

## Evolution after toe amputation related to diabetic foot

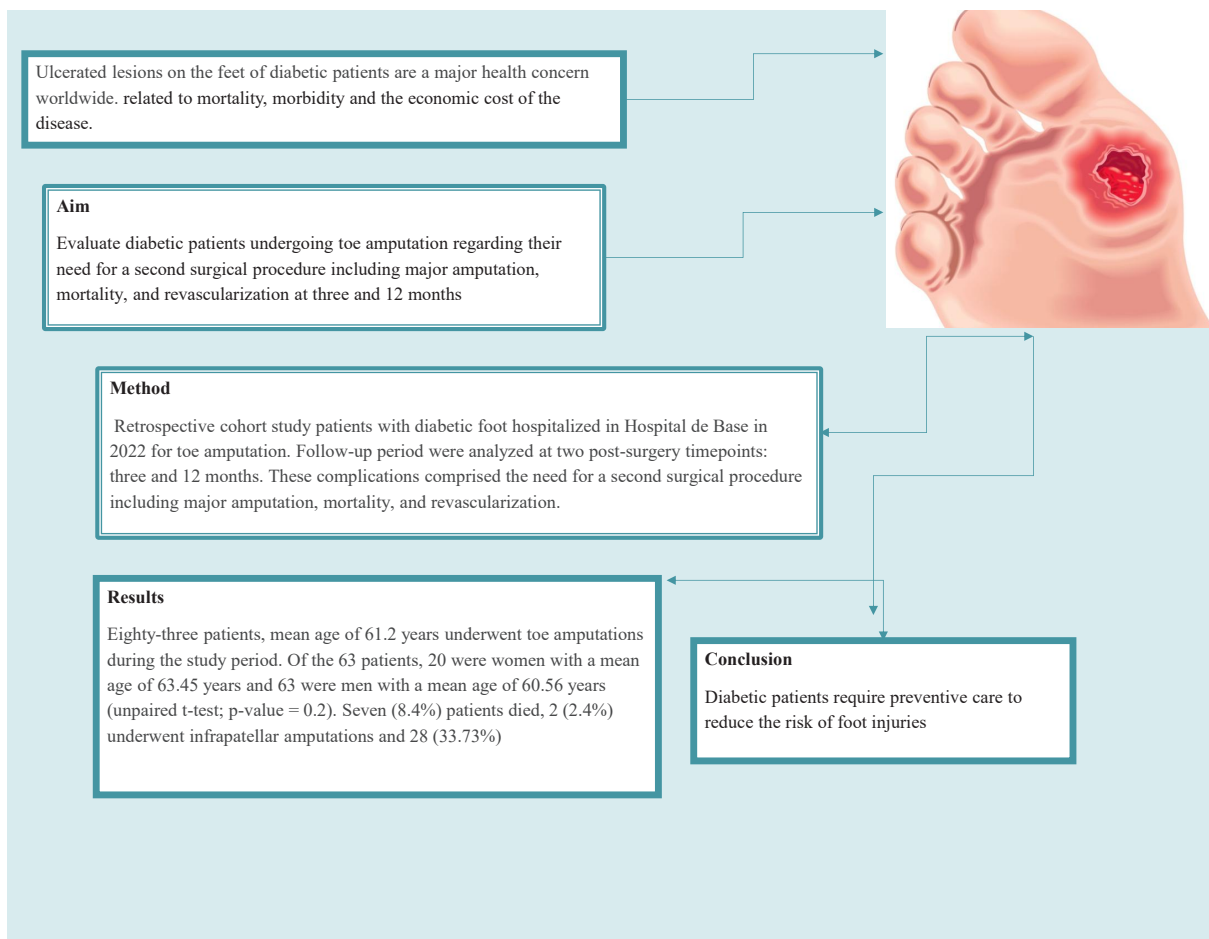
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### Graphical Abstract



## Abstract

Ulcerated lesions on the feet of diabetic patients are a major health concern worldwide. They are responsible for the greatest burden related to mortality, morbidity and the economic cost of the disease. The objective of this study was to evaluate diabetic patients undergoing toe amputation regarding their need for a second surgical procedure including major amputation, mortality, and revascularization at three and 12 months of follow-up as well as glycated hemoglobin levels. A retrospective cohort study was performed evaluating the evolution of consecutive patients with diabetic foot hospitalized in *Hospital de Base* in 2022 for toe amputation. Complications and glycated hemoglobin levels in the follow-up period were analyzed at two post-surgery timepoints: three and 12 months. These complications comprised the need for a second surgical procedure including major amputation, mortality, and revascularization. Eighty-three patients with an overall mean age of 61.2 years underwent toe amputations during the study period. Of the 63 patients, 20 were women with a mean age of 63.45 years and 63 were men with a mean age of 60.56 years (unpaired t-test; p-value = 0.2). Seven (8.4%) patients died, 2 (2.4%) underwent infrapatellar amputations and 28 (33.73%) were submitted to revascularization during this period. Glycated hemoglobin levels ranged from 6.9-14.2% with a mean of 9.2%. Diabetic patients require preventive care to reduce the risk of foot injuries and rapid treatment of wounds, prioritizing a vascular assessment to check whether the blood flow is sufficient to heal lesions with adequate infection control using bacterial wound cultures and antibiograms.

**Keywords:** Diabetes. Amputation. Follow-up. Diabetic Foot.

## INTRODUCTION

Ulcerated lesions on the feet of diabetic patients are a major health concern worldwide. They are responsible for the greatest burden related to mortality, morbidity and the economic cost of the disease<sup>1</sup>. Constant monitoring of diabetic patients with a view to provide preventive guidance against injuries is recommended, even for those at low risk, in order to avoid the principal complication, diabetic foot<sup>2</sup>. However, there are few long-term studies on amputation after a diagnosis of osteomyelitis in diabetic patients, even though these patients have higher rates of lower limb amputation and hospital readmission, longer hospitalization, and higher 2-year mortality rates<sup>3</sup>.

The main factors used to assess lesions related to diabetic foot in the clinical practice emphasize neurological changes, peripheral arterial disease and infection<sup>4</sup>. An accurate assessment of peripheral arterial disease in patients with diabetes and foot ulceration is important, so that the best interventions can be defined, including the need for revascularization.

Non-invasive tests are available but there is no consensus on the most useful test

or the accuracy of these investigations<sup>5</sup>. The clinical diagnosis of a soft tissue infection in diabetic foot based on local or systemic signs and symptoms of inflammation and suspicion of osteomyelitis, is essential<sup>6</sup>. One literature review reported that the most useful non-invasive tests to inform about the probability of healing are skin perfusion pressure  $\geq 40$  mmHg, toe pressure  $\geq 30$  mmHg and transcutaneous oxygen pressure (TcPO<sub>2</sub>)  $\geq 25$  mmHg. Ankle pressure  $< 50$  mmHg, an ankle-brachial index (ABI)  $< 0.5$ , toe pressure  $< 30$  mmHg and TcPO<sub>2</sub>  $< 25$  mmHg predicts major amputation<sup>7</sup>.

When suspected, a positive probe-to-bone test and an erythrocyte sedimentation rate test are recommended, as the results of these exams can clearly indicate suspicion of diabetic foot osteomyelitis. Bacterial cultures of the wound or bone samples and plain x-rays remain the first-line tests<sup>8</sup>. The objective of this study was to evaluate diabetic patients undergoing toe amputation regarding their need for a second surgical procedure including major amputation, mortality, and revascularization at three and 12 months of follow-up as well as glycated hemoglobin levels.

## METHOD

### *Patients and setting*

A retrospective cohort study was performed evaluating the evolution of consecutive patients with diabetic foot, who underwent toe amputation.

The medical records of diabetic patients who underwent toe amputation in 2022 at *Hospital de Base* in São Jose do Rio Preto were revisited. Data related to age, sex, and complications, such as the need for a second surgical procedure including major amputation, mortality, and revascularization at three and 12 months were collected as were data on glycated hemoglobin levels.

The inclusion criteria were consecutive diabetic patients who underwent toe amputation.

Non-diabetic and trauma patients undergoing toe amputation were excluded from the study.

### *Statistical analysis*

Data were tabulated in an Excel spreadsheet and descriptive statistical analysis was performed. Data are reported as absolute numbers, means and percentages with differences being compared using the unpaired t-test and Fisher's exact test. Statistical significance was defined as an alpha error of 5% (p-value <0.05).

### *Ethical considerations*

The study was approved by the research ethics committee (CEP) in Medicine School of Sao Jose do Rio Preto-FAMERP-Brazil # 5.012.332.

## RESULTS

Eighty-three patients with a mean age of 61.2 years underwent toe amputation during the study period. Of the 83 patients, 20 were women with a mean age of 63.45 years and 63 were men with a mean age of 60.56 years (unpaired t-test; p-value = 0.2). Seven (8.4%) patients died, 2 (2.4%) underwent infrapatellar amputations and 28 (33.73%) were submitted to revascularization during this period (Table 1). Glycated hemoglobin levels ranged from 6.9-14.2% with a mean of 9.2%.

Four (20%) of the 20 women returned to the vascular surgery service within three months for a second surgical procedure; two other female patients had orthopedist consultations and one consulted a cardiologist. Between three and 12 months,

three (15%) patients returned to the vascular surgery service for procedures related to foot infections, totaling seven (35%) during one year of follow up. Ten (50%) required limb revascularization, four of whom underwent two procedures each and there were two deaths (Table 1).

Of the 63 male patients, 14 (22.22%) had new surgical interventions for foot infections within three months and 17 (26.9%) were submitted to second procedures in the period covering 3-12 months after the first surgery. Eighteen (28.5%) of these required revascularizations and 13 (20.6%) further amputations: 11 (17.4%) of toes and two (3.1%) amputations below the knee. Five (7.9%) men died within the first post-surgery year.

**Table 1** - Number of vascular readmissions, revascularizations, mortalities and major amputations due to diabetic foot. Hospital de Base-Sao Jose do Rio Preto/2020.

Second interventions	Female (n = 20)	Male (n = 63)	Total (n = 83)	P Value*
	n (%)	n (%)	n (%)	n (%)
3 months post-surgery	4 (20)	14 (22.2)	18 (21.7)	P= 0.86
3-12 months post-surgery	3 (15)	17 (26.9)	20 (24.1)	P= 0.2
Revascularization	10 (50)	18 (10)	28 (33.7)	P= 0.09

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... continuation - Table 1.

Second interventions	Female (n = 20)	Male (n = 63)	Total (n = 83)	P Value*
	n (%)	n (%)	n (%)	n (%)
Death	2 (28.5)	5 (7.9)	7 (8.4)	P= 0.7
Leg amputation	0	2(3.1)	2 (2.4)	

Fisher's exact test p-value\*.

## DISCUSSION

The present study reports the evolution and complications during the first three months and from 3-12 months after toe amputations in diabetic patients. Specific evaluations of the need for further surgical procedures including major amputation and revascularization, the mortality rate and measurement of glycated hemoglobin levels in the first year of follow up were not found in the literature, however one study evaluating the risk factors that led to amputation within two years was identified<sup>3</sup>.

There are three important factors in critical clinical practice associated with ulcers on the feet of diabetic patients: neuropathy, ischemia and infection. Neuropathies are responsible for skin lesions that these patients often do not realize have occurred. The main approach to neuropathies must be on an outpatient basis; in the case of a foot injury, the first step is to see whether there is sufficient circulation to heal the wound and, simultaneously, to evaluate possible infections using a bacterial wound culture and antibiogram.

Non-invasive exams should be the first choice in particular the ABI, toe blood pressure and transcutaneous oximetry. Data in the literature suggest that an ankle pressure <50 mmHg, ABI <0.5, toe pressure <30 mmHg or TcPO<sub>2</sub> <25 mmHg is predictive for the necessity of amputation<sup>7</sup>.

The Vascular Surgery Discipline of *Hospital de Base* has performed more than 10,000 major and minor amputations in 39 years. Routinely, in this service, an initial non-invasive assessment is made followed by imaging tests such as arterial duplex when necessary. When revascularization is a possible solution, tests such as arteriography are perfor-

med followed by an immediate endovascular or surgical intervention when indicated. We observed that in the clinical practice systolic pressure of >80 mmHg rarely leads to healing and when healing does occur it is very slow and can be aggravated by wound infections; the protracted length of this process is a worrying factor. A cure occurred in less than 5% of cases when the systolic pressure in the tibial arteries was <80 mmHg and systemic blood pressure was within the normal range (≤14 mmHg) (unpublished study).

The present study highlights the mandatory need for the first assessment to identify whether there is sufficient blood flow to heal the wound. Around 34% of patients in the current study required revascularization during this period. An ischemic wound can favor anaerobic infection, which increases mortality from around 2% after toe amputation to more than 22% (a study in press). Biopsies and wound cultures are mandatory to define the best therapeutic option.

Only two major amputations occurred in the present study suggesting successful revascularization and infection control. One-year mortality in these diabetic patients was 8.4%, close to that detected after toe amputations in general, but without other complications such as anaerobic infections in the service<sup>9-11</sup>.

Another aspect observed in diabetic patients is that, in most cases, they already have necrotic lesions of the ulcers and it is necessary to evaluate possible osteomyelitis by a simple X-ray of the foot as this type of infection can progress to amputation of the affected toe. Soft tissue, tendon and bone cultures are routinely collected to guide an-

tibiotic therapy.

The present study draws attention to the greater risk of diabetic patients losing parts of their extremities in some cases due to necrosis caused by trauma, ischemia or infection. Therefore, prevention measures such as primary care must be routine, even in patients who have good irrigation in their limbs. For more severely ill patients, where the neuropathy is more advanced, protection of the foot using special shoes adapted for each case is recommended. Consider hospitalizing all diabetics with severe infections, those with moderate, complex infections or with infections and associated significant morbidities and any with suspicion of osteomyelitis of the foot.

Another detail is the physical examination where the presence of a palpable pulse does not necessarily exclude the possibility of chronic arterial disease therefore, the ABI must be assessed and, if necessary, other complementary tests must be carried out.

In one of the authors' studies, 108 minor amputations were analyzed: 48 patents (44.44%) had only diabetes<sup>9</sup>, (12.5%) had only chronic arterial insufficiency and 52 (48.14%) had diabetes and chronic arterial insufficiency. Among the 80 major amputa-

tions, 16 patients (20%) had diabetes only, 38 (47.5%) had chronic arterial insufficiency alone, and 26 (32.5%) had both diabetes and chronic arterial insufficiency<sup>12</sup>. Hence chronic arterial disease is the major aggravating factor for diabetic patients. For this, preventing the progression of arteriosclerosis together with better control of diabetes is essential; in the present study, the glycated hemoglobin level was very high.

In relation to the treatment carried out in the service, in addition to surgical procedures, the usual dressings are used and, when necessary, a hyperbaric chamber is utilized. In respect to surgery, secondary intention healing is avoided, and the wound is constantly assessed. Antibiotic therapy was guided by wound cultures and antibiograms with the timing being defined by the infectious diseases of each patient.

The current guidelines state that when osteomyelitis is suspected, a standard radiography of the foot is the first-line imaging exam, and a bone biopsy should be performed for microbiological documentation. Histological analysis of the bone sample is no longer recommended. High doses of antibiotics are recommended in cases of confirmed osteomyelitis<sup>13</sup>.

## CONCLUSION

Diabetic patients require preventive care to reduce the risk of foot injuries and rapid treatment of wounds, prioritizing a vascular assessment to

check whether the blood flow is sufficient to heal lesions with adequate infection control using bacterial wound cultures and antibiograms.

### CRediT author statement

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All authors have read and agreed to the published version of the manuscript.

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