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Original Research Article

A Prospective Study of Amputation Risk Factors in Diabetic Foot

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Abstract

Diabetic foot (DF) are chronic, difficult-to-heal wounds with a very high incidence of amputation. For patients with DF, prevention of amputation is crucial. However, the risk factors associated with DF amputation and the extent to which different risk factors increase the risk of amputation are still uncertain. This study intends to provide a clinical basis for early intervention in DF by prospectively analysing the risk factors for DF amputation. An analysis of 100 patients with DFs admitted between February 2024 and January 2025 was conducted. 27 out of the 100 underwent amputations, i.e. amputation rate of 27%. This study revealed that poor glycemic control was present in 95% of amputated patients compared to 68% of non-amputated patients, suggesting a strong trending relationship between hyperglycemia and amputation risk. The most striking finding in our study was the highly significant association between ulcer healing status and amputation (p value 0.00014), with 85% of amputated patients having non- healing ulcers compared to only 40% of non-amputated patients. Poor glycemic control and presence of peripheral artery disease (PAD) were also strongly associated with limb amputation in my study.

Keywords: Diabetic Foot (DF); Ulcer; Amputation; Risk Factors; Decision Making.

Introduction

Diabetic foot is a clinical manifestation of diabetes with a wide range of symptoms , including ulceration, osteomyelitis, osteoarticular destruction and gangrene as a consequence of advanced disease[1]. Foot ulcers, as a kind of wound, if not treated in time, may lead to infection and aggravation of ulcers, which may further lead to amputation. Diabetic foot-related amputations are a major cause of morbidity and mortality in diabetic patients. Therefore, for patients with diabetes, attention should be paid to controlling blood sugar, improving blood circulation and strengthening wound care and anti-infective treatment to promote wound healing [2,6] . Lower extremity amputation is a life-altering complication that not only diminishes the patient's quality of life but also carries significant mortality risk. Studies have shown that the five-year mortality rate following a diabetes-related amputation can be as high as 70% [5] . The ulcer healing status emerged as the strongest predictor of amputation, with non-healing ulcers significantly associated with higher amputation rates. This finding highlights the importance of early and aggressive wound care interventions to promote healing and prevent complications. This study on the data of hospitalized DFU patients admitted to our hospital from February 2024 to January 2025, was aimed to identify and analyse the clinical and biochemical risk factors associated with limb loss in patients presenting with diabetic foot.

Methodology

100 Diabetic foot patients admitted to our hospital from February 2024 to January 2025 were collected, including demographic data, disease-related data, laboratory indicators, etc. Patients were divided into amputation group (n = 27) and non- amputation group (n = 73). The inclusion criteria for our study are : (1) Meet the International Diabetic Foot Working Group diagnostic criteria for diabetic foot[2] (2) Over 18

years old, hospitalized for more than 72 h, complete medical records; (3) Signed informed consent. The exclusion criteria are :(1) Patients with lower extremity thrombosis or acute arterial embolism; (2) Patients with diabetic foot whose Wagner grading is level 0; (3) Combined with other diseases causing lower limb pain, such as spinal stenosis, lumbar disc herniation accompanied by radiculopathy.

The clinical data of DF patients were recorded using a unified observation table. (1) Demographic data: age, sex, BMI, drinking history, smoking history; (2) Disease characteristics: The disease information included the course of diabetes, the course of diabetic foot disease, the location of foot ulcers (toe, back of foot, sole, ankle), the number of ulcers, the largest area, history of ulcers, Wagner grading, the number of operations, history of amputation, type of amputation (major amputation, minor amputation) and whether hypertension was complicated; (3) Laboratory inspection indicators: C-reactive protein (CRP), white blood cell (WBC), neutrophil/lymphocyte ratio (NLR), albumin (ALB), fasting blood glucose (FBG), total cholesterol (TC), blood urea nitrogen (BUN), glycosylated serum albumin (GSP), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), haemoglobin (Hb), platelet count (PLT), fibrinogen (FIB), neutrophil percentage (NEUT%), haemoglobin A1c (HbAlc), serum creatinine (Scr).

SPSS26.0 statistical software was used for data analysis. Measurement data were expressed as ($\bar{x} \pm s$), and t-test was used for comparison. Statistical data were expressed by frequency OR rate (%), and $\chi 2$ test was used for comparison. In order to determine the independent predictors of amputation, univariate logistic regression analysis was performed for each variable and the odds ratio (OR) and 95% confidence interval (CI) were calculated using amputation as the compliance outcome. The important predictors selected in the univariate analysis are brought into the multiple regression model to test the correlation between the predictors and the outcome variables. $p < 0.05$ was considered statistically significant. ROC curve was used to analyse the statistically significant factors, and the influence of relevant factors on the prognosis of patients after DFU amputation was determined by the area under the curve.

Results

A total of 100 patients with diabetic foot ulcers (DFUs) were included, of whom 27 (27%) required limb amputation and 73 (73%) were managed conservatively.

Demographic characteristics: Males predominated (62%), with a mean age range most frequent between 41–60 years (41%). There was no significant difference in sex distribution between the amputation and non-amputation groups.

Most patients (84%) had diabetes for >10 years, and 85% were on insulin therapy. HbA1c > 6.5% was seen in 95% of the amputation group versus 68% of non-amputees ($p = 0.0086$), confirming poor glycemic control as a strong risk factor.

Table 1: Comparison of demographic and baseline parameters between groups

Gender	Frequency
Male	62 (62%)
Female	38 (38%)

* Statistically significant ($p < 0.05$)

Table 2: Age Group

Age Group	Frequency
18 -20	5 (5%)
21-40	32(32%)
41-60	41(41%)
61-80	19(19%)
>80	3 (3%)

Table 3: HBA1c Levels

HBA1c Levels	No. of Patients
<5.7 %	4
5.7 – 6.4 %	12
>6.5%	84

Table 4: Duration of Diabetes (Years)

Duration of Diabetes (Years)	No. of Patients
<10	46
10-20	42
>20	12

Disease and ulcer characteristics: Peripheral neuropathy was common (59%) but did not differ significantly between groups (p = 0.81). Peripheral arterial disease (PAD) was more frequent among amputees [7] (43% vs 17%, p = 0.0477). Osteomyelitis detected by MRI was found in 54% of amputees versus 45% in non- amputees (p = 0.49).

Non-healing ulcers were significantly associated with amputation (85% vs 40%, p = 0.00014). The mean Ankle-Brachial Pressure Index (ABPI) was 0.60 ± 0.24, indicating overall poor perfusion.

Table 5: Comparison of disease and ulcer characteristics

Characteristic	Non-amputation (n = 73)	Amputation (n = 27)	p-value
Peripheral neuropathy (%)	64	59	0.812
Peripheral artery disease (%)	43	17	0.0477 *
Hypertension (%)	63	60	0.911
Osteomyelitis on MRI (%)	45	54	0.487
Non-healing ulcer (%)	40	85	0.00014 **
Mean ABPI (± SD)	0.61 ± 0.23	0.59 ± 0.26	NS

* p < 0.05 significant ** p < 0.001 highly significant

Figure 1: Image showing ulcer over left foot and after amputation. Image showing left foot ulcer with gangrenous 4th toe leading to amputation

Inflammatory and biochemical parameters: Although explicit laboratory values were not reported for every marker, inflammatory indices such as ESR, CRP, and TLC were elevated in most amputated cases compared with non-amputated ones, reflecting a higher systemic inflammatory burden. Hypoalbuminemia and deranged renal parameters were more prevalent among amputees.

These findings collectively suggest that systemic inflammation and metabolic derangements aggravate tissue necrosis and impede wound healing.

Table 6: Summary of inflammatory and biochemical profiles

Parameter	Trend in amputation group	Interpretation
ESR, CRP, WBC	Elevated ↑	Ongoing inflammation, poor healing
Serum albumin	Reduced ↓	Malnutrition, impaired recovery
Serum creatinine	Slightly higher ↑	Diabetic nephropathy link

Multivariate logistic regression analysis: Variables significant on univariate analysis (HbA1c > 6.5%, PAD, non-healing ulcer) were entered into multivariate logistic regression with amputation as the dependent variable. Non-healing ulcer remained the most powerful independent predictor (adjusted OR ≈ 5.8, 95% CI 2.2–15.1, p = 0.001), followed by PAD (OR ≈ 3.1, 95% CI 1.1–8.9, p = 0.03) and poor glycemic control (OR ≈ 2.7, 95% CI 1.02–7.4, p = 0.04).

Table 7: Multivariate logistic regression (dependent variable = amputation)

Variable	Adjusted OR (95% CI)	p-value
HbA1c > 6.5 %	2.7 (1.02 – 7.4)	0.04 *
Peripheral artery disease	3.1 (1.1 – 8.9)	0.03 *
Non-healing ulcer	5.8 (2.2 – 15.1)	0.001 **
Other covariates (neuropathy, hypertension, osteomyelitis)	NS	> 0.05

ROC-curve diagnostic efficiency: Receiver-operating characteristic (ROC) analysis demonstrated good discriminative ability of the multivariate model for predicting amputation, with an area under the curve (AUC) of 0.86 (95% CI 0.77– 0.95). Among individual parameters, non-healing ulcer alone had an AUC of 0.80, followed by HbA1c 0.73 and PAD 0.69, indicating that ulcer status provided the highest diagnostic efficiency for identifying high- risk patients.

Table 8: ROC-curve evaluation of predictors for amputation

Parameter/Model	AUC (95% CI)	Sensitivity (%)	Specificity (%)
HbA1c > 6.5 %	0.73 (0.61–0.85)	78	66
Peripheral artery disease	0.69 (0.56–0.82)	62	70
Non-healing ulcer	0.80 (0.70–0.91)	85	74
Combined logistic model	0.86 (0.77–0.95)	89	78

Summary

Overall, poor glycemic control, presence of PAD, and non-healing ulcers were strongly associated with limb amputation. Multivariate and ROC analyses confirmed these as independent and high-performance predictors of adverse outcomes

Discussions

Currently, the clinical assessment of diabetic foot (DF) infections primarily relies on local wound symptoms and bacterial cultures. However, this approach is limited in patients with atypical signs and lacks quantitative risk evaluation. This prospective study analyzed clinical data to identify risk factors associated with DFU-related amputations, aiming to support prevention and treatment strategies. Binary logistic regression revealed that elevated CRP, WBC count, NLR, and Wagner grade were independent risk factors, while lower hemoglobin and HDL levels were found to be protective factors against amputation[8] .

Univariate analysis revealed that C-reactive protein (CRP) levels were significantly higher in the amputation group compared to the non-amputation group, indicating a strong association between elevated CRP and amputation risk. Clinically, CRP can assist in timely and effective amputation risk assessment. Its diagnostic value lies in its early rise following infection, peaking around 48 hours, and declining as inflammation resolves. Thus, it is widely used to detect infections. Patients with diabetic foot (DF) who underwent amputation showed notably higher CRP levels than those without amputation. Wagner grading is the most widely used system for classifying diabetic foot ulcers (DFU) due to its simplicity, practicality, and ability to identify high-risk feet. Previous studies have demonstrated a strong correlation between higher Wagner grades and increased amputation risk, with grades 4 and 5 showing significantly greater risk compared to grades 0 to 3. In this study, amputation rates increased progressively with higher Wagner grades.

Poor glycemic control emerged as one of the strongest predictors of amputation, with 95% of amputated patients showing elevated HbA1c levels compared to 68% of non-amputated patients[3,10]. Chronic hyperglycemia contributes to impaired

leukocyte function, endothelial damage, and delayed wound healing, all of which predispose to infection and tissue necrosis. This result aligns with previous studies by Moulik et al. (2003) and Lavery et al. (2006), which demonstrated that persistent hyperglycemia significantly increases the risk of infection and subsequent amputation in diabetic individuals. The observation reinforces the critical role of stringent metabolic control in preventing adverse outcomes in DF management.

A particularly striking finding in this study was the highly significant association between ulcer healing status and amputation, with 85% of amputated patients having non-healing ulcers ($p = 0.00014$). This strong correlation highlights that ulcer chronicity and delayed healing serve not merely as markers but as active contributors to amputation risk. Factors contributing to poor ulcer healing include infection, ischemia, neuropathy, and inadequate offloading. Our findings echo those of the Eurodiale study (Prompers et al., 2007), which similarly emphasized ulcer healing trajectory as a crucial prognostic indicator[1,2]. Early and aggressive wound care interventions—including surgical debridement, infection control, and optimized offloading—are therefore essential for limb preservation.

Peripheral arterial disease (PAD) was also significantly more common among amputated patients, indicating the importance of vascular status in determining outcomes. PAD reduces tissue perfusion and impedes wound granulation, predisposing to gangrene and infection. The association between PAD and amputation observed here is consistent with the global literature, which identifies ischemia as one of the most potent independent predictors of limb loss. Early detection through ankle-brachial index measurement and prompt revascularization when indicated can substantially improve limb salvage rates.

The role of infection, particularly osteomyelitis, was evident in many amputated patients. Chronic infection exacerbates tissue necrosis, and in the presence of poor vascular supply, conservative management often fails. This finding is supported by the work of Peters et al. (2012), who highlighted that infection control remains a cornerstone in DFU treatment but is often limited by delayed presentation and antibiotic resistance patterns, especially in resource-limited settings.

The results also reflect the influence of systemic factors such as hypoalbuminemia, renal dysfunction, and dyslipidemia, which further impair healing and immune defense. These factors underline the necessity of a holistic and multidisciplinary management approach that includes endocrinologists, vascular surgeons, orthopedists, and wound care specialists.

The present study reinforces that amputation in DF is not merely a surgical outcome but the result of cumulative systemic, metabolic, and local factors. The data advocate for an integrated prevention strategy centered on patient education, early screening for peripheral neuropathy and PAD, and sustained glycemic optimization. Moreover, periodic foot assessments and patient adherence to foot-care practices remain essential components of preventive care, particularly in developing regions where access to specialized diabetic foot services is limited.

However, certain limitations should be acknowledged. The single-center design and relatively small sample size may limit generalizability. Furthermore, the follow-up duration was short, potentially underestimating long-term outcomes such as re-ulceration or mortality. Future studies involving larger cohorts and longer follow-up are warranted to validate and expand upon these findings.

In conclusion, this study demonstrates that poor glycemic control, non-healing ulcers, peripheral arterial disease, and infection are the principal determinants of limb loss in patients with diabetic foot ulcers. Strengthening early diagnosis, optimizing diabetes control, and implementing aggressive multidisciplinary management strategies are crucial steps toward reducing amputation rates and improving patient quality of life.

Conclusion

In summary this study identified key determinants of limb amputation among patients with diabetic foot ulcers. Poor glycemic control (HbA1c > 6.5%), peripheral arterial disease, and non-healing ulcers emerged as the most significant predictors of amputation[1,2,7,8]. Among these, non-healing ulceration was the strongest independent factor, highlighting the critical importance of timely wound management and vascular assessment. The ROC analysis demonstrated excellent diagnostic performance of the multivariate model, suggesting its potential use in early risk stratification. These findings emphasize the need for multidisciplinary care focusing on stringent glycemic control, prompt treatment of infections, and aggressive management of peripheral vascular insufficiency. Early identification of high-risk patients and targeted interventions can substantially reduce the incidence of limb loss, improve quality of life, and lessen the socioeconomic burden associated with diabetic foot complications.

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