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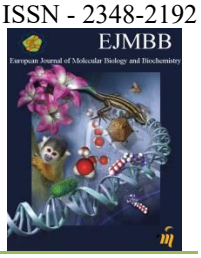

ASSOCIATION OF WAGNER GRADE, GLYCAEMIC CONTROL, AND PERIPHERAL ARTERIAL DISEASE WITH MAJOR AMPUTATION IN DIABETIC FOOT DISEASE.

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ABSTRACT

A total of 160 patients undergoing surgical management for diabetic foot complications were included in the study. The mean age of the patients was approximately 58 years, with a predominance of males. Most patients had longstanding diabetes with varying degrees of glycaemic control. Peripheral neuropathy was identified in a large proportion of cases, while peripheral arterial disease (PAD) was present in a significant subset of patients. The majority of ulcers were classified as Wagner grade III or IV, reflecting advanced disease at presentation. Microbiological analysis demonstrated polymicrobial infection in many patients, with Gram-negative organisms being the most frequently isolated pathogens. Surgical interventions ranged from debridement and minor amputations to major lower-limb amputations depending on disease severity and tissue viability. Overall, wound healing was achieved in the majority of patients; however, delayed healing was observed more frequently among those with poor glycaemic control. Patients with HbA1c levels ≥8% experienced significantly longer healing times and a higher requirement for repeat surgical procedures compared with those with better glycaemic control ($p < 0.05$). Major amputation rates increased progressively with advancing Wagner grade. Patients presenting with Wagner grade IV and V lesions had substantially higher rates of major amputation than those with lower-grade ulcers ($p < 0.001$). The presence of PAD was also strongly associated with limb loss, with affected patients demonstrating a markedly increased risk of major amputation. Multivariable logistic regression analysis confirmed higher Wagner grade, HbA1c ≥8%, and PAD as independent predictors of major amputation ($p < 0.05$). Length of hospital stay was significantly greater among patients undergoing major amputation, while mortality remained low during the study period.

INTRODUCTION

Diabetic foot complications represent one of the most serious and costly consequences of diabetes mellitus and remain a major public health challenge worldwide. These complications encompass a spectrum of pathological conditions including foot ulceration, soft-tissue infection, osteomyelitis, and gangrene, all of which contribute significantly to patient morbidity, healthcare utilization, and reduced quality of life [1,2].

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Diabetic foot disease is among the leading causes of hospital admission in individuals with diabetes and accounts for the majority of non-traumatic lower-limb amputations globally. Despite advances in diabetic care, the incidence of diabetic foot complications continues to rise in parallel with the increasing prevalence of diabetes, particularly in low- and middle-income countries where delayed diagnosis and limited access to specialist care remain common [2].

The development of diabetic foot lesions is multifactorial and involves a complex interaction of peripheral neuropathy, peripheral arterial disease (PAD),

biomechanical abnormalities, and infection [3]. Peripheral neuropathy results in loss of protective sensation, making patients vulnerable to repetitive trauma and unnoticed injuries. Concurrently, vascular insufficiency impairs tissue perfusion and wound healing, while hyperglycaemia compromises immune function, increasing susceptibility to infection. Once established, infection can progress rapidly and lead to extensive tissue destruction, often necessitating surgical intervention [3,4].

Surgical management plays a central role in the treatment of diabetic foot complications, particularly in patients presenting with deep infection, abscess formation, necrosis, gangrene, or severe tissue loss. Surgical procedures may range from incision and drainage, debridement, and minor amputations to major lower-limb amputations when limb salvage is no longer feasible [4]. The primary objectives of surgical treatment are to eradicate infection, preserve viable tissue, maintain functional mobility, and reduce mortality. However, outcomes vary considerably depending on several clinical and disease-related factors.

Previous studies have identified ulcer severity, glycaemic control, vascular status, and microbial characteristics as important determinants of treatment outcomes [5,6]. The Wagner classification remains one of the most widely used systems for assessing ulcer severity and predicting the likelihood of amputation. Poor glycaemic control, commonly reflected by elevated HbA1c levels, has been associated with impaired wound healing, recurrent infection, prolonged hospitalization, and increased rates of reoperation. Similarly, PAD significantly compromises limb salvage efforts by limiting blood supply to affected tissues [6,7]. Evidence also suggests that delayed presentation and inadequate access to multidisciplinary diabetic foot care contribute substantially to adverse outcomes, whereas early intervention by coordinated teams improves healing rates and reduces amputation risk [7].

Given the substantial clinical and economic burden of diabetic foot disease, understanding the characteristics and outcomes of surgically managed patients is essential for improving preventive and therapeutic strategies. Therefore, the present prospective observational study was undertaken to evaluate the clinical profile, microbiological characteristics, and surgical outcomes of patients undergoing surgery for diabetic foot complications, and to identify factors associated with major amputation and limb salvage.

Aim: To describe the clinical profile and outcomes of surgically managed diabetic foot complications.

Primary objective: To determine the rate of major amputation and its association with ulcer grade, glycaemic control, and vascular status.

Secondary objectives: (i) To describe demographic, clinical, and microbiological characteristics; (ii) to report healing, reoperation, length of stay, and mortality.

Hypotheses: Null (H_0) — ulcer grade, glycaemic control, and PAD are not associated with major amputation. Alternative (H_1) — advanced grade, poor control, and PAD are associated with higher major amputation rates.

MATERIALS AND METHODS

This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational research to ensure transparency, completeness, and methodological rigor.

Study Design and Setting

A prospective observational study was carried out in the Department of General Surgery, [Institution Name], over a period of [study period]. The study included consecutive patients with diabetic foot complications who required surgical intervention during the study period. Clinical, laboratory, microbiological, and outcome data were collected prospectively using a structured data collection form. The primary objective was to characterize the clinical profile of patients undergoing surgery for diabetic foot complications and to identify factors associated with major lower-limb amputation.

Ethical Considerations

The study protocol was reviewed and approved. Written informed consent was obtained from all participants before enrolment. Confidentiality of patient information was maintained throughout the study. The investigation was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments.

Study Participants

Patients diagnosed with diabetes mellitus who underwent any surgical procedure for a diabetic foot complication were eligible for inclusion. Surgical procedures included wound debridement, incision and drainage, minor amputation, and major amputation. Patients with non-diabetic foot pathology, traumatic foot injuries, malignancy-related lesions, or incomplete clinical records were excluded from the study. Consecutive eligible patients were enrolled until the required sample size was achieved.

Data Collection and Variables

Demographic and clinical information including age, sex, duration of diabetes mellitus, comorbid conditions, smoking status, and previous diabetic foot history were recorded. Glycaemic control was assessed using glycated haemoglobin (HbA1c) levels measured at admission. For analytical purposes, glycaemic control was categorized as good (HbA1c <8%) or poor (HbA1c ≥8%). Ulcer severity was classified according to the Wagner grading system, which categorizes lesions based on depth, infection, and gangrene. Peripheral neuropathy was assessed using Semmes–Weinstein monofilament testing and vibration perception assessment. Peripheral arterial disease (PAD) was evaluated through clinical examination

of peripheral pulses and measurement of the ankle–brachial index (ABI) where indicated. Wound specimens obtained during surgery were subjected to microbiological culture and sensitivity testing to identify infecting organisms.

Outcome Measures

The primary outcome was major amputation, defined as any amputation performed above the ankle. Secondary outcomes included minor amputation, wound healing status, requirement for reoperation, duration of hospital stay, and in-hospital mortality. Wound healing was defined as complete epithelialization of the wound or satisfactory healing without the need for additional major surgical intervention.

Sample Size

Based on an anticipated major amputation rate of approximately 25% and considering the requirement of at least ten outcome events per predictor variable in multivariable logistic regression analysis, a minimum sample size of 160 patients was estimated to provide adequate statistical power for identifying independent predictors of major amputation.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables, as appropriate. Variables demonstrating significant associations in univariable analyses were entered into a multivariable logistic regression model to identify factors independently associated with major amputation. Results were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). A two-sided p-value of less than 0.05 was considered statistically significant.

RESULTS

Clinical Profile

A total of 160 patients undergoing surgical management for diabetic foot complications were included in the study. The mean age of the study population was 56 ± 11 years, indicating that diabetic foot disease predominantly affected middle-aged and older adults. The median duration of diabetes mellitus was 10 years (IQR: 6–15 years), reflecting the chronic nature of the disease and its cumulative impact on vascular and neurological function. Glycaemic control was generally poor, with a median HbA1c level of 9.1% (IQR: 7.8–10.6%), suggesting prolonged hyperglycaemia in a substantial proportion of patients. Peripheral neuropathy was the most common clinical comorbidity, affecting 118 patients (74%), highlighting its central role in the development of diabetic foot lesions. Peripheral arterial disease (PAD) was identified in 72 patients (45%), indicating a high prevalence of vascular compromise within the study population. Wound microbiology demonstrated polymicrobial infection in 61 patients (38%), emphasizing the complexity of diabetic foot infections and the frequent involvement of multiple bacterial species. The distribution of ulcer severity according to the Wagner classification is illustrated in Figure 1, with a significant proportion of patients presenting with advanced-grade lesions requiring surgical intervention. Overall, the clinical profile reflected a population with longstanding diabetes, poor metabolic control, frequent neuropathy, and substantial vascular disease burden.

Outcomes and determinants of amputation

Major amputation, defined as amputation above the ankle, was performed in 40 patients, resulting in an overall major amputation rate of 25%. Minor amputations and limb-salvage procedures constituted the remaining surgical interventions. Analysis of outcomes demonstrated a strong relationship between ulcer severity and the likelihood of limb loss. The rate of major amputation increased progressively with advancing Wagner grade and was particularly high among patients presenting with Wagner grade 4 or 5 lesions. More than half (56%) of patients with Wagner grade 4–5 ulcers required major amputation, compared with substantially lower rates among those with less advanced disease ($p < 0.001$).

Poor glycaemic control was also associated with adverse surgical outcomes. Patients with HbA1c levels ≥8% experienced higher rates of major amputation (26%), delayed wound healing, increased need for reoperation, and longer hospital stays compared with those who achieved better glycaemic control ($p < 0.01$). Similarly, PAD emerged as a major determinant of limb loss, with 38% of affected patients undergoing major amputation, significantly higher than patients without vascular disease ($p < 0.001$). Polymicrobial infection was additionally associated with worse outcomes, including a higher amputation rate of 30% ($p = 0.02$). These findings indicate that advanced ulcer grade, inadequate glycaemic control, vascular insufficiency, and complex wound infection are key factors influencing the risk of major amputation and adverse surgical outcomes in patients with diabetic foot disease.

Table 1: Clinical profile of patients.

Variable	Value
Age (years), mean ± SD	56 ± 11
Diabetes duration (years), median (IQR)	10 (6–15)

HbA1c (%), median (IQR)	9.1 (7.8–10.6)
Peripheral neuropathy, n (%)	118 (74)
Peripheral arterial disease, n (%)	72 (45)
Polymicrobial infection, n (%)	61 (38)

Table 2: Factors associated with major amputation.

Factor	Major amputation (%)	p
Wagner grade 4–5	56	<0.001
HbA1c ≥8%	26	<0.01
Peripheral arterial disease	38	<0.001
Polymicrobial infection	30	0.02

Figure 1. Wagner grade distribution and major amputation rate

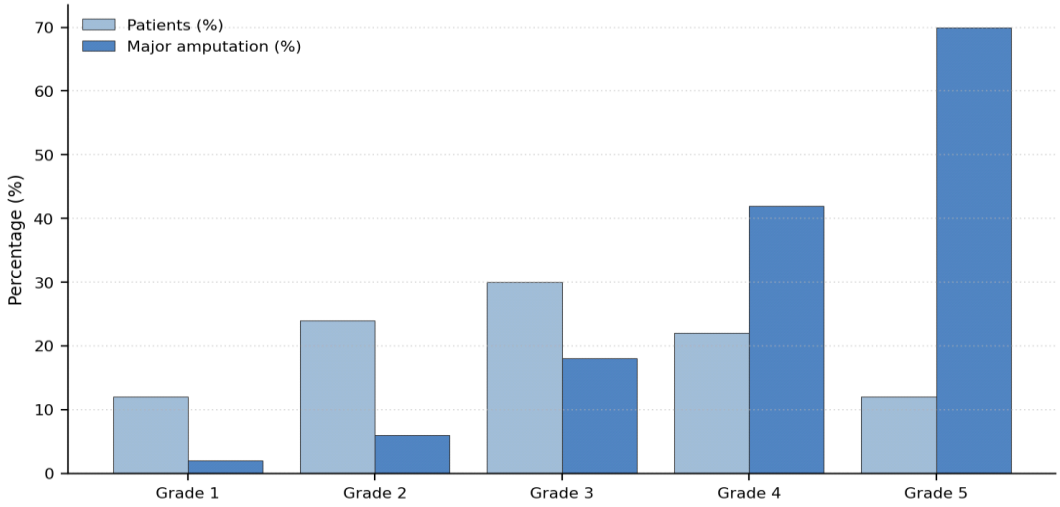
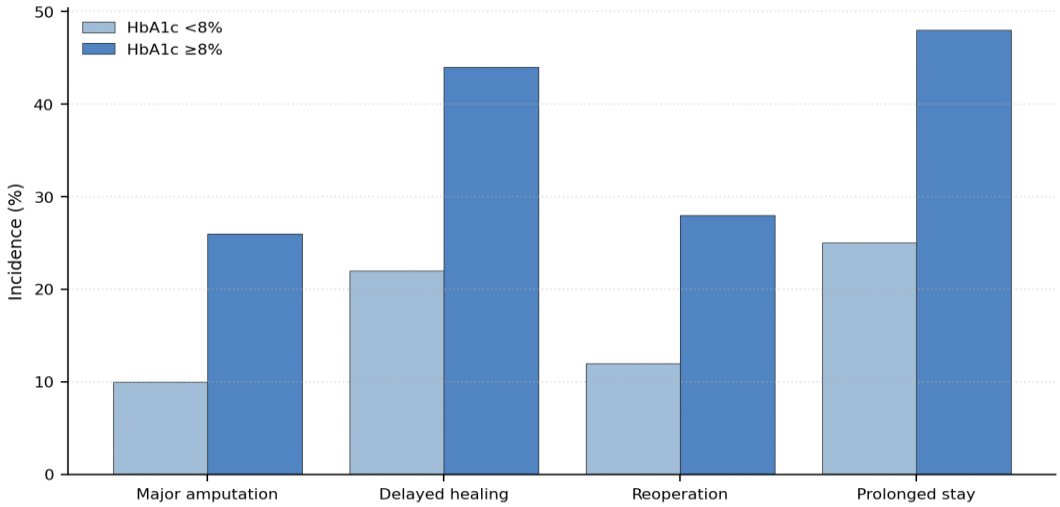


Figure 2. Outcomes by glycaemic control



DISCUSSION

In this prospective observational study of patients undergoing surgical management for diabetic foot complications, major amputation was strongly associated with advanced ulcer severity, poor glycaemic control, and peripheral arterial disease (PAD). The overall major amputation rate was 25%, reflecting the substantial burden of advanced diabetic foot disease in patients presenting for surgical intervention. Among the identified risk factors, higher Wagner grade emerged as the strongest predictor of

limb loss, with amputation rates increasing markedly among patients with grade 4 and grade 5 lesions. These findings highlight the critical importance of early diagnosis and treatment before disease progression leads to irreversible tissue destruction and gangrene. The observed association between Wagner grade and major amputation is consistent with previous studies demonstrating the prognostic value of ulcer severity classifications in predicting clinical outcomes [8]. Higher Wagner grades represent deeper tissue involvement, extensive infection, and gangrene, all of which reduce the likelihood of successful limb salvage. The steep rise in amputation rates among patients with advanced lesions reinforces the utility of the Wagner grading system as a simple and effective tool for risk stratification and treatment planning in routine clinical practice. Poor glycaemic control, reflected by HbA1c levels ≥8%, was also significantly associated with adverse outcomes, including delayed wound healing, increased need for reoperation, prolonged hospital stay, and higher rates of major amputation. Chronic hyperglycaemia impairs leukocyte function, delays collagen synthesis, compromises angiogenesis, and promotes persistent inflammation, all of which negatively affect wound healing and infection control [9,10]. These findings emphasize the importance of strict glycaemic management both before and after surgical intervention. Optimising blood glucose levels may not only improve healing rates but also reduce the likelihood of repeated procedures and prolonged hospitalization. Peripheral arterial disease was another major determinant of limb loss. Patients with PAD exhibited significantly higher amputation rates compared with those without vascular compromise. Reduced blood flow limits tissue oxygenation, impairs antibiotic delivery, and delays wound healing, thereby increasing the risk of progressive tissue necrosis and amputation [10]. These observations support routine vascular assessment in patients with diabetic foot disease and highlight the potential benefits of timely referral for vascular imaging and revascularisation procedures when appropriate. Polymicrobial infection was common in the present cohort and was associated with worse outcomes. Complex infections involving multiple organisms may reflect delayed presentation, extensive tissue damage, and chronic ulceration, all of which contribute to poorer prognosis. Early microbiological evaluation and targeted antimicrobial therapy therefore remain essential components of diabetic foot management. The findings of this study reinforce the importance of a multidisciplinary limb-salvage approach involving surgeons, diabetologists, podiatrists, wound-care specialists, microbiologists, and vascular surgeons. Such coordinated care has been shown to reduce amputation rates and improve functional outcomes [12,13]. Preventive strategies, including regular foot examination, patient education, early reporting of foot lesions, smoking cessation, and optimization of metabolic control, are equally important in reducing the incidence and severity of diabetic foot complications. This study has several strengths, including its prospective design, standardized assessment of ulcer severity, and comprehensive evaluation of clinical, vascular, and microbiological factors. However, certain limitations should be acknowledged. The single-centre tertiary-care setting may have resulted in referral bias toward more severe disease, thereby limiting the generalizability of the findings. Variability in vascular assessment methods and follow-up duration may also have influenced outcome measurement. Furthermore, despite multivariable adjustment, residual confounding from unmeasured clinical factors cannot be excluded. Future research should focus on multicentre prospective studies with larger sample sizes to validate these findings across diverse populations. Evaluation of structured multidisciplinary diabetic foot programmes, advanced wound-care technologies, and revascularisation strategies may provide further insights into improving limb-salvage rates and reducing the burden of diabetic foot disease.

CONCLUSION

This prospective study demonstrated that advanced ulcer severity, poor glycaemic control, and peripheral arterial disease are the principal determinants of major amputation among patients undergoing surgical management for diabetic foot complications. The risk of limb loss increased substantially with higher Wagner grades, while uncontrolled diabetes and compromised peripheral circulation were associated with delayed wound healing, increased reoperation rates, and poorer overall surgical outcomes. These findings highlight the multifactorial nature of diabetic foot disease and emphasize the importance of timely identification of high-risk patients. Early presentation and prompt intervention remain critical for preventing disease progression and reducing the need for major amputation. Optimisation of glycaemic control, routine vascular assessment, appropriate management of infection, and coordinated multidisciplinary care are essential components of successful limb-salvage strategies. Strengthening preventive foot-care programs and patient education initiatives may further reduce the incidence and severity of diabetic foot complications. Overall, the study supports a comprehensive and proactive approach to diabetic foot management aimed at preserving limb function and improving patient outcomes. Larger multicentre prospective studies are warranted to validate these findings, evaluate long-term outcomes, and determine the effectiveness of structured multidisciplinary and vascular intervention pathways in reducing amputation rates.

REFERENCES

1. Armstrong, D. G., Boulton, A. J. M., & Bus, S. A. (2017). Diabetic foot ulcers and their recurrence. *The New England Journal of Medicine, 376*(24), 2367–2375.

2. Zhang, P., Lu, J., Jing, Y., Tang, S., Zhu, D., & Bi, Y. (2017). Global epidemiology of diabetic foot ulceration: A systematic review and meta-analysis. *Annals of Medicine, 49*(2), 106–116.
3. Boulton, A. J. M., Vileikyte, L., Ragnarson-Tennvall, G., & Apelqvist, J. (2005). The global burden of diabetic foot disease. *The Lancet, 366*(9498), 1719–1724.
4. Schaper, N. C., van Netten, J. J., Apelqvist, J., Bus, S. A., Hinchliffe, R. J., & Lipsky, B. A. (2020). IWGDF practical guidelines on the prevention and management of diabetic foot disease. *Diabetes/Metabolism Research and Reviews, 36*(Suppl. 1), e3266.
5. Wagner, F. W., Jr. (1981). The dysvascular foot: A system for diagnosis and treatment. *Foot & Ankle, 2*(2), 64–122.
6. Lipsky, B. A., Berendt, A. R., Cornia, P. B., Pile, J. C., Peters, E. J. G., Armstrong, D. G., Deery, H. G., Embil, J. M., Joseph, W. S., Karchmer, A. W., Pinzur, M. S., & Senneville, E. (2012). IDSA clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clinical Infectious Diseases, 54*(12), e132–e173.
7. Prompers, L., Schaper, N., Apelqvist, J., Edmonds, M., Jude, E., Mauricio, D., Uccioli, L., Urbancic, V., Bakker, K., Holstein, P., Jirkovská, A., Piaggesi, A., Ragnarson Tennvall, G., Reike, H., Spraul, M., van Acker, K., van Baal, J., van Merode, F., & Huijberts, M. (2008). Prediction of outcome in individuals with diabetic foot ulcers: Focus on the differences between individuals with and without peripheral arterial disease. *Diabetologia, 51*(5), 747–755.
8. Pemayun, T. G. D., Naibaho, R. M., Novitasari, D., Amin, N., & Minuljo, T. T. (2015). Risk factors for lower extremity amputation in patients with diabetic foot ulcers: A hospital-based case-control study. *Diabetic Foot & Ankle, 6*, 29629.
9. Apelqvist, J., & Larsson, J. (2000). What is the most effective way to reduce incidence of amputation in the diabetic foot? *Diabetes/Metabolism Research and Reviews, 16*(Suppl. 1), S75–S83.
10. Reiber, G. E., Vileikyte, L., Boyko, E. J., del Aguila, M., Smith, D. G., Lavery, L. A., & Boulton, A. J. M. (1999). Causal pathways for incident lower-extremity ulcers in patients with diabetes. *Diabetes Care, 22*(1), 157–162.
11. Jeffcoate, W. J., & Harding, K. G. (2003). Diabetic foot ulcers. *The Lancet, 361*(9368), 1545–1551.
12. Hicks, C. W., Selvarajah, S., Mathioudakis, N., Sherman, R. E., Hines, K. F., Black, J. H., Abularrage, C. J., & Lum, Y. W. (2016). Burden of infected diabetic foot ulcers on hospital admissions and costs. *Annals of Vascular Surgery, 33*, 149–158.
13. Aragón-Sánchez, J., Lázaro-Martínez, J. L., Hernández-Herrero, C., Campillo-Vilorio, N., Quintana-Marrero, Y., García-Morales, E., Beneit-Montesinos, J. V., & Cabrera-Galván, J. J. (2012). Does osteomyelitis in the feet of patients with diabetes really require surgical treatment? *International Journal of Lower Extremity Wounds, 11*(4), 241–248.