

Factors associated with amputation in people with foot ulcers as a consequence of Diabetes Mellitus

Fatores associados à amputação em pessoas com úlcera do pé decorrente do diabetes mellitus

Factores asociados a la amputación en personas con úlceras en los pies como consecuencia de la Diabetes Mellitus

Álvaro Sepúlveda Carvalho Rocha^I; Lídy Tolstenko Nogueira^{II}; Jefferson Abraão Caetano Lira^{III}; Sandra Marina Gonçalves Bezerra^{III}; Ana Maria Ribeiro dos Santos^I; Claudia Daniella Avelino Vasconcelos^I

^IUniversidade Federal do Piauí. Teresina, PI, Brasil; ^{II}Universidade Estadual do Ceará. Fortaleza, CE, Brasil;

^{III}Universidade Estadual do Piauí. Teresina, PI, Brasil

ABSTRACT

Objective: to analyze the factors associated with amputation in people with foot ulcers as a consequence of Diabetes *Mellitus*.

Methods: a cross-sectional and analytical study conducted with 132 individuals with Diabetes *Mellitus* hospitalized in an Emergency hospital. The data were collected by means of interviews and by checking medical records. The data analysis was performed using the following statistical tests: Pearson's chi-square, Fisher's exact, Mann-Whitney's U and binary logistic regression. **Results:** in the bivariate analysis, dry skin and/or cracks, onychocryptosis, interdigital maceration, calluses and cold, cyanotic and pale feet were associated with amputation ($p < 0.05$). In the multivariate model, the female gender was a protective factor against amputation ($p = 0.049$). The individuals with peripheral neuropathy were 34.98 times more likely to suffer amputations ($p = 0.005$); in turn, having a previous amputation history increased the amputation chances by 869.8 times ($p < 0.001$). **Conclusion:** amputation was associated with foot complications, biological sex, peripheral neuropathy and previous amputations.

Descriptors: Diabetes Mellitus; Foot Ulcers; Diabetes Complications; Surgical Amputation; Nursing.

RESUMO

Objetivo: analisar os fatores associados à amputação em pessoas com úlcera do pé decorrente do diabetes *mellitus*.

Método: estudo transversal analítico realizado com 132 pessoas com diabetes *mellitus* internadas em um hospital de urgência. Os dados foram coletados mediante entrevista e consulta em prontuário. A análise dos dados ocorreu por meio dos testes estatísticos Qui quadrado Pearson, Exato de Fisher, Mann-Whitney e regressão logística binária. **Resultados:** na análise bivariada, pele seca e/ou rachadura, onicocriptose, maceração interdigital, calosidades, pés frios, cianóticos e pálidos apresentaram associação com a amputação ($p < 0,05$). No modelo multivariado, o sexo feminino apresentou fator de proteção para amputação ($p = 0,049$). As pessoas com neuropatia periférica tiveram 34,98 mais chances de sofrerem amputação ($p = 0,005$) e possuir histórico de amputação anterior aumentou as chances de amputação em 869,8 vezes ($p < 0,001$). **Conclusão:** a amputação teve associação com complicações nos pés, sexo biológico, neuropatia periférica e amputação anterior.

Descritores: Diabetes *Mellitus*; Úlcera do Pé; Complicações do Diabetes; Amputação Cirúrgica, Enfermagem.

RESUMEN

Objetivo: analizar los factores asociados a la amputación en personas con úlceras de pe pie como consecuencia de la Diabetes *Mellitus*. **Método:** estudio transversal y analítico realizado con 132 personas que padecen Diabetes *Mellitus* internadas en un hospital de Urgencias. Los datos se recolectaron por medio de entrevistas y consultando historias clínicas. Se utilizaron las siguientes pruebas estadísticas para analizar los datos: Chi-cuadrado de Pearson, Exacta de Fisher, Mann-Whitney y Regresión logística binaria. **Resultados:** en el análisis bivariado, piel seca y/o grietas, onicocriptosis, maceración interdigital, callos y pies fríos, cianóticos y pálidos estuvieron asociados a la amputación ($p < 0,05$). En el modelo multivariado, pertenecer al sexo femenino representó un factor de protección contra la amputación ($p = 0,049$). Las personas con neuropatía periférica fueron 34,98 veces más propensas a sufrir amputaciones ($p = 0,005$), mientras que poseer antecedentes de amputaciones previas aumentó 869,8 veces las probabilidad de amputación ($p < 0,001$). **Conclusión:** la amputación estuvo asociada con complicaciones en los pies, sexo biológico, neuropatía periférica y antecedentes de amputaciones previas.

Descriptor: Diabetes Mellitus; Úlceras en los Pies; Complicaciones de la Diabetes; Amputación Quirúrgica, Enfermería.

INTRODUCTION

Foot ulcers as a consequence of Diabetes *Mellitus* are characterized by ruptures in the deepest foot tissues, favored by the neuropathy and peripheral arterial disease associated with Diabetes *Mellitus* complications. These conditions lead to sensitivity loss and to deficient circulation in the lower limbs, which favors infections and lesions that are easily worsened. Amputation is among the main complications of foot ulcers and is frequently caused by deep infections or by untreated ischemia¹.

At the global level, foot ulcers as a consequence of Diabetes *Mellitus* represent a relevant problem, preceding nearly 80% of all lower limb amputations in people with Diabetes *Mellitus*. It is estimated that 18.6 million people are

This study was financed in part by the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* – Brazil (CAPES); process number #88887.953478/2024-00.

Corresponding author: Álvaro Sepúlveda Carvalho Rocha. E-mail: alvaro_scr@hotmail.com

Editor in Chief: Cristiane Helena Gallasch; Scientific Editor: Thelma Spindola

affected by this complication every year, with approximately 20% of the severe cases evolving to amputation. The high frequency of these outcomes reflect difficulties in early diagnosis and in access to specialized treatments, especially in low- and middle- income countries².

Foot ulcers as a consequence of Diabetes *Mellitus* emerge as an important Public Health problem with a substantial impact on morbidity, mortality and assistance-related costs. A recent review estimates the lifetime ulcer risk at between 19% and 34% and signals inequalities in access to specialized services, determining factors for these cases to evolve to amputation. International guidelines³ recommend prevention by means of periodic screening, ulcer risk stratification and interventions to reduce plantar pressure.

The situation is worrisome in Brazil, as a significant increase in the number of foot ulcer complications is noticed, as identified between January and August 2023, period during which 6,982 Diabetes *Mellitus*-associated lower limb amputations were recorded, with a mean of 28 a day. In 2022, the country recorded 10,168 amputation procedures, representing a 3.9% increase in relation to the preceding year. Considering the procedures performed in the Unified Health System (*Sistema Único de Saúde, SUS*), this figure reached 31,190 in the same year, which equals nearly 85 amputations a day⁴.

The most common factors for foot ulcers to evolve to amputation include peripheral neuropathy, peripheral arterial disease, severe infections like osteomyelitis and gangrene, and inadequate glycemic control. In addition to that, not undergoing periodic clinical foot examinations, advanced age, smoking habit and absence self-care guidelines are factors associated with higher amputation risks^{5,6}.

Amputations impose important consequences such as reduced mobility, functional losses, dependence on care measures and worse quality of life; in addition, they are associated with high mortality rates, which can exceed 70% five years after major amputation procedures. Costs are also high for health services, as amputation procedures alone cost BR\$ 78.7 million to the SUS in 2022, with a mean of BR\$ 2,962 per surgery and without including expenses due to prolonged hospitalizations and rehabilitation^{2,4}.

The main strategy to avoid ulcers and amputations in people with Diabetes *Mellitus* is prevention. Periodic clinical foot examinations, self-care health education and early treatment of the first lesions are some of the recommended actions. Measures such as glycemic control, debriding, infection control and using pressure redistribution devices like total “contact casting” are fundamental. In addition, multiprofessional performance contributes significantly to reducing the number of amputations and improving clinical outcomes^{2,7}.

The World Health Organization (WHO) 2030 Agenda set forth the need to reduce inequalities and to promote health for all⁸. This study is justified because it provides aids for the assistance to be provided to people with Diabetes *Mellitus* and to assess public policies targeted at the following Sustainable Development Goals (SDGs): SDG 3 (Health and Well-Being), SDG 10 (Reduced Inequalities) and SDG 11 (Sustainable Cities and Communities). In addition to that, this study can be fundamental in evaluating the efficacy and scope of the National Policy for Diabetes Prevention and Comprehensive care for People with Diabetes *Mellitus*, instituted by Law No. 3,895 of 2019, as well as to offer aids to improve the care provided to people with Diabetes *Mellitus*⁹.

Despite the existence of countless studies on amputation risk factors in people with foot ulcers as a consequence of Diabetes *Mellitus*, there are gaps regarding the profile of the patients served in specialized Emergency hospitals and about the strength of the associations in high-complexity contexts. Identifying factors associated with amputation in these units may support devising immediate assistance strategies and prevention policies. Thus, the objective of this study was to analyze the factors associated with amputation in people with foot ulcers as a consequence of Diabetes *Mellitus*.

METHOD

This is a cross-sectional and analytical study conducted at the wards from an Emergency hospital from Teresina, Piauí, which is a reference in Traumatology and has 368 beds, distributed as follows: 270 wards for adults, 38 pediatric wards, 17 semi-intensive care beds, 33 intensive care beds for adults and 10 for children.

The population was comprised by 345 individuals with Diabetes *Mellitus* that had foot ulcers as a consequence of Diabetes *Mellitus* and were hospitalized in an Emergency hospital from the state of Piauí. The sample was calculated based on a proportional formula for finite populations, using a 95% confidence interval, maximum error of 5% and 50% assumed prevalence, totaling 132 participants. Sampling was of the non-probability and for convenience type.

The inclusion criteria were as follows: people with Type 1 or 2 Diabetes *Mellitus*, aged at least 18 old and hospitalized for the treatment of foot ulcers as a consequence of neuropathic, ischemic or neuroischemic Diabetes *Mellitus*. The subjects excluded were those with cognitive deficit as assessed by means of the Mini Mental State Examination. The independent variables were as follows: sociodemographic and clinical ones, self-care, foot

complications and aspects from the patients' current clinical condition. The dependent variable was "amputation due to foot ulcers as a consequence of Diabetes *Mellitus*".

The data were collected between October 2024 and January 2025 (encompassing 12 weeks in all), by means of semi-structured interviews and using an adapted form that addressed five domains: Sociodemographic aspects (Domain 1); Diabetes-associated clinical aspects (Domain 2); Self-care and foot ulcers as a consequence of Diabetes *Mellitus* (Domain 3); Aspects related to the clinical foot examination (Domain 4); and Aspects inherent to the patients' current clinical condition (Domain 5). Domains 1 and 2 were created based on the lower limb clinical evaluation form for the prevention of foot ulcers as a consequence of Diabetes *Mellitus*¹⁰. Domains 3 and 4 were created based on the Script for screening foot ulcers as a consequence of Diabetes *Mellitus* in Primary Health care prepared following the Brazilian Diabetes Society guidelines, with Domain 4 being put into practice while performing the physical examinations¹¹. Domain 5 was assembled by the authors based on the Amputee Care Guidelines¹².

It is noted that a pilot test was performed with the form using 10% of the sample, encompassing a total of 13 patients, who were discarded from the final sample. In addition to that, medical records were consulted to identify the patients and survey data referring to the clinical conditions related to foot ulcers as a consequence of Diabetes *Mellitus* (previous diabetic ulcers, previous amputations, neuropathy and ischemia) by means of a Data Use Commitment Form (DUCF). The interviews were conducted in the wards and at the patients' bedside, allowing a responsible companion to be present.

The data were tabulated in Excel 2019 by double typing to debug the database and correct errors and exported to the *Statistical Package for the Social Sciences* (SPSS), version 29.0, where descriptive and inferential statistical analyses were performed. Absolute and percentage frequencies were calculated for the categorical variables in the descriptive statistical analysis. Central tendency (mean and median), dispersion (standard deviation) and variability (minimum and maximum values) measures were employed for the numerical variables

The inferential analysis was carried out based on association tests such as Pearson's chi-square and Fisher's exact to associate the independent categorical variables with the categorical outcome one. Association strength was measured by means of the Odds Ratio, considering a 95% Confidence Interval. Kolmogorov-Smirnov's normality test was used to verify the distribution pattern corresponding to the numerical variables, which presented non-normal distribution. Thus, the Mann-Whitney test was employed to compare the numerical variables to the categorical outcome one.

A binary logistic regression model following the "stepwise forward" method was created in the multivariate statistical analysis, firstly introducing the variable with the highest statistical significance to subsequently do the same with the others, following the decreasing association order identified in the bivariate analysis. The criterion to include variables in the multivariate model corresponded to obtaining $p\text{-values} \leq 0.20$ in the bivariate analysis, as recommended by Katz (2003), as adopting this broader cutoff value avoids early excluding possible confounding factors and ensures that variables with potential epidemiological relevance are properly assessed in the adjusted model¹³.

Multicollinearity among the independent variables was identified with the Variance Inflation Factor (VIF), where values over four were adopted as cutoff for the VIF multicollinearity diagnosis¹⁴. Consequently, 18 variables were included in the multivariate model. Only 14 variables remained in the multivariate model after the multicollinearity analysis. $p\text{-values} < 0.05$ were considered significant for all the statistical tests used.

The study complied with National Health Council Resolution No. 466 from 2012 and was approved by a Research Ethics Committee (*Comitê de Ética em Pesquisa*, CEP). All the participants signed the Free and Informed Consent Form (FICF).

RESULTS

As for their sociodemographic characterization, the participants has a mean age of 63.72 years old ($SD \pm 12.82$), varying from 31 to 94, with predominance of the male gender (62.1%) and of individuals that had a partner (53.8%). Their mean number of children was 4.58 ($SD \pm 4.34$), with Complete Elementary School (34.8%) and retirement (59.8%) as the most frequent conditions; in addition, 81.1% earned monthly incomes of up to BR\$ 1,331.05.

In relation to the clinical aspects, all had a Type 2 Diabetes *Mellitus* diagnosis, with a mean time of 10 years since the disease was detected and oral hypoglycemic agents as the most frequently used treatment (50%). There was high incidence of comorbidities (83.3%), with Systemic Arterial Hypertension standing out (77.3%). As for life habits, 61.4% stated being smokers or former smokers for a mean time of 13 years and 70.5% current or previous alcohol consumption for nearly 15 years. The vast majority (92.4%) stated not having being diagnosed with Peripheral Obstructive Arterial Disease; in turn, peripheral neuropathy was detected in 56.8% of the cases, with a

mean evolution time of four years. It was also observed that 84.1% did not perform physical activity and that 74.2% presented altered blood glucose levels at hospital admission.

As for self-care, the mean evolution time of the foot ulcers as a consequence of Diabetes *mellitus* was three years. Most of the participants (71.2%) had never attended Nursing appointments in Basic Health units and 77.3% had not undergone any foot examination in this or other type of health care services. Foot care was aided in 87.9% of the cases, mainly by family members (82.6%). In turn, 68.2% had never been provided professional self-care guidelines, 99.2% did not use adapted shoes and 87.1% were not in the habit of walking barefoot (earthing).

In the physical examination, it was verified that 84.8% presented dry skin and cracks, 81.1% had onychocryptosis or improperly cut nails and 74.2% presented callouses. Absence of interdigital maceration was observed in 64.4% of the participants; in turn, 58.3% had no previous ulceration history. As for perfusion and color, 76.5% reported cold, cyanotic or ale feet and 56.8% presented erythema or edema. In addition, 83.3% had no previous amputation history.

In relation to the sociodemographic aspects, the female gender represented a protection factor against amputation (OR: 0.278; 95% CI: 0.105-0.732). However, marital status, schooling, occupation/profession and income were not associated with amputation ($p>0.05$). Regarding the clinical aspects, it was identified that individuals with peripheral neuropathy were 24.32 times more likely to suffer amputations. However, type of treatment, comorbidities, smoking habit, alcoholism, Peripheral Obstructive Arterial Disease, performing physical activity and blood glucose at admission did not present any association with amputation ($p>0,05$), as shown in Table 1.

Table 1: Association of the sociodemographic and clinical aspects of people with foot ulcers as a consequence of Diabetes *Mellitus* with amputation (n=132). Teresina, Piauí, Brazil, 2025.

Variables		Amputation		Unadjusted OR	95% CI	p-value
		Yes n (%)	No n (%)			
Marital status	With a partner	15 (21.1)	56 (78.9)	0.64	0.290-1.413	0.268*
	Without a partner	18 (29.5)	43 (70.5)			
Gender	Female	6 (12.0)	44 (88.0)	0.278	0.105-0.732	0.007*
	Male	27 (32.9)	55 (67.1)			
Schooling level	Illiterate	9 (26.5)	25 (73.5)	1.237	0.548-2.793	0.608*
	Can read and write	8 (25.8)	23 (74.2)			
	Complete Elementary School	14 (30.4)	32 (69.6)			
	Complete High School	2 (9.5)	19 (90.5)			
Occupation/Profession	Retired	21 (26.6)	58 (73.4)	1.237	0.548-2.793	0.608*
	Active/Working	12 (22.6)	41 (77.4)			
Income	Up to one minimum wage	26 (24.3)	81 (75.7)	0.731**		
	Up to two minimum wages	5 (25.0)	15 (75.0)			
	From three to five minimum wages	2 (40.0)	3 (60.0)			
Type of treatment	Insulin	3 (21.4)	11 (78.6)	0.256**		
	Oral medications	13 (19.7)	53 (80.3)			
	Insulin and oral medications	17 (32.7)	35 (67.3)			
Comorbidities	Yes	25 (22.7)	85 (77.3)	0.515	0.194-1.367	0.178*
	No	8 (36.4)	14 (63.6)			
Which coorbiditie(s)	Systemic Arterial Hypertension	24 (23.5)	78 (76.5)	0.317**		
	Others	1 (12.5)	7 (87.5)			
	Not applicable	8 (36.4)	14 (63.6)			
Smoker	Yes	21 (25.9)	60 (74.1)	1.138	0.503-2.572	0.757*
	No	12 (23.5)	39 (76.5)			
Alcohol consumption	Yes	27 (29.0)	66 (71.0)	2.25	0.846-5.985	0.099*
	No	6 (15.4)	33 (84.6)			
Peripheral Obstructive Arterial Disease	Yes	3 (30.0)	7 (70.0)	1.314	0.320-5.404	0.071**
	No	30 (24.6)	92 (75.4)			
Peripheral neuropathy	Yes	32 (42.7)	43 (57.3)	24.32	3.425-172.712	<0.001*
	No	1 (1.8)	56 (98.2)			
Performs physical activity	Yes	4 (19.0)	17 (81.0)	0.665	0.207-2.141	0.492*
	No	29 (26.1)	82 (73.9)			
Blood glucose at admission	Normal	8 (25.0)	24 (75.0)	0.712**		
	Altered	25 (25.5)	73 (74.5)			
	Not recorded	0 (0.0)	2 (100.0)			

Notes: *Pearson's chi-square test; **Fisher's exact test.

In relation to self-care and foot complications, not evaluating the feet in the Nursing appointments (OR: 2.571; 95% CI: 1.073-6,162), onychocryptosis or improperly cut nails (OR: 10.24; 95% CI: 1.328-78,968), interdigital maceration (OR: 4.103; 95% CI: 1.795-9,376), previous ulcer history (OR: 7.188; 95% CI: 2.910-17.753), callouses (OR: 3.152; 95% CI: 1.018-9.757) and presence of erythema/edema (OR: 3.657; 95% CI: 1.590-8.411) presented more amputation chances. In addition to that, having a previous amputation history increases the amputation chances 74.615 times. On the other hand, not presenting dry skin and/or cracks (OR: 0.705; 95% CI: 0.626-0,795) and not having cold/cyanotic/pale feet (OR: 0.673; 95% CI: 0.588-0.771) proved to be protective factors against amputation, as indicated in Table 2.

Table 2: Association between the aspects related to self-care and to foot complications in people with foot ulcers because of Diabetes *Mellitus* and amputation. Teresina, Piauí, Brazil, 2025. (n=132)

Variables		Amputation		Unadjusted OR	95% CI	p-value
		Yes n (%)	No n (%)			
Attended a Nursing appointment at the BHU	Yes	26 (27.7)	68 (72.3)	1.693	0.664-4.319	0.267*
	No	7 (18.4)	31 (81.6)			
Foot evaluation in the Nursing appointment	Yes	12 (40.0)	18 (60.0)	2.571	1.073-6.162	0.031*
	No	21 (20.6)	81 (79.4)			
Has help with foot care	Yes	31 (26.7)	85 (73.3)	2.553	0.549-11.880	0.356**
	No	2 (12.5)	14 (87.5)			
Who helps with foot care	Family members	29 (26.6)	80 (73.4)	0.309**		
	Friends	0 (0.0)	1 (100.0)			
	Caregiver	1 (16.7)	5 (83.3)			
	Health institution	1 (100.0)	0 (0.0)			
Self-care guidance from some health professional	Yes	11 (26.2)	31 (73.8)	1.097	0.474-2.538	0.829*
	No	22 (24.4)	68 (75.6)			
Dry skin and/or cracks	Yes	33 (29.5)	79 (70.5)	0.705	0.626-0.795	0.005*
	No	0 (0.0)	20 (100.0)			
Onychocryptosis or improperly cut nails	Yes	32 (29.9)	75 (70.1)	10.24	1.328-78.968	0.007*
	No	1 (4.0)	24 (96.0)			
Interdigital maceration	Yes	20 (42.6)	27 (57.4)	4.103	1.795-9.376	<0.001*
	No	13 (15.3)	72 (84.7)			
Previous ulcer history	Yes	25 (45.5)	30 (54.5)	7.188	2.910-17.753	<0.001*
	No	8 (10.4)	69 (89.6)			
Callouses	Yes	29 (29.6)	69 (70.4)	3.152	1.018-9.757	0.039*
	No	4 (11.8)	30 (88.2)			
Cold/Cyanotic/Pale feet	Yes	33 (32.7)	68 (67.3)	0.673	0.588-0.771	<0.001*
	No	0 (0.0)	31 (100.0)			
Presence of erythema/edema	Yes	22 (38.6)	35 (61.4)	3.657	1.590-8.411	0.002*
	No	11 (14.7)	64 (85.3)			
Used and/or uses adapted shoes	Yes	1 (100.0)	0 (0.0)	4.094	3.029-5.533	0.250**
	No	32 (24.4)	99 (75.6)			
Has the habit of walking barefoot (earthing)	Yes	7 (41.2)	10 (58.8)	2.396	0.830-6.917	0.132**
	No	26 (22.6)	89 (77.4)			
Previous amputation history	Yes	20 (90.9)	2 (9.1)	74.615	15.602-356.710	<0.001*
	No	13 (11.8)	97 (88.2)			

Notes: *Pearson's chi-square test; **Fisher's exact test.

As for the patients' current clinical condition, 63.6% had been hospitalized for more than 30 days, 25% had been subjected to foot amputation procedures (totaling 33 amputations as a consequence of foot ulcers), 73.5% did not present neuropathy in the other limb and 22% had their limb partially healed. The mean hospitalization time was 10.5 days (SD±19.2). In addition to that, a statistically significant difference was noticed between amputation and time since the Diabetes *Mellitus* diagnosis (p=0.005), as well as with time since peripheral neuropathy was detected (p=0.002), in the individuals with foot ulcers as a consequence of Diabetes *Mellitus*. In addition to that, having had the current problem for one month at the most (OR: 0.381; 95% CI: 0.151-0.961; p=0.037) was a protective factor for not being subjected to amputation procedures. In turn, having the other foot affected by neuropathy (OR: 368.125; 95% CI: 4.283-2,108.103; p<0.001) presented 368.125 more amputation chances. In addition to that, the foot healing stage at the collection moment was associated with amputation (p<0.001).

Table 3 shows the results for multivariate analysis.

Table 3: Logistic regression corresponding to the differences between sociodemographic/clinical variables, self-care and foot complications in people with foot ulcers as a consequence of Diabetes *Mellitus* in relation to amputation (n=132). Teresina, Piauí, Brazil, 2025.

Variables	Adjusted OR	95% CI	p-value
Gender			
Female	0.15	0.02-0.99	0.049
Peripheral neuropathy			
Yes	34.98	2.90-421.22	0.005
Foot evaluation in the Nursing appointment			
No	0.86	0.14-5.32	0.877
Dry skin and/or cracks			
No	0	0.00-0.00	0.998
Onychocryptosis or improperly cut nails			
Yes	63.96	0.28-1.47	0.292
Interdigital maceration			
Yes	0.23	0.26-2.15	0.202
Previous ulcer history			
Yes	0.79	0.08-7.73	0.843
Callouses			
Yes	0.39	0.04-3.79	0.418
Cold/Cyanotic/Pale feet			
No	0	0.00-0.00	0.997
Presence of erythema/edema			
Yes	1.22	0.19-7.88	0.829
Previous amputation history			
Yes	869.8	19.02-397.57	<0.001
Time since onset of the current problem			
One month at the most	3.85	0.71-20.82	0.117
Time since DM diagnosis (in years)	0.961	0.87-1.05	0.398
Time with ulcer(s) as a consequence of Diabetes Mellitus (in years)	1.04	0.81-1.33	0.744

Female gender represented a protection factor against amputations due to foot ulcers as a consequence of Diabetes *Mellitus* (ORa: 0.15; 95% IC: 0.02-0.99). In addition to that, the individuals with peripheral neuropathy were 34.98 times more likely to suffer amputations, whereas those with a previous amputation history presented 869.8 more chances of being subjected to another amputation.

DISCUSSION

In the multivariate model, female gender represented a protection factor against amputations in the foot as a consequence of ulcers. The higher amputation prevalence among men reflects differences in the self-care patterns between the genders, as women seek health services more frequently and adhere more to self-care measures whereas men tend to present more hospitalizations due to neglect. In this sense, a study analyzed the gender-related differences in clinical outcomes among patients with foot ulcers as a consequence of Diabetes *Mellitus* treated in a tertiary-level reference center and verified that belonging to the male gender was a negative predictive factor for healing time and mortality; in addition, men presented higher prevalence of comorbidities, previous ulcers and revascularization procedures¹⁵.

Not undergoing a foot evaluation in the Nursing appointment was one of the risk factors for amputation due to foot ulcers as a consequence of Diabetes *Mellitus* in the bivariate analysis, reinforcing the need to include this care measure in the assistance routine for people with Diabetes *Mellitus*. The International Work Group on foot ulcers as a consequence of Diabetes *Mellitus* recommends that people with diabetes and very low risk of foot ulcers are examined once a year for loss of plantar protective sensitivity and peripheral arterial disease; in turn, those at higher risk need to be evaluated more frequently depending on the risk factors for ulcers identified in the anamnesis and in the clinical foot examination¹⁶.

The association between peripheral neuropathy and amputation evidenced in this study reinforces recent findings that identify the former as one of the main predictors of foot ulcers as a consequence of Diabetes *Mellitus*. Peripheral neuropathy favors the loss of the protective sensation, resulting in repeated micro-traumas and ulceration. Systematized screening programs to identify plantar protective sensitivity, vascular evaluations and pressure relief

interventions (consisting in “off-loading”) are all recommended strategies to reduce the incidence of ulcers and of progression to amputation and are supported by international guidelines¹⁷.

Prevention and early treatment of foot complications such as dry skin and/or cracks, onychocryptosis, interdigital maceration, cold/cyanotic/pale feet and presence of erythema and edema are fundamental to reduce lower limb ulcers and amputations in people with Diabetes *Mellitus*, as foot complications were associated with amputation in the bivariate analysis. This evidences the importance of intensifying the self-care guidelines provided to these people, as a population-based study identified that 37.8% and 6% of the individuals with Diabetes *Mellitus* had complications and foot ulcers or amputations, respectively¹⁸.

Callouses are pre-ulcerative lesions that increased 3.15 times de amputation chances in the bivariate analysis. Thus, pressure relief techniques such as pressure redistribution shoes, load relief dressings, felt foam or padding, callous debridement, rest, using crutches, gait retraining, foot-related physical exercises and patient education are essential to prevent and treat callouses in people with Diabetes *Mellitus*¹⁹. Consequently, these technologies and care measures need to be accessible to the entire population to prevent and treat callouses, which would contribute to reducing foot ulcers.

Previous history of foot ulcers was associated with amputation, emphasizing that the monitoring strategies for these individuals with Diabetes *Mellitus* in Primary Health Care needs to be effective (including foot evaluations, risk stratification and screening of foot complications) for the assistance provided to these people can be suitable, timely, fast and resolute. A systematic review conducted in China found that a history of ulcers presenting Wagner grades over 3 and peripheral vascular disease were the main risk factors associated with the incidence of amputation in Chinese patients with diabetes, reinforcing the need for preventive care measures²⁰.

In Guatemala, age, time since the diabetes diagnosis and previous ipsilateral amputations were associated with lower limb amputation procedures related to infections in foot ulcers as a consequence of Diabetes *Mellitus*, corroborating the results of this study, where time since the Diabetes *Mellitus* diagnosis and amputation history were associated with amputation, evidencing the urgent need to implement programs for Diabetes *Mellitus* control adherence and foot care²¹.

Early treating foot ulcers is indispensable to prevent complications, as having had the current problem for one month at the most was a protective factor against being subjected to an amputation procedure in the bivariate analysis. A study conducted in Finland identified that major amputations, wound ischemia and advanced age reduced overall survival after a foot ulcer as a consequence of Diabetes *Mellitus* and that survival after five years of a major amputation was 8.3%; this underscores the importance of early managing wounds and ischemia to prevent severe complications, which contributes to improving life expectancy and quality in people with Diabetes *Mellitus*²².

Time since the peripheral neuropathy diagnosis and having the other foot affected by this condition were associated with amputation in the bivariate analysis, which evidences the severity of peripheral neuropathy as a risk factor for more severe complications. Oftentimes silent, neuropathy leads to a significant sensitivity loss in the feet, increasing the probability of lesions that result in amputations if not properly treated. A study evidenced that neuropathy, peripheral arterial disease, high post-prandial blood glucose and low hemoglobin were more significant predictive factors for amputation, showing the relevance of periodic examinations for the clinical monitoring of people with Diabetes *Mellitus*²³.

The foot healing stage at the collection moment was associated with amputation in the bivariate analysis, reinforcing that inadequate or slow ulcer healing is a predictor of more severe complications, such as the need for amputations. The healing process quality is directly influenced by glycemic control, presence of infections and adequate care measures; as such, constant monitoring is crucial to improve clinical outcomes. A study conducted in Piauí in the Primary Health Care context identified that fewer foot complications were a protective factor against developing foot ulcers as a consequence of Diabetes *Mellitus* and that inadequate control of the capillary blood glucose levels, unwillingness to take care of the feet and not undergoing frequent foot examinations were risk factors for developing ulcers, underscoring the importance of self-care²⁴.

The treatment for foot ulcers as a consequence of Diabetes *Mellitus* requires interdisciplinary assistance. In addition to that, the evolution in the healing process for these ulcers requires systematized assistance, duly qualified professionals and availability of resources like special supplies and dressings suitable to the characteristics of the lesions and to the healing process stages, which contributes to reducing healing times and to enhancing full healing, rendering hospitalization time shorter and lowering costs. A retrospective cohort study that analyzed the patients' evolution after a toe amputation related to foot ulcers as a consequence of Diabetes

Mellitus found that patients with this disease require fast wound treatment and prioritization of the vascular evaluation to verify if blood flow is sufficient for wound healing, with the purpose of optimizing and easing healing of foot ulcers in people with Diabetes *Mellitus* and prevent amputation²⁵.

The risk factors for amputation in patients with foot ulcers as a consequence of Diabetes *Mellitus* are multiple and frequently inter-related, such as peripheral neuropathy, peripheral arterial disease and previous ulcer history as consistent predictors of unfavorable outcomes, including amputation. In this context, the loss of plantar protective sensitivity caused by peripheral neuropathy eases the appearance of micro-traumas, which can evolve to ulceration, infection and amputation if not identified early in time. The IWGDF guidelines reinforce the importance of systematically screening plantar protective sensitivity and peripheral arterial disease as part of the risk stratification strategy to prevent foot ulcers and, consequently, reduce the number of lower limb amputations²⁶.

In the multivariate model, the patients with peripheral neuropathy had 34.98 more amputation chances, emphasizing the relevance of clinical foot examinations to screen plantar protective sensitivity, deformities and skin dryness, which are signs and symptoms of impairment in the autonomic, motor and sensitive fibers in peripheral diabetic polyneuropathy. In this context, when assessing the foot ulcer risk in people with Diabetes *Mellitus* in Primary Health Care, a study identified that the patients with dry skin, deformities and altered ankle reflexes and vibration perceptions in the hallux were more likely to presenting foot ulcers²⁷.

In addition to the association between neuropathy and amputation, amputation history and long-standing pre-existing ulcers are predictors of subsequent amputations in patients with foot ulcers as a consequence of Diabetes *Mellitus*, highlighting the need for early interventions and ongoing monitoring in individuals with previous complications²⁸. The presence of peripheral neuropathy combined with systemic factors such as extended time since the diabetes diagnosis and vascular comorbidities intensify the risk of progression to amputation, which demands a more detailed analysis of these risk factors, emphasizing the importance of Nursing assistance in Primary Health Care in early identifying risk factors, during longitudinal follow-up, in health education and in implementing preventive strategies targeted at reducing the number of foot complications in people with Diabetes *Mellitus*²⁹.

Having a previous amputation history also increased the reamputation chances 869.8 times in the multivariate model, which underscores the importance of paying attention to healing of the surgical wound and of rehabilitating these people resorting to orthoses, prostheses, adapted shoes and self-care guidelines. In this sense, a systematic review with meta-analysis verified that educational technologies (especially the soft-hard and hard ones) were a protective factors to prevent the incidence of lower limb amputations in people with Diabetes *Mellitus* and that they can be a powerful health education resource for self-care, with the objective of preventing foot complications³⁰.

Proper and ongoing management of foot ulcers should encompass integrated ulcer prevention strategies, structured health education programs and adaptation of therapeutic devices such as adapted shoes, orthoses and insoles, aiming at reducing plantar pressure and at improving gait, which would contribute to reducing the number of recurrent foot complications and lower the incidence of amputations. Thus, these care measures need to be implemented in a comprehensive and multiprofessional way, including vascular evaluation, skin care and ongoing self-care education³¹, with the objective of reducing the incidence of ulcers and amputations in the feet as a consequence of Diabetes *Mellitus*.

Study cross-sectional design stands out as a limitation, as it precludes causal inferences between exposure instances and outcome. In addition to that, the for convenience sampling and the fact that the study was conducted in an Emergency hospital that is a reference in Traumatology may have influenced sample composition, for having patients with more severe cases and higher amputation chances. Thus, the results may not be totally representative of the entire population with foot ulcers treated in Primary Health Care or in outpatient services. It is recommended to conduct longitudinal studies with more robust sampling strategies and in other health care contexts, with the aim of ensuring greater representativeness and understanding about the factors associated with amputations due to foot ulcers as a consequence of Diabetes *Mellitus* complications.

CONCLUSION

The factors associated with amputation in people with foot ulcers as a consequence of Diabetes *Mellitus* in the bivariate analysis were as follows: biological sex; presenting peripheral neuropathy, not having undergone a foot evaluation in the Nursing appointment; having dry skin and/or cracks; onychocryptosis or improperly cut nails; interdigital maceration, callouses, cold/cyanotic/pale feet; presence of erythema and edema; previous ulcer and amputation history; time since the diabetes and peripheral neuropathy diagnoses; time with the current problem; having the other foot affected by neuropathy; and healing stage at the collection moment. This emphasizes the need to

evaluate the feet in the care routine for people with Diabetes *Mellitus*, as well as to intensify self-care guidelines and early treatment of foot complications.

In the multivariate model, amputation was associated with biological sex, peripheral neuropathy and previous amputation history. This reinforces the importance of screening plantar protective sensitivity loss and vasculopathies in people with Diabetes *Mellitus* in Primary Health Care, in addition to proper monitoring these individuals and to longitudinal care according to the ulcer risk stratification, with the objective of preventing skin injuries and, consequently, lower limb amputations.

REFERENCES

1. McDermott K, Fang M, Boulton AJM, Selvin E, Hicks CW. Etiology, epidemiology, and disparities in the burden of diabetic foot ulcers. *Diabetes Care*. 2023 [cited 2025 Aug 20]; 46(1):209–21. DOI: <https://doi.org/10.2337/dci22-0043>.
2. Edmonds M, Manu C, Vas P. Diabetic foot ulcers: a review of current management. *Diabet Med*. 2023 [cited 2025 Aug 20]; 40(6):e15084. DOI: <https://doi.org/10.1001/jama.2023.10578>.
3. International Working Group on the Diabetic Foot. IWGDF guideline on the prevention of foot ulcers in persons with diabetes. Brussels: IWGDF; 2019 [cited 2025 Aug 20]. Available from: <https://iwgdfguidelines.org/wp-content/uploads/2019/05/IWGDF-Guideline-on-the-prevention-of-foot-ulcers-in-persons-with-diabetes.pdf>.
4. Agência Brasil. Diabetes behind 28 amputations in Brazil every day [Site de Internet]. 2023 [cited 2025 Aug 29]. Available from: <https://agenciabrasil.ebc.com.br/en/saude/noticia/2023-11/diabetes-behind-28-amputations-brazil-every-day>.
5. Frykberg RG, Banks J. Challenges in the treatment of chronic wounds. *Adv Wound Care (New Rochelle)*. 2022 [cited 2025 Aug 20]; 11(12):659-70. DOI: <https://doi.org/10.1089/wound.2015.0635>.
6. Santos ICRV, Carvalho EF, Souza WV, Albuquerque EC. Factors associated with diabetic foot amputations. *J Vasc Bras*. 2022 [cited 2025 Aug 20]; 21:e20210049. DOI: <http://dx.doi.org/10.1590/1677-5449.20140049>.
7. Bus SA, Armstrong DG, van Netten JJ. The role of footwear and offloading interventions in preventing and healing foot ulcers in diabetes. *Endocrinol Metab Clin North Am*. 2023 [cited 2025 Aug 20]; 52(3):477-93. DOI: http://dx.doi.org/10.1007/978-3-319-89869-8_27.
8. World Health Organization. Sustainable Development Goals. Geneva: World Health Organization; 2017 [cited 2025 Aug 20]. Available from: <https://www.who.int/europe/news-room/questions-and-answers/item/sustainable-development-goals>.
9. Ministério da Saúde (Br). Estratégias para o cuidado da pessoa com doença crônica: diabetes mellitus. Brasília (DF): Ministério da Saúde; 2019 [cited 2025 Jun 16]. Available from: https://bvsm.sau.gov.br/bvs/publicacoes/estrategias_cuidado_pessoa_diabetes_mellitus_cab36.pdf.
10. Mello RFA, Pires MLE, Kede J. Ficha de avaliação clínica de membros inferiores para prevenção do pé diabético. *Rev. Pesqui. (Univ. Fed. Estado Rio J., Online)*. 2017 [cited 2025 Aug 20]; 9(3):899–913. DOI: <https://doi.org/10.9789/2175-5361.2017.v9i3.899-913>.
11. Secretaria Municipal Da Saúde De Ribeirão Preto. Roteiro para rastreamento do pé diabético na atenção primária. Ribeirão Preto: Coordenadoria de Atenção às Pessoas com Doenças Crônicas não Transmissíveis; 2023 [cited 2025 Aug 26]. Available from: <https://www.ribeiraopreto.sp.gov.br/portal/pdf/saude669202302.pdf>.
12. Ministério da Saúde (Br). Secretaria de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. Diretrizes de atenção à pessoa amputada. 1. ed. Brasília: Ministério da Saúde, 2013 [cited 2025 Jan 12]. Available from: https://bvsm.sau.gov.br/bvs/publicacoes/diretrizes_atencao_pessoa_amputada.pdf.
13. Katz MH. Multivariable analysis: a primer for readers of medical research. *Ann Intern Med*. 2003 [cited 2025 Aug 20]; 138(8):644-50. DOI: <https://doi.org/10.7326/0003-4819-138-8-200304150-00012>.
14. Garson GD. Structural equation modeling. Asheboro: Statistical Publishing Associates; 2010.
15. Iacopi E, Pieruzzi L, Riitano N, Abbruzzese L, Goretti C, Piaggese A. The weakness of the strong sex: differences between men and women affected by diabetic foot disease. *Int J Low Extrem Wounds*. 2021 [cited 2025 Aug 20]; 22(1):9-26. DOI: <https://doi.org/10.1177/1534734620984604>.
16. Bus AS, Sacco ICN, Monteiro-Soares M, Raspovic A, Paton J, Rasmussen A, et al. Guidelines on the prevention of foot ulcers in persons with diabetes. The International Working Group on the Diabetic Foot. IWGDF Guidelines, 2023 [cited 2025 Aug 20]. DOI: <https://doi.org/10.1002/dmrr.3651>.
17. International Working Group on the Diabetic Foot. IWGDF guidelines on prevention and management of diabetic foot disease 2023 update. Brussels: IWGDF; 2023 [cited 2025 Aug 20]. Available from: <https://iwgdfguidelines.org/wp-content/uploads/2023/07/IWGDF-Guidelines-2023.pdf>.
18. Neves RG, Tomasi E, Duro SMS, Saes-Silva E, Saes MO. Complications due to diabetes mellitus in Brazil: 2019 nationwide study, 2019. *Cien Saude Colet*. 2023 [cited 2025 Aug 20]; 28(11):3183-90. DOI: <https://doi.org/10.1590/1413-812320232811.11882022>.
19. Bus SA, Armstrong DG, Crews RT, Gooday C, Jarl G, Kirketerp-Moller K. Guidelines on offloading foot ulcers in persons with diabetes. The International Working Group on the Diabetic Foot. IWGDF Guidelines, 2023 [cited 2025 Aug 20]. DOI: <https://doi.org/10.1002/dmrr.3647>.
20. Zhang Y, Liu H, Yang Y, Feng C, Cui L. Incidence and risk factors for amputation in Chinese patients with diabetic foot ulcers: a systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2024 [cited 2025 Aug 20]; 30(15):1405301. DOI: <https://doi.org/10.3389/fendo.2024.1405301>.
21. Rayna T, Flores M, Quiñonez E, Mendoza JA, Corzo VF, Ortiz C, et al. Factors associated with major lower extremity amputations in diabetic foot infections at a county hospital in Guatemala. *J Surg Res*. 2024 [cited 2025 Aug 20]; 302:100-5. DOI: <https://doi.org/10.1016/j.jss.2024.07.033>.

22. Vuorlaakso M, Kiiski J, Salonen T, Karpelin M, Helminen M, Kaartinen I. Major amputation profoundly increases mortality in patients with diabetic foot infection. *Front Surg*. 2021 [cited 2025 Aug 20]; 30(8):655902. DOI: <https://doi.org/10.3389/fsurg.2021.655902>.
23. Mansoor Z, Modaweb A. Predicting amputation in patients with diabetic foot ulcers: a systematic review. *Cureus*. 2022 [cited 2025 Aug 20]; 14(7):e27245. DOI: <https://doi.org/10.3389/fsurg.2021.655902>.
24. Lira JAC, Nogueira LT, Oliveira BMA, Soares DR, Santos AMR, Araújo TME. Factors associated with the risk of diabetic foot in patients with diabetes mellitus in Primary Care. *Rev Esc Enferm USP*. 2021 [cited 2025 Aug 20]; 55:e03757. DOI: <https://doi.org/10.1590/S1980-220X2020019503757>.
25. Godoy JMP, Mazzocchi JC, Westin LG, Monteiro LB, Silva GL, Lopes TAS. Evolução após amputação de dedo do pé relacionada ao pé diabético. *Mundo Saúde (Online)*. 2024 [cited 2025 Aug 29]; 48:e16402024. DOI: <https://doi.org/10.15343/0104-7809.202448e16402024P>.
26. International Working Group on the Diabetic Foot. Guidelines on the prevention of foot ulcers in persons with diabetes 2023 update. *Diabetes Metab Res Rev*. 2023 [cited 2025 Aug 20]; ePublished. DOI: <https://doi.org/10.1002/dmrr.3651>.
27. Lira JAC, Oliveira BMA, Soares DR, Benício CDAV, Nogueira LT. Risk evaluation of feet ulceration in people with diabetes mellitus in primary care. *REME: Rev Min Enferm*. 2020 [cited 2025 Aug 20]; 24:e1327. DOI: <http://dx.doi.org/10.5935/1415-2762.20200064>.
28. Singh S, Bhimani Z, Malik M, Shah N, Eswar PS. Assessment of risk factors for amputation in patients with diabetic foot ulcers. *Int J Diabetes Res*. 2025 [cited 2025 Aug 20]; 7(1):18–22. DOI: <https://doi.org/10.33545/26648822.2025.v7.i1a.21>.
29. Farine F, Rapisarda AM, Roani C, Giuli C, Comisi C, Mascio A, et al. Predictive factors of amputation in diabetic foot. *Biomedicine*. 2024 [cited 2025 Aug 20]; 12(12):2775. DOI: <https://doi.org/10.3390/biomedicine12122775>.
30. Lira JAC, Rocha ASC, Bezerra SMG, Nogueira PC, Santos AMR, Nogueira LT. Effects of educational technologies on the prevention and treatment of diabetic ulcers: A systematic review and meta-analysis. *Rev. Latino-Am. Enfermagem*. 2023 [cited 2025 Aug 20]; 31:e3945. DOI: <https://doi.org/10.1590/1518-8345.6628.3945>.
31. Bus SA, Armstrong DG, van Netten JJ, et al. IWGDF guidelines on the prevention of foot ulcers in persons with diabetes: 2023 update. *Diabetes Metab Res Rev*. 2024 [cited 2025 Aug 20]; 40(1):e3746. DOI: <https://doi.org/10.1002/dmrr.3746>.

Authors contributions

Conceptualization, A.S.C.R., L.T.N. and J.A.C.L.; methodology, A.S.C.R., L.T.N. and J.A.C.L.; formal analysis, A.S.C.R., L.T.N., J.A.C.L., S.M.G.B, A.M.R.S. and C.D.A.V.; investigation, A.S.C.R., L.T.N., J.A.C.L., S.M.G.B, A.M.R.S. and C.D.A.V.; data curation, A.S.C.R., L.T.N. and J.A.C.L.; manuscript writing, A.S.C.R., L.T.N. and J.A.C.L.; review and editing, A.S.C.R., L.T.N., J.A.C.L., S.M.G.B., A.M.R.S. and C.D.A.V.; visualization, A.S.C.R., L.T.N., J.A.C.L., S.M.G.B., A.M.R.S. and C.D.A.V.; supervision, L.T.N. and J.A.C.L.; project administration, L.T.N. and J.A.C.L. All authors read and agreed with the published version of the manuscript.

Preprint Publication

Authors declare that research data are available in the repository https://sigaa.ufpi.br/sigaa/public/programa/defesas.jsf?lc=pt_BR&id=345.

Use of artificial intelligence tools

Authors declare that no artificial intelligence tools were used in the composition of the manuscript “*Factors associated with amputation in people with foot ulcers as a consequence of Diabetes Mellitus*”.