Predictors of Major Lower Limb Amputation Among Type II Diabetic Patients

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Abstract:

Background: Diabetic foot syndrome (DFS) is a severe complication of Type II diabetes mellitus (T2DM) and is a leading cause of lower limb amputations globally. Peripheral neuropathy, peripheral arterial disease (PAD), and poor glycemic control significantly contribute to this condition. Early identification of predictors of amputation is essential for effective prevention and management.

Aim: The purpose of this study was to determine the factors that predict individuals with Type II diabetes mellitus to have a significant lower limb amputated.

Methods: A cross-sectional observational study was conducted at Jawaharlal Nehru Medical College and Hospital, Bhagalpur, involving 160 patients with T2DM and diabetic foot complications. Data on demographics, clinical history, laboratory parameters, and comorbidities were collected. Logistic regression analysis was used to identify significant predictors of amputation, with statistical significance set at $p < 0.05$.

Results: Out of 160 participants, 44 (27.5%) underwent major lower limb amputations. Peripheral neuropathy (OR: 4.21, $p < 0.001$), peripheral vascular disease (OR: 5.12, $p < 0.001$), and poor glycemic control (HbA1c > 8%; OR: 3.35, $p = 0.017$) were identified as significant predictors of amputation. Advanced age (≥60 years) and hypertension also showed associations but were not statistically significant in multivariate analysis.

Conclusion: In individuals with type 2 diabetes, peripheral neuropathy, peripheral vascular disease, and inadequate glycemic management are important predictors of major lower limb amputation. The significance of early screening and risk factor management is emphasized by these findings.

Recommendations: Targeted preventive strategies, including stringent glycemic control, regular screening for neuropathy and vascular disease, and patient education on foot care, are crucial to reducing the burden of amputations in diabetic populations.

Keywords: Diabetes mellitus, diabetic foot, lower limb amputation, peripheral neuropathy, glycemic control.

Introduction

Millions of people worldwide suffer with type 2 diabetes, a chronic metabolic disease marked by insulin resistance and hyperglycemia. In 2021, more than 537 million persons had diabetes, and by 2030, that number is expected to rise to 643 million, according to the IDF [1]. Among the myriad complications associated with T2DM, (DFS) is particularly debilitating. It encompasses a spectrum of conditions, including (DFUs), infections, and gangrene, often culminating in lower limb amputations if not managed timely.

The pathophysiology of DFS is complex, involving neuropathy, ischemia, and impaired wound healing. Peripheral neuropathy leads to sensory loss, making patients vulnerable to unnoticed trauma, while peripheral arterial disease (PAD) compromises blood flow, delaying tissue repair [2]. These processes, coupled with chronic hyperglycemia, create a conducive environment for infections, escalating the risk of amputation. The global burden of diabetic foot complications is immense, with up to 85% of amputations being preceded by DFUs [3]. Recent research underscores the role of glycemic control and comorbidities in predicting the risk of major amputations. A 2020 study by Zhang et al. identified poor glycemic control, with HbA1c levels above 8%, as a significant risk factor for DFUs progressing to severe infections and amputations [4]. Similarly, a 2022 systematic

review highlighted the contribution of PAD and advanced Wagner classification grades in predicting major lower limb amputations [5]. Early identification of these predictors is critical for timely interventions that can mitigate progression to severe outcomes.

Economic implications of diabetic foot complications are staggering. A 2021 study reported that the annual healthcare cost of managing DFUs ranges from $9 to $13 billion in the United States alone [6]. Mortality rates post-amputation further accentuate the gravity of this condition, with five-year survival rates being as low as 50%, comparable to some cancers [7]. Understanding the factors that predict major lower limb amputation in people with type 2 diabetes is essential in light of these difficulties. Identifying high-risk individuals, coupled with aggressive management of risk factors such as glycemic control and vascular health, can significantly reduce the burden of amputations and improve patient outcomes. The purpose of this study was to determine the factors that predict individuals with Type II diabetes mellitus to have a significant lower limb amputated.

Methodology

Study Design: This study was conducted as a cross-sectional observational study.

Study Setting: The study was conducted at the Department of Endocrinology and Diabetology, Jawaharlal Nehru Medical College and Hospital (JLNMCH), Bhagalpur. Data collection spanned six months, ensuring an adequate timeframe for participant recruitment and evaluation.

Participants: The study comprised 160 people with a diagnosis of Type II diabetes. Strict eligibility requirements were used to enroll patients who presented with diabetic foot problems and needed to be evaluated for the risk of amputation.

Inclusion Criteria

- Patients aged 18 years or older.
- Confirmed diagnosis of T2DM.
- History or evidence of diabetic foot ulcers or gangrene.
- Patients who are prepared to give their informed permission.

Exclusion Criteria

- Patients with Type I diabetes mellitus.

- Individuals with amputations due to non-diabetic causes.
- Pregnant or lactating women.
- Patients who chose not to participate or whose medical information are incomplete.

Bias: In order to reduce selection bias, participants were enlisted consecutively during the study period. Observer bias was mitigated by ensuring that the investigators collecting the data were blinded to the study hypothesis. Data entry errors were minimized by double-checking the dataset before analysis.

Data Collection: Data was collected using a structured proforma that included demographic information, clinical history, laboratory parameters, as well as the existence of concomitant conditions like hypertension, peripheral neuropathy, or vascular disease. Information was also obtained about the characteristics of foot ulcers, infection severity, and previous treatments.

Procedure: Participants were assessed through clinical examinations and investigations, including blood sugar levels, HbA1c, and vascular imaging as necessary. The Wagner grading system was used to classify diabetic foot ulcers. Details of amputations performed, including indications and levels, were recorded.

Statistical Analysis: The SPSS software, version 23.0, was used to enter and analyze the data. While frequencies and percentages were used to summarize categorical variables, descriptive statistics such as mean and standard deviation were computed for continuous variables. Chi-square tests and logistic regression analysis were used to find significant predictors of major lower limb amputation. Statistical significance was defined as a p-value of less than 0.05.

Results

The study comprised 160 T2DM patients in total. The findings are categorized as follows: clinical and demographic traits, factors linked to major lower limb amputation, and statistically based amputation predictions.

The mean age of participants was 58.4 ± 10.7 years, with a male predominance (65%, n = 104). The majority of patients (82.5%, n = 132) had diabetes for over 10 years. Comorbidities such as hypertension (70%, n = 112) and peripheral neuropathy (62.5%, n = 100) were predominant among the study population.

Table 1: Demographic and Clinical Characteristics of the Study Population

Variable	Frequency (n)	Percentage (%)
Gender: Male	104	65.0
Gender: Female	56	35.0
Age ≥ 60 years	96	60.0
Diabetes duration > 10 years	132	82.5
Hypertension	112	70.0
Peripheral neuropathy	100	62.5
Peripheral vascular disease	78	48.8
HbA1c > 8%	126	78.8

Among the 160 participants, 44 (27.5%) underwent major lower limb amputations (above or below knee). Clinical features of patients who had amputations and those who did not showed significant variations.

Table 2: Comparison of Clinical Characteristics Between Amputation and Non-Amputation Groups

Variable	Amputation (n = 44)	No Amputation (n = 116)	p-value
Age ≥ 60 years	34 (77.3%)	62 (53.4%)	0.012
Male gender	32 (72.7%)	72 (62.1%)	0.210
Diabetes duration > 10 years	40 (90.9%)	92 (79.3%)	0.105
Hypertension	36 (81.8%)	76 (65.5%)	0.047
Peripheral neuropathy	38 (86.4%)	62 (53.4%)	<0.001
Peripheral vascular disease	36 (81.8%)	42 (36.2%)	<0.001
HbA1c > 8%	40 (90.9%)	86 (74.1%)	0.020

According to logistic regression analysis, major lower limb amputation was significantly predicted by peripheral neuropathy, peripheral vascular disease, and HbA1c > 8%. Below are the multivariate logistic regression's findings.

Table 3: Multivariate Logistic Regression Analysis for Predictors of Major Lower Limb Amputation

Predictor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Peripheral neuropathy	4.21	2.01–8.80	<0.001
Peripheral vascular disease	5.12	2.56–10.26	<0.001
HbA1c > 8%	3.35	1.23–9.12	0.017
Hypertension	1.89	0.95–3.78	0.070

Discussion

A total of 160 patients were evaluated, with 27.5% (n = 44) undergoing major amputations. The findings revealed significant correlations between various clinical characteristics and the risk of amputation, providing insights into the factors contributing to this adverse outcome. Demographic analysis showed that the majority of participants were male (65%) and older adults, with 60% aged 60 years or older. Prolonged diabetes duration (over 10 years) was observed in 82.5% of patients, reflecting the chronic nature of the disease in this cohort. Common comorbidities included hypertension (70%) and peripheral neuropathy (62.5%), both of which were more prevalent among those who underwent amputation.

A statistical analysis revealed that peripheral neuropathy, peripheral vascular disease, and poor glycemic control (HbA1c > 8%) were considerably more common in patients who had major amputations. These factors emerged as strong predictors of amputation risk. For instance, peripheral neuropathy and vascular disease increased the odds of amputation by more than four- and five-fold, respectively, indicating their critical role in disease progression. Similarly, uncontrolled diabetes significantly heightened the risk, as reflected by an odds ratio of 3.35 for HbA1c > 8%. In the multivariate analysis, age and hypertension also demonstrated correlations with amputation, although they fell short of statistical significance. The amputation group had greater numbers of people of older age (≥60 years), which may exacerbate the effects of complications from diabetes.

In individuals with Type II diabetes, the study emphasizes the importance of early detection and treatment of peripheral neuropathy, vascular disease, and poor glycemic control. Targeted interventions, including aggressive control of blood sugar levels and monitoring for vascular complications, may reduce the risk of limb loss. Moreover, these findings emphasize the importance of routine screening for high-risk individuals to enable timely preventive measures.

Critical factors for significant lower limb amputation in people with type 2 diabetes have been found in recent research. The risk of major amputations was shown to be considerably increased by the presence of gangrenous tissue and poor glycemic control (HbA1c ≥8%). Additionally, patients with diabetes for over 15 years and those with hypertension, cardiac diseases, chronic renal impairment, and ischemia were at heightened risk [8]. A cross-sectional study highlighted that a diabetes duration exceeding 20 years, hypertension, and severe diabetic foot ulcers (Wagner grade ≥4) were independent predictors for lower limb amputation. Patients with micro-albuminuria or uncontrolled LDL cholesterol levels also demonstrated a higher risk [9]. Another study revealed that insufficient guidance and support for diabetes management at the primary care level contributed to a higher prevalence of severe amputations. Factors like cardiovascular disease and older age (above 67 years) compounded these risks [10].

Moreover, biomarkers such as Tumor Necrosis Factor Receptor 1 (TNFR1) and ischemia-modified albumin (IMA) were associated with an elevated risk of amputations in diabetic patients, further suggesting that micro- and macrovascular diseases play a pivotal role in amputation outcomes. Elevated systolic blood pressure and a history of peripheral arterial disease (PAD) were also strongly correlated with major amputations [11]. Lastly, a cohort study emphasized the role of glycemic control, where intensive glucose control reduced the risk of lower extremity amputation significantly, underlining the importance of early and stringent diabetes management [12].

Conclusion

Patients with Type II diabetes who have peripheral neuropathy, peripheral vascular disease, or poor glycemic control (HbA1c > 8%) are at a significantly higher risk of major lower limb amputation. Reducing the risk of limb loss requires efficient glycemic control, early identification, and management of these risk factors. Clinical risk assessments can be improved and patients' quality of life preserved by including these predictors to help target preventive measures.

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