²⁰ because it improves the growth of granulation tissue and reduces edema, bacterial growth and infection, thus decreasing the risk of amputation.^{21,22} In addition to increasing tissue perfusion, this technology encourages rest and foot discharge because it hinders walking.23

In order to manage the ulcerations, weekly surgical debridement was performed on almost every patient by trained nurses. A requirement for ulcer healing is the distribution of pressure and adequate debridement.²⁴ When performed systematically, debridement is probably as important as the suspension of plantar pressure to reduce the inflammatory reactions of a wound.¹⁶ A randomized study has reported a significantly higher healing rate in centers where surgical debridement was performed.²⁵ In this study and in other research conducted in Brazil, ulceration was more prevalent among men (64.7%), which may be related to an active life as family providers and, consequently, to a lower attendance of medical appointments and worse control of the disease and the wound.²⁶

Most of the patients were at risk of ulceration because they had already been diagnosed with neuropathy. Therefore, they lacked protective plantar sensation and deformities, which are key aspects of ulceration, and other signs, such as dry skin, fissures, and callosities. Neuropathic ulcers were the most prevalent, followed by neuro-ischemic ulcers (ABI below 0.90). Multicenter studies in Latin America and other countries have also demonstrated the prevalence of neuropathic ulcers,²⁶ in contrast with European multicenter studies where ischemic or neuroischemic ulcers were the most prevalent.²⁷ Peripheral artery disease was less frequent than neuropathy; 32.4% of the individuals had neuro-ischemic ulcers with ABI <0.90. In the Eurodiale multicenter study, 50% had peripheral artery disease, and 12% had critical ischemia.²⁶

The infection diagnosis was clinical and also based on non-specific inflammatory markers, such as ESR and CRP, which were used for laboratory monitoring, mainly in cases of osteomyelitis. An elevated ESR or CRP indicates sensitivity to bone infection; however, evidence is still scarce, and there is no consensus about laboratory capacity for the diagnosis of osteomyelitis;²⁸ therefore, osteomyelitis was diagnosed with magnetic resonance imaging. Given that the majority of the participants in this study were outpatients, ertapenem was prevalent because it can be used in outpatient care and has a broad spectrum; other surgically.²⁹ studies have treated osteomyelitis Amputations were associated with osteomyelitis, and the risk of amputation for patients with osteomyelitis was 3.625 times greater than for those without osteomyelitis. This result differs from a retrospective study that described the depth of the wound as a predictive factor.²⁶ Another prevalent factor found in this investigation was that an increase of one unit in BMI was associated with a 1.113 times higher probability of a patient's foot ulcer taking longer than one year to heal. Although no study considering this outcome was found, it is known that individuals

with increased BMI and waist circumference are at higher risk for heart diseases and mortality.^{30,31}

Although all the individuals in this study were followed by a nutritionist, most of them had gained weight by the end of the study. The gain was not significant and may have been influenced by the recommendation of absolute rest and time off work. A retrospective study has shown that patients with ulcers and neuropathy have higher mortality from ischemic heart disease.³² An HbA1c level <7% is an international recommendation to avoid ulceration;²³ however, in this study, the average HbA1c was 8.13%, similar to the findings of other research. Other studies have found that HbA1c levels above the goal (>9) are an independent risk factor for reulceration. Most of the patients, however, did not receive insulin. Intensified glycemic control may decrease amputations and microvascular diseases, but there is no evidence that it reduces mortality.33 Despite the overweight rates, the lipid and triglyceride levels of most of the patients were normal because they were undergoing medical treatment.

Limitations

This study presented two limitations. The first is related to the restricted number of participants involved. Despite the relevant information collected and the prospective followup, we cannot exclude the possibility that the results could vary with a larger sample size. The second limitation is that the study was conducted in the only specialized center that offers care to diabetic patients with foot ulcers in the city of Brasília. This means that certain sociodemographic characteristics and specific diseases may vary according to each region of the country, although people assisted in this center come from different locations, including other states.

Despite these limitations, this was the first prospective study using this approach that was performed in the city of Brasília. All the data collected assisted our team in identifying the factors that may influence the outcome of ulceration and the need to strengthen specialized teamwork.

Conclusion

Although some outcomes were present, such as low education level, infection, neuropathic ulcer, uncontrolled blood glucose levels, and reduced glomerular filtration rate, only 11.8% of the patients in this study required amputations. The more complex ulcers healed earlier, which may be related to more advanced therapy in the management of the wounds and better self-care, due to the risk of amputation. Osteomyelitis was the only complication related to the risk of amputation and – with raised body mass index – was significantly related to a delay in healing. The mean healing time was 10 months, although 61.8% healed after one year. In spite of the factors that limited healing, it is possible to state that having a multidisciplinary team specialized in caring for the diabetic foot is essential for avoiding amputations, as, in spite of there being deep and complex ulcers, few patients required amputation.

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Author contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

- Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. *Lancet*. 2005;366 (9498):1719–1724. doi:10.1016/S0140-6736(05)67528-9
- Lipsky BA, Aragon-Sanchez J, Diggle M, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. *Diabetes Metab Res Rev.* 2016;32(Suppl 1):45–74. doi:10.1002/dmrr.2699
- 3. Canadian Association of Wound Care (Wounds Canada). Foundations of Best Practice for Skin and Wound Management: Best Practice Recommendations for the Prevention and Management of Diabetic Foot Ulcers. North York: Wounds Canada; 2018. 68. Available from: https://www.woundscanada.ca/ docman/public/health-care-professional/bpr-workshop/895-wc-bprprevention-and-management-of-diabetic-foot-ulcers-1573r1e-final /file. Accessed November 8, 2018.
- Markakis K, Bowling FL, Boulton AJ. The diabetic foot in 2015: an overview. *Diabetes Metab Res Rev.* 2016;32(Suppl 1):169–178. doi:10.1002/dmrr.2740
- Oliveira JEP, Vencio S. [Guidelines of the Brazilian Diabetes Society: 2014–2015]. Oliveira JEP, Vencio S, editors. São Paulo: AC Pharmaceuticals; 2016. Portuguese.
- Boulton AJ. The pathway to foot ulceration in diabetes. *Med Clin* North Am. 2013;97(5):775–790. doi:10.1016/j.mcna.2013.04.001
- 7. Guo S, DiPietrio LA. Factors affecting wound healing. *J Dent Res.* 2010;89(3):219–229. doi:10.1177/0022034510366903

- Grigoropoulou P, Eleftheriadou I, Jude EB, Tentolouris N. Diabetic foot infections: an update in diagnosis and management. *Curr Diab Rep.* 2017;17(1):3. doi:10.1007/s11892-017-0902-3
- Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. *Diabetes Care*. 1998;21(5):855–859.
- Hao D, Hu C, Zhang T, Feng G, Chai J, Li T. Contribution of infection and peripheral artery disease to severity of diabetic foot ulcers in Chinese patients. *Int J Clin Pract.* 2014;68(9):1161–1164. doi:10.1111/ijcp.12440
- World Obesity [homepage on the Internet]. *About Obesity*. London: World Obesity Federation; c2015. Available from: https://www.worl dobesity.org/what-we-do/aboutobesity/. Accessed March 8, 2017.
- Brazilian Society of Diabetes (BSD). [Tripartite Official Positioning N° 01/2016 SBD/SBEM/SBN: Diagnosis and Therapeutic Management in Diabetes Kidney Disease]. São Paulo: SBD; 2017. Available from: http://www.diabetes.org.br/publico/images/posiciona mento-sbd-sbem-sbn.pdf. Accessed November 8, 2018. Portuguese.
- WHO. Obesity: Preventing and Managing the Global Epidemic. Report on a WHO Consultation on Obesity, Geneva. June 3–5, 1997. WHO/NUT/NCD/98.1. Technical Report Series Number 894. Geneva: World Health Organization; 2000.
- Aydin K, Isildak M, Karakaya J, Gürlek A. Change in amputation predictors in diabetic foot disease: effect of multidisciplinary approach. *Endocrine*. 2010;38(1):87–92. doi:10.1007/s12020-010-9352-2
- Jeong EG, Cho SS, Lee SH, et al. Depth and combined infection is important predictor of lower extremity amputations in hospitalized diabetic foot ulcer patients. *Korean J Intern Med.* 2018;33 (5):952–960. doi:10.3904/kjim.2016.165
- Pound N, Chipchase S, Treece K, Game F, Jeffcoate W. Ulcer-free survival following management of foot ulcers in diabetes. *Diabet Med.* 2005;22(10):1306–1309. doi:10.1111/dme.2005.22.issue-10
- Bus SA, Waaijman R, Arts M, et al. Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. *Diabetes Care*. 2013;36(12):4109–4116. doi:10.2337/ dc13-0996
- Chu YJ, Li XW, Wang PH, et al. Clinical outcomes of toe amputation in patients with type 2 diabetes in Tianjin, China. *Int Wound J.* 2016;13(2):175–181. doi:10.1111/iwj.12249
- Fernando ME, Crowther RG, Pappas E, et al. Plantar pressure in diabetic peripheral neuropathy patients with active foot ulceration, previous ulceration and no history of ulceration: a meta-analysis of observational studies. *PLoS One.* 2014;9(6):e99050. doi:10.1371/ journal.pone.0099050
- 20. Dzieciuchowicz L, Kruszyna L, Krasiński Z, Espinosa G. Monitoring of systemic inflammatory response in diabetic patients with deep foot infection treated with negative pressure wound therapy. *Foot Ankle Int.* 2012;33(10):832–837. doi:10.3113/FAI.2012.0832
- 21. Hassan R, Mohammad-Hadi SM, Gholam HK, et al. Comparison of vacuum-assisted closure and moist wound dressing in the treatment

of diabetic foot ulcers. J Cutan Aesthet Surg. 2013;6(1):17–20. doi:10.4103/0974-2077.110091

- 22. Liu S, He CZ, Cai YT, et al. Evaluation of negative-pressure wound therapy for patients with diabetic foot ulcers: systematic review and meta-analysis. *Ther Clin Risk Manag.* 2017;13:533–544. doi:10.2147/ TCRM.S131193
- 23. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. *J Vasc Surg.* 2016;63(2Suppl):3S–21S. doi:10.1016/j.jvs.2015.10.003
- Dumville JC, Hinchliffe RJ, Cullum N, et al. Negative pressure wound therapy for treating foot wounds in people with diabetes mellitus. *Cochrane Database Syst Rev.* 2013;(10):CD010318.
- 25. Steed DL, Donohoe D, Webster MW, Lindsley L. Effect of extensive debridement and treatment on the healing of diabetic foot ulcers: Diabetic Ulcer Study Group. J Am Coll Surg. 1996;183(1):61–64.
- 26. Parisi MCR, Neto AM, José M, Saad A. Baseline characteristics and risk factors for ulcer, amputation and severe neuropathy in diabetic foot at risk: the BRAZUPA study. *Diabetol Metab Syndr.* 2016;8:25. doi:10.1186/s13098-016-0126-8
- Prompers L, Huijberts M, Apelqvist J, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. *Diabetologia*. 2007;50(1):18–25. doi:10.1007/ s00125-006-0491-1
- Malhotra R, Shu-Yi Chan C, Nather A. Osteomyelitis in the diabetic foot. *Diabet Foot Ankle*. 2014;5(1):24445. doi:10.3402/dfa.v5.24445
- 29. Ulcay A, Karakas A, Mutluoglu M, Uzun G, Turhan V, Ay H. Antibiotherapy with and without bone debridement in diabetic foot osteomyelitis: a retrospective cohort study. *Pak J Med Sci.* 2014;30 (1):28–31. doi:10.12669/pjms.306.5684
- 30. Carmienke S, Freitag MH, Pischon T, et al. Comment on 'General and abdominal obesity parameters and their combination in relation to mortality: a systematic review and meta-regression analysis'. *Eur J Clin Nutr.* 2013;67(6):573–585. doi:10.1038/ejcn.2013.134
- 31. Finucane MM, Stevens GA, Cowan M, et al. National, regional, and global trends in body mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011;377 (9765):557–567. doi:10.1016/S0140-6736(10)62037-5
- 32. Chammas NK, Hill RLR, Edmonds ME. Increased mortality in diabetic foot ulcer patients: the significance of ulcer type. *J Diabetes Res.* 2016;2016(2879809):7. doi:10.1155/2016/2879809
- 33. Hemmingsen B, Lund SS, Gluud C, et al. Targeting intensive glycaemic control versus targeting conventional glycaemic control for type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2011;15(6): CD008143.

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